UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2017

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____

001-33357
(Commission file number)

PROTALIX BIOTHERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**65-0643773**
State or other jurisdiction of incorporation or organization	**(I.R.S. Employer Identification No.)**
2 Snunit Street Science Park POB 455 Carmiel, Israel	**20100**
(Address of principal executive offices)	**(Zip Code)**

972-4-988-9488
Registrant's telephone number, including area code

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common stock, par value $0.001 per share	**NYSE AMERICAN**

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definition of “large accelerated filer,” “accelerated filer” and “smaller reporting company” in Rule 12b-2 of the Exchange Act. (check one):

Large accelerated filer	☐		Accelerated filer	☒
Non-accelerated filer	☐	(Do not check if a smaller reporting company)	Smaller reporting company	☐
			Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting common equity held by non-affiliates of the Registrant, as of June 30, 2017 was approximately $105.4 million, based upon a per share price equal to $0.84, the closing price for shares of the Registrant’s common stock reported by the NYSE American for such date.

On March 1, 2018, approximately 145,569,955 shares of the Registrant’s common stock, par value $0.001 per share, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant’s definitive Proxy Statement for its 2018 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission no later than May 1, 2018 and to be delivered to shareholders in connection with the 2018 Annual Meeting of Stockholders, are herein incorporated by reference in Part III of this Form 10-K.

FORM 10-K
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PART I

Except where the context otherwise requires, the terms, "we," "us," "our" or "the Company," refer to the business of Protalix BioTherapeutics, Inc. and its consolidated subsidiaries, and "Protalix" or "Protalix Ltd." refers to the business of Protalix Ltd., our wholly-owned subsidiary and sole operating unit.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

The statements set forth under the captions "Business," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Risk Factors," and other statements included elsewhere in this Annual Report on Form 10-K, which are not historical, constitute "forward-looking statements" within the meanings of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, including statements regarding expectations, beliefs, intentions or strategies for the future. When used in this report, the terms "anticipate," "believe," "estimate," "expect," "can," "continue," "could," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" and other words or phrases of similar import, as they relate to our company or our subsidiaries or our management, are intended to identify forward-looking statements. We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are only predictions and reflect our views as of the date they are made with respect to future events and financial performance, and we undertake no obligation to update or revise, nor do we have a policy of updating or revising, any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events, except as may be required under applicable law. Forward-looking statements are subject to many risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements.

Examples of the risks and uncertainties include, but are not limited to, the following:

- failure or delay in the commencement or completion of our preclinical studies and clinical trials, which may be caused by several factors, including: slower than expected rates of patient recruitment; unforeseen safety issues; determination of dosing issues; lack of effectiveness during clinical trials; inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; inability to monitor patients adequately during or after treatment; and or lack of sufficient funding to finance our clinical trials;

- the risk that the results of our clinical trials will not support the applicable claims of superiority, safety or efficacy and that our product candidates will not have the desired effects or will have undesirable side effects or other unexpected characteristics;

- risks relating to our ability to manage our relationship with Chiesi Farmaceutici S.p.A., or Chiesi, and any other collaborator, distributor or partner;

- risks relating to our ability to make scheduled payments of the principal of, to pay interest on or to refinance or satisfy conversions of our outstanding convertible notes or any other indebtedness;

- risks relating to our ability to defease the remaining outstanding 4.5% convertible notes on or prior to June 16, 2018;

- risks relating to the compliance by Fundação Oswaldo Cruz, or Fiocruz, an arm of the Brazilian Ministry of Health, or the Brazilian MoH, with its purchase obligations under our supply and technology transfer agreement, which may have a material adverse effect on our company and may also result in the termination of such agreement;

- our dependence on performance by third-party providers of services and supplies, including without limitation, clinical trial services;

- risks relating to our ability to finance our research programs;

- delays in preparing and filing applications for regulatory approval of our product candidates in the United States, the European Union and elsewhere;
- the impact of development of competing therapies and/or technologies by other companies;
- the risk that products that are competitive to our product candidates may be granted orphan drug status in certain territories and, therefore, one or more of our product candidate may become be subject to potential marketing and commercialization restrictions;
- risks related to our supply of drug product to Pfizer Inc., or Pfizer, pursuant to our amended and restated exclusive license and supply agreement with Pfizer;
- risks related to the commercialization efforts for taliglucerase alfa in Brazil;
- risks related to our expectations with respect to the potential commercial value of our product and product candidates;
- the inherent risks and uncertainties in developing the types of drug platforms and products we are developing;
- potential product liability risks, and risks of securing adequate levels of product liability and clinical trial insurance coverage;
- the possibility of infringing a third party's patents or other intellectual property rights;
- the uncertainty of obtaining patents covering our products and processes and in successfully enforcing our intellectual property rights against third parties;
- risks relating to changes in healthcare laws, rules and regulations in the United States or elsewhere; and
- the possible disruption of our operations due to terrorist activities and armed conflict, including as a result of the disruption of the operations of regulatory authorities, our subsidiaries, our manufacturing facilities and our customers, suppliers, distributors, collaborative partners, licensees and clinical trial sites.

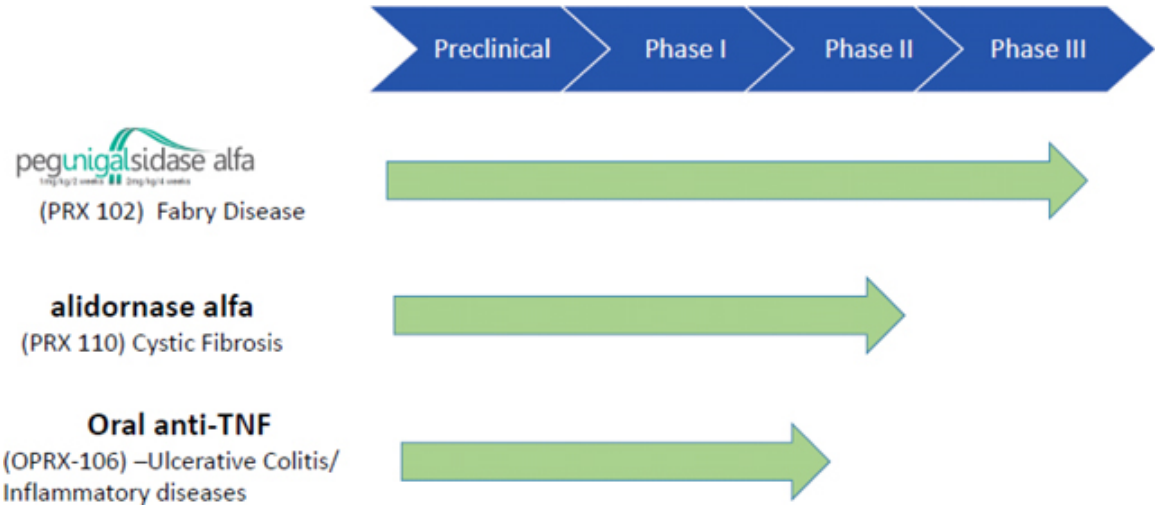
Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced or late-stage clinical trials, even after obtaining promising earlier trial results or preliminary findings for such clinical trials. Even if favorable testing data is generated from clinical trials of a drug product, the U.S. Food and Drug Administration, or the FDA, or foreign regulatory authorities may not accept or approve a marketing application filed by a pharmaceutical or biotechnology company for the drug product.

These forward-looking statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These and other risks and uncertainties are detailed under the heading "Risk Factors" in this Annual Report and are described from time to time in the reports we file with the U.S. Securities and Exchange Commission, or the Commission.

Item 1. Business

We are a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins based on our proprietary ProCellEx® protein expression system. We developed our first commercial drug product, Elelyso®, using our ProCellEx system and we are now focused on utilizing the system to develop a pipeline of proprietary, clinically superior versions of recombinant therapeutic proteins that primarily target large, established pharmaceutical markets and that in most cases rely upon known biological mechanisms of action. With our experience to date, we believe ProCellEx will enable us to develop additional proprietary recombinant proteins that are therapeutically superior to existing recombinant proteins currently marketed for the same indications, including applying the unique properties of our ProCellEx system for the oral delivery of therapeutic proteins.

The following table summarizes our current product candidates and their respective stages of clinical development:



On October 19, 2017, Protalix Ltd., our wholly-owned subsidiary, and Chiesi entered into an Ex-US license and collaboration agreement, which we refer to as the Chiesi Agreement, pursuant to which Chiesi was granted an exclusive, license for all markets outside of the United States to develop and commercialize pegunigalsidase alfa. Pegunigalsidase alfa, or PRX-102, is our chemically modified version of the recombinant protein alpha-Galactosidase-A protein that is currently being evaluated in phase III clinical trials for the treatment of Fabry disease. Under the terms and conditions of the Chiesi Agreement, Protalix Ltd. retained the right to commercialize pegunigalsidase alfa in the United States. Under the Chiesi Agreement, Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to $25 million in development costs, capped at $10 million per year. Protalix Ltd. is also eligible to receive an additional up to $320 million, in the aggregate, in regulatory and commercial milestone payments. Protalix Ltd. and Chiesi have agreed to a specific allocation of the responsibilities for the continued development efforts for pegunigalsidase alfa. Protalix Ltd. will manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi will make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa. The Chiesi Agreement also provides for reimbursement by Chiesi of certain costs to be incurred by Protalix Ltd.

In December 2017, the European Commission granted Orphan Drug Designation for pegunigalsidase alfa for the treatment of Fabry disease. The designation was granted after the EMA's Committee for Orphan Medicinal Products, or the COMP, issued a positive opinion supporting the designation noting that we had established that there was medically plausible evidence that pegunigalsidase alfa will provide a significant benefit over existing approved therapies in the European Union for the treatment of Fabry disease. The COMP cited clinical and non-clinical justifications we provided to establish the significant benefit of pegunigalsidase alfa, noting that the COMP considered the justifications to constitute a clinically relevant advantage. Orphan Drug Designation for pegunigalsidase alfa qualifies Protalix Ltd. for access to a centralized marketing authorization procedure, including applications for inspections and for protocol assistance. If the orphan drug designation is maintained at the time pegunigalsidase alfa is approved for marketing in the European Union, if at all, we expect that PRX-102 will benefit from 10 years of market exclusivity within the European Union. The market exclusivity will not have any effect on Fabry disease treatments already approved at that time.

In January 2018, FDA granted Fast Track designation to PRX-102. Fast Track designation is a process designed to facilitate the development and expedite the review of drugs and vaccines for serious conditions that fill an unmet medical need.

On May 1, 2012, the FDA approved for sale our first commercial product, taliglucerase alfa for injection, an enzyme replacement therapy, or ERT, for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease. Subsequently, taliglucerase alfa was approved for marketing by the regulatory authorities of other countries. Taliglucerase alfa is called alfataliglicerase in Brazil and certain other Latin American countries, where it is marketed under the name alfataliglicerase. Taliglucerase alfa is marketed under the name Elelyso in other territories.

Since its approval by the FDA, taliglucerase alfa has been marketed by Pfizer, as provided in the exclusive license and supply agreement by and between Protalix Ltd. and Pfizer, which we refer to as the Pfizer Agreement. In October 2015, we entered into an Amended and Restated Exclusive License and Supply Agreement, or the Amended Pfizer Agreement, which amends and restates the Pfizer Agreement in its entirety. Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso in exchange for a cash payment equal to $36.0 million. As part of the sale, we agreed to transfer our rights to Elelyso in Israel to Pfizer, while gaining full rights to Elelyso in Brazil. We will continue to manufacture drug substance for Pfizer, subject to certain terms and conditions. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all revenues, globally for Elelyso, excluding Brazil, where we are responsible for all expenses and retain all revenues.

For the first 10-year period after the execution of the Amended Pfizer Agreement, we have agreed to sell drug substance to Pfizer for the production of Elelyso, and Pfizer maintains the right to extend the supply period for up to two additional 30-month periods subject to certain terms and conditions. Any failure to comply with our supply commitments may subject us to substantial financial penalties, which will have a material adverse effect on our business, results of operations and financial condition. The Amended Pfizer Agreement also includes customary provisions regarding cooperation for regulatory matters, patent enforcement, termination, indemnification and insurance requirements.

On June 18, 2013, we entered into a Supply and Technology Transfer Agreement, or the Brazil Agreement, with Fiocruz, an arm of the Brazilian MoH, for taliglucerase alfa.

In 2017, we received a purchase order from the Brazilian MoH for the purchase of approximately $24.3 million of alfataliglicerase for the treatment of Gaucher patients in Brazil. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in the best interest of our company.

Our Strategy

Our strategy centers around prioritizing existing and new pipeline candidates to focus on products that we believe offer a clear competitive advantage over existing treatments. The strategy was the culmination of an intensive review by our management of our internal resources and of the markets in which we expect we can operate. The following highlights the details of the strategic plan as it relates to our development of an innovative product pipeline using our ProCellEx protein expression system.

Pegunigalsidase alfa (PRX-102) for the Treatment of Fabry Disease. pegunigalsidase alfa, or PRX-102, is designed to be an improved enzyme replacement therapy product for the treatment of Fabry disease given its potential for clinically superior outcomes and enhanced safety when compared to currently marketed enzyme replacement therapies. The product candidate is a key focus for us. We are continuing to enroll patients and recruit clinical sites for our phase III clinical trials of PRX-102, and our phase I/II clinical trial remains ongoing in an extension period.

alidornase alfa (PRX-110) for the Treatment of Cystic Fibrosis. alidornase alfa, our proprietary plant cell recombinant human Deoxyribonuclease 1, is under development for the treatment of cystic fibrosis (CF), to be administered by inhalation. alidornase alfa has an actin inhibition resistance that is designed to improve lung function and lower the incidence of recurrent infections by enhancing the enzyme's efficacy in patients' sputa. We released the final results of our phase II clinical trial of alidornase alfa for the treatment of CF in April 2017. We are currently studying the final results of the trial and are considering different collaboration alternatives as part of our further development plans.

Oral Anti-TNF (OPRX-106) Anti Inflammatory. Oral anti-TNF represents a novel mode of administering a recombinant anti-TNF protein. It is under development as an orally-delivered anti-inflammatory treatment using plant cells as a natural capsule for the expressed protein. Currently, the first 14 patients have completed our phase II proof of concept efficacy study of OPRX-106 for the treatment of ulcerative colitis, and four patients are currently in treatment and follow-up. The trial is evaluating key efficacy endpoints including clinical response and remission utilizing the Mayo score, as well as safety and pharmacokinetics. Interim data generated from the first 14 patients that completed the trial was released in January 2018. We expect to release complete results by the end of March, 2018. Upon review of the final proof of concept data, we intend to identify and collaborate with a well-suited partner for further development.

Potential Pipeline Candidates. We aim to expand our pipeline by leveraging the advantages of our proprietary ProCellEx protein expression technology. The focus is expected to be on biologics with significantly improved clinical profiles than the currently marketed proteins for these indications. Biosimilars will not be a market on which we focus, and will only be considered in the case of proteins that are highly difficult to express or that represent opportunities for early market entry arising from the intellectual property advantages arising from ProCellEx.

Except for the rights to commercialize taliglucerase alfa worldwide (other than Brazil), which we licensed to Pfizer, and the rights to PRX-102 which we licensed to Chiesi for territories outside the United States, we hold the worldwide commercialization rights to all of our proprietary development candidates. We continuously evaluate potential strategic marketing partnerships as well as collaboration programs with biotechnology and pharmaceutical companies and academic research institutes.

ProCellEx: Our Proprietary Protein Expression System

ProCellEx is our proprietary production system. We have developed our ProCellEx system based on our plant cell culture technology for the development, expression and manufacture of recombinant proteins. Our protein expression system does not involve mammalian or animal components or transgenic field-grown, whole plants at any point in the production process. Our ProCellEx system consists of a comprehensive set of capabilities and proprietary technologies, including advanced genetic engineering and plant cell culture technology, which enables us to produce complex, proprietary and biologically equivalent proteins for a variety of human diseases. This protein expression system facilitates the creation and selection of high expressing, genetically stable cell lines capable of expressing recombinant proteins. The entire protein expression process, from initial nucleotide cloning to large-scale production of the protein product, occurs under cGMP-compliant, controlled processes. Our plant cell culture technology uses plant cells, such as carrot and tobacco cells, which undergo advanced genetic engineering and are grown on an industrial scale in a flexible bioreactor system. Cell growth, from scale up through large-scale production, takes place in flexible, sterile, polyethylene bioreactors which are confined to a clean-room environment. Our bioreactors are well-suited for plant cell growth using a simple, inexpensive, chemically-defined growth medium as a catalyst for growth. The reactors are custom-designed and optimized for plant cell cultures, easy to use, entail low initial capital investment, are rapidly scalable at a low cost and require less hands-on maintenance between cycles.

Our ProCellEx system is capable of producing proteins with an amino acid sequence and three dimensional structure practically equivalent to that of the desired human protein, and with a very similar, although not identical, glycan, or sugar, structure, as demonstrated in our internal research and external laboratory studies. In collaboration with the Weizmann Institute of Science, we have demonstrated that the three-dimensional structure of a protein expressed in our proprietary plant cell-based expression system retains the same three-dimensional structure as exhibited by the mammalian cell-based expressed version of the same protein. In addition, proteins produced by our ProCellEx system maintain the biological activity that characterize that of the naturally-produced proteins. Based on these results, we believe that proteins developed using our ProCellEx protein expression system have the intended composition and correct biological activity of their human equivalent proteins.

We believe that our ProCellEx system will enable us to develop recombinant therapeutic proteins yielding substantial cost advantages, accelerated development and other competitive benefits when compared to mammalian cell-based protein expression systems. In addition, our ProCellEx system may enable us, in certain cases, to develop and commercialize recombinant proteins without infringing upon the method-based patents or other intellectual property rights of third parties. The major elements of our ProCellEx system are patent protected in most major countries. Moreover, we expect to enjoy method-based patent protection for the proteins we develop using our proprietary ProCellEx protein expression technology, although there can be no assurance that any such patents will be granted. In some cases, we may be able to obtain patent protection for the compositions of the proteins themselves. We have filed for United States and international composition of matter patents for taliglucerase alfa.

We have successfully demonstrated the feasibility of our ProCellEx system through: (i) the FDA's approval of taliglucerase alfa, and its subsequent approval by other regulatory authorities; (ii) the clinical and preclinical studies we have performed to date, including the positive efficacy and safety data in our clinical trials for taliglucerase alfa, pegunigalsidase alfa, alidornase alfa and OPRX-106 for the treatment of ulcerative colitis; (iii) preclinical results in well-known models in our enzyme for each of Fabry disease, DNase and antiTNF; and (iv) by expressing, on an exploratory, research scale, many additional complex therapeutic proteins belonging to different drug classes, such as enzymes, hormones, monoclonal antibodies, cytokines and vaccines. The therapeutic proteins we have expressed to date in research models have produced the intended composition and similar or superior biological activity compared to their respective human-equivalent proteins. Moreover, several of such proteins demonstrated advantageous biological activity when compared to the biotherapeutics currently available in the market to treat the applicable disease or disorder. We believe that the FDA's approval of taliglucerase alfa represents a strong proof-of-concept of our ProCellEx system and plant cell-based protein expression technology. We also believe that the significant benefits of our ProCellEx system, if further substantiated in clinical trials and in the successful commercialization of taliglucerase alfa and our other product candidates, have the potential to transform the industry standard for the development of complex therapeutic proteins.

Mammalian cell-based expression technology is based on the introduction of a human gene encoding for a specific therapeutic protein into the genome of a mammalian cell, and such systems have become the dominant system for the expression of recombinant proteins due to their capacity for sophisticated, proper protein folding (which is necessary for proteins to carry out their intended biological activity), assembly and post-expression modification, such as glycosilation (the addition of sugar residues to a protein which is necessary to enable specific biological activity by the protein). Many of the biotechnology industry's largest and most successful therapeutic proteins, including Epogen®, Neupogen®, Cerezyme®, Rituxan®, Humira®, Enbrel®, Neulasta®, Remicade® and Herceptin® are produced through mammalian cell-based expression systems. Mammalian cell-based expression systems can produce proteins with superior quality and efficacy compared to proteins expressed in bacteria and yeast cell-based systems. As a result, the majority of currently approved therapeutic proteins, as well as those under development, are produced in mammalian cell-based systems.

While bacterial and yeast cell-based expression systems were the first protein expression systems developed by the biotechnology industry and remain cost-effective compared to mammalian cell-based production methodologies, proteins expressed in bacterial and yeast cell-based systems lack the capacity for sophisticated protein folding, assembly and post-expression modifications, which are key factors of mammalian cell-based systems. Accordingly, such systems cannot be used to produce glycoproteins or other complex proteins and, therefore, bacterial and yeast cell-based systems are limited to the expression of the most basic, simple proteins, such as insulin and growth hormones.

Several companies and research institutions have been exploring the expression of human proteins in genetically-modified organisms, or GMOs, such as transgenic field-grown, whole plants and transgenic animals. However, these alternate techniques may be restricted by regulatory and environmental risks regarding contamination of agricultural crops and by the difficulty in applying cGMP standards of the pharmaceutical industry to these expression technologies and none of these technologies have been approved by the regulatory agencies with jurisdiction over any substantial market.

To date, our manufacturing facility, in which we utilize our ProCellEx system, was determined to be acceptable by each of the FDA, the European Medicines Agency, or the EMA, ANVISA, the Israeli MOH, the Australian Therapeutic Goods Administration, or the TGA, and Health Canada, after GMP inspections were performed as part of their respective reviews for marketing approval of taliglucerase alfa.

Competitive Advantages of Our ProCellEx Protein Expression System

We intend to continue to leverage the multiple unique advantages of our proprietary ProCellEx protein expression system, including our advanced genetic engineering technology and plant cell-based protein expression methods, to develop our pipeline. Significant advantages of our ProCellEx system over mammalian, bacterial, yeast and transgenic cell-based expression technologies, include the following:

Biologic Optimization. ProCellEx has internal capabilities developed to improve the biologic dynamics of an expressed protein. For example, the proteins produced through our system have uniform glycosilation patterns and therefore do not require the lengthy and expensive post-expression modifications that are required for certain proteins produced by mammalian cell-based systems. Such post-expression modifications in mammalian cell-produced proteins are made in order to expose the terminal mannose sugar residues, which are structures on a protein that are key elements in allowing the expressed protein to bind to a target cell and subsequently be taken into the target cell for therapeutic benefit. In addition, these steps do not guarantee the exposure of all of the required terminal mannose sugar residues, resulting in potentially lower effective yields and inconsistency in potency from batch to batch. We believe this quality increases the potency and consistency of the expressed proteins, and thus, the effectiveness of the protein which presents an additional cost advantage of ProCellEx over competing protein expression methodologies.

Ability to Penetrate Certain Patent-Protected Markets. ProCellEx has the potential to provide workaround manufacturing that does not infringe the method-based patents or other intellectual property rights of third parties. Certain biotherapeutic proteins available for commercial sale are not protected by patents that cover the compound and are available for use in the public domain. Rather, the process of expressing the protein product in mammalian or bacterial cell systems is protected by method-based patents. Using our plant cell-based protein expression technology, we are able to express an equivalent protein without infringing upon these method-based patents. Moreover, we expect to enjoy method-based patent protection for the proteins we develop using our ProCellEx system, although there can be no assurance that any such patents will be granted. In some cases, we may be able to obtain patent protection for the compositions of the proteins themselves. We have filed for U.S. and international composition of matter patents for PRX-102 and certain of our other product candidates.

Broad Range of Expression Capabilities. ProCellEx is able to produce a broad array of complex glycosilated proteins, which are difficult to produce in other systems, such as bacterial and yeast cell-based systems, as well as CHO systems. We have successfully demonstrated the feasibility of our ProCellEx system by producing, on an exploratory, research scale, a variety of therapeutic proteins belonging to different classes of recombinant drugs, such as enzymes, hormones, monoclonal antibodies, cytokines and vaccines. We have demonstrated that the recombinant proteins we have expressed to date have the intended composition and correct biological activity of their human-equivalent protein, with several of such proteins demonstrating advantageous biological activity compared to the currently available biotherapeutics. In specific cases, we have been successful in expressing proteins that have not been successfully expressed in other production systems.

Significantly Lower Capital and Production Costs. ProCellEx entails a lower cost of scale-up and of production. Plant cells grow rapidly under a variety of conditions and are not as sensitive as mammalian cells are to temperature, pH and oxygen levels which generally can only be grown under near perfect conditions. Our system, therefore, does not require the highly complex, expensive, stainless steel bioreactors typically used in mammalian cell-based production systems to maintain very specific temperature, pH and oxygen levels. Instead, we use simple polyethylene bioreactors that can be maintained at the room temperature of the clean-room in which they are placed. This system also reduces ongoing production and monitoring costs typically associated with mammalian cell-based expression technologies. Furthermore, while mammalian cell-based systems require very costly growth media at various stages of the production process to achieve target yields of proteins, plant cells require only simple and much less expensive solutions based on sugar, water and microelements at infrequent intervals to achieve target yields. Mammalian cell-based expression systems require large quantities of sophisticated and expensive growth medium to accelerate the expression process.

Elimination of the Risk of Viral Transmission or Infection by Mammalian Components. By nature, plant cells do not carry the risk of infection by human or other animal viruses. Mammalian cells, to the contrary, are susceptible to viral infections, including human viruses, and several cases of viral contamination have occurred. As a result, the risk of contamination of our products under development and the potential risk of viral transmission from our product and product candidates to future patients, whether from known or unknown mammalian viruses, is eliminated. Because our products and product candidates do not bear the risk of mammalian viral transmission, we are not required by the FDA or other regulatory authorities to perform the constant monitoring procedures for mammalian viruses during the protein expression process that are required in mammalian cell-based production. In addition, the production process of our ProCellEx system is void of any mammalian components which are susceptible to the transmission of prions, such as those related to bovine spongiform encephalopathy (commonly known as "mad-cow disease"). These factors further reduce the risks and operating costs of ProCellEx compared to mammalian cell-based expression systems.

The FDA and other regulatory authorities require viral inactivation and other rigorous and detailed procedures for mammalian cell-based manufacturing processes in order to address these potential hazards, thereby increasing the cost and time demands of such expression systems. Furthermore, the current FDA and other procedures only ensure screening for scientifically identified, known viruses. Accordingly, compliance with current FDA and other procedures does not fully guarantee that patients are protected against transmission of unknown or new potentially fatal viruses that may infect mammalian cells.

Potential ability to administer active therapeutic proteins orally. We are using ProCellEx to produce active recombinant proteins through oral administration of plant cells expressing biotherapeutic proteins. In such method, an enzyme is naturally encapsulated within plant cells genetically engineered to express the targeted enzyme. Plant cells have the unique attribute of a cellulose cell wall which makes them resistant to enzyme degradation when passing through the digestive tract. The plant cell itself serves as a delivery vehicle, once released and absorbed, to transport an enzyme in active form to the bloodstream. If proven effective, this would be the first time an enzyme will be administered orally rather than through intravenous therapy. To date we have completed successful preclinical animal studies for oral GCD and oral antiTNF, and early clinical trials of oral GCD in Gaucher patients. In addition, we have completed a phase IIa proof of concept trial of oral antiTNF as well as a phase I clinical trial of oral antiTNF in healthy volunteers.

Our First Commercial Product – Elelyso for the Treatment of Gaucher Disease

Elelyso (taliglucerase alfa), our first commercial product, is a plant cell expressed recombinant glucocerebrosidase enzyme (GCD) for the treatment of Gaucher disease. On May 1, 2012, the FDA approved Elelyso for injection as an enzyme replacement therapy (ERT) for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease. It was subsequently approved by the Israeli MOH, ANVISA and the regulatory authorities of other countries. In August 2014, the FDA approved Elelyso for injection for pediatric patients, and other jurisdictions, including Brazil, approved pediatric indications thereafter.

Gaucher disease, a hereditary, genetic disorder with severe and debilitating symptoms, is the most prevalent lysosomal storage disorder in humans. Lysosomal storage disorders are metabolic disorders in which a lysosomal enzyme, a protein that degrades cellular substrates in the lysosomes of cells, is mutated or deficient. Lysosomes are small membrane-bound cellular structures within cells that contain enzymes necessary for intracellular digestion. Gaucher disease is caused by mutations or deficiencies in the gene encoding GCD, a lysosomal enzyme that catalyzes the degradation of the fatty substrate, glucosylceramide (GlcCer). Patients with Gaucher disease lack or otherwise have dysfunctional GCD and, accordingly, are not able to break down GlcCer. The GlcCer accumulates in lysosomes of certain white blood cells called macrophages which consequently become highly enlarged. The enlarged cells accumulate in the spleen, liver, lungs, bone marrow and brain. Signs and symptoms of Gaucher disease may include enlarged liver and spleen, abnormally low levels of red blood cells and platelets and skeletal complications. In some cases, the patient may suffer an impairment of the central nervous system.

The standard of care for Gaucher disease is enzyme replacement therapy using recombinant GCD to replace the mutated or deficient natural GCD enzyme. Enzyme replacement therapy is a medical treatment in which recombinant enzymes are injected into patients in whom the enzyme is lacking or dysfunctional. Cerezyme® and VPRIV® are the only other ERTs currently available for the treatment of Gaucher disease. In addition, Cerdelga® (eliglustat) is a substrate reduction therapy for Gaucher disease that was approved for marketing by the FDA in August 2014 and by the European Commission in January 2015. Finally, Zavesca (miglustat) is a small molecule drug for the treatment of Gaucher disease. Zavesca has been approved by the FDA for use in the United States as an oral treatment. However, it has many side effects and the FDA has approved it only for administration to those patients who cannot be treated through ERT, and, accordingly, have no other treatment alternative. As a result, the use of Zavesca has been limited with respect to the treatment of Gaucher disease. However, Zavesca is also used to treat other rare disorders.

We have licensed to Pfizer the worldwide rights to Elelyso with the exception of Brazil, a market where we have retained own full rights.

Our Pipeline Drug Candidates

PRX-102 for the Treatment of Fabry Disease

We are developing PRX-102, our proprietary plant cell expressed chemically modified version of the recombinant alpha-GAL-A protein, a therapeutic enzyme, for the treatment of Fabry disease, a rare genetic lysosomal storage disorder. We believe that PRX-102 has the potential to be a significantly improved version of the currently marketed Fabry disease enzymes, Fabrazyme® and Replagal®, with improved activity in the Fabry disease target organs and significantly longer half-life due to higher stability, which together can potentially lead to improved substrate clearance and significantly lower formation of antibodies, as observed in our phase I/II clinical trial in Fabry patients. We believe that the treatment of Fabry disease is a specialty clinical niche with the potential for high growth as there is a significant unmet medical need for Fabry disease treatments.

Fabry Disease Background

Fabry disease is a serious, life-threatening condition. It is a disease or condition associated with morbidity that has a substantial impact on survival, day-to-day function, and the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. Fabry disease is an X-linked multisystem lysosomal storage disorder caused by the absence or reduction of α-galactosidase-A (α-Gal-A) activity, which is a lysosomal enzyme that catalyzes the hydrolysis of globotriaosylceramide (Gb3) from oligosaccharides, glycoproteins and glycolipids. The absence or reduction of this enzymatic activity leads to the progressive accumulation of glycolipids, especially Gb3, in capillary endothelial cells, podocytes, tubular cells, glomerular endothelial cells, mesangial cells, interstitial cells, cardiomyocytes, fibroblasts, and neurons. The accumulation of glycosphingolipids (e.g., Gb3) leads to chronic pain, skin lesions, cardiac, deficiencies, and, in particular, renal involvement. End-stage renal failure and cardiomyopathy often lead to early death in Fabry patients. Fabry disease causes substantial reduction in life-expectancy, by an average of 15 years in female patients and 20 years in male patients, compared to the general population.

Current Treatments of Fabry Disease

Currently there are two enzyme replacement therapies drugs available on the market to treat Fabry disease. Fabrazyme, marketed by Genzyme Corporation (acquired by Sanofi), is approved for the treatment of Fabry disease in the United States and the European Union. Sanofi reported €722 million (approximately $865 million) in worldwide sales of Fabrazyme in 2017. The other approved enzyme replacement therapy for the treatment of Fabry disease in the European Union is Replagal, which is marketed by Shire. Shire reported $472 million in sales of Replagal in 2017. In April 2016, Galafold™, a chaperone therapy manufactured by Amicus Therapeutics, Inc., or Amicus, was approved in the European Union as a monotherapy for Fabry disease in patients with amenable mutations. Galafold has also been accepted for marketing in a number of other countries. Amicus reported revenues of approximately $36 million in sales of Galafold in 2017.

PRX-102 Development Program

In October 2016, the first patient was dosed in our global phase III clinical trial of PRX-102 for the treatment of Fabry disease. Over 40 sites are currently participating in this trial. The phase III efficacy and safety clinical trial, which we refer to as the BALANCE Study, is a multi-center, randomized, double-blind, active control study of PRX-102 in Fabry patients with impaired renal function. The trial is designed to enroll 78 patients previously treated with Fabrazyme (agalsidase beta) with a stable dose for at least six months. Enrolled patients are randomized to continue treatment with 1 mg/kg of either Fabrazyme or PRX-102, at a 2:1 ratio of PRX-102 to Fabrazyme, respectively. Patients are to be treated via intravenous (IV) infusions every two weeks. The sites are recruiting adult symptomatic Fabry patients with plasma and/or leucocyte alpha galactosidase activity (by activity assay) less than 30% mean normal levels. All patients must have had treatment with a dose of 1 mg/kg agalsidase beta per infusion every two weeks for at least one year. In addition, to be included in the trial, patients need to have certain eGFR values and a meaningful decline in annualize eGFR slope.

The primary endpoint for the BALANCE study, which was agreed with both the FDA and the EMA, is the comparison in the rate of decline of eGFR slope between Fabrazyme and PRX-102. At 12 months, we intend to conduct an interim analysis to test for non-inferiority to support an anticipated regulatory filing with the EMA. At the same time, we intend to approach the FDA to request its review of the then totality of data. Notwithstanding, patients enrolled in the study will continue to be treated for a total of 24 months, at which point the data will be analyzed to test for superiority, which is the original guidance we received from the FDA.

Concurrently with the BALANCE study, we are also performing a supportive phase III clinical trial of PRX-102, which we refer to as the BRIDGE Study. The BRIDGE study is an open-label, single-arm, switchover study to assess the efficacy and safety of PRX-102 in Fabry patients currently treated with Replagal. The trial is designed to enroll 22 patients. The objective of the study is to generate safety and efficacy data of patients switched from Replagal to PRX-102 over a 12-month period. The endpoints of the study are safety, mean annualized change (slope) in eGFR, pain, plasma lyso GB3, immunogenicity and Quality of Life.

In addition to the BALANCE and BRIDGE studies, we are performing a third clinical trial to evaluate the safety and efficacy of administering 2 mg/kg of PRX-102 once monthly in Fabry patients. PRX-102 with a 2 mg/kg dose was found to be safe and well tolerated with no formation of antibodies in our phase I/II clinical trial of PRX-102 for the treatment of Fabry disease. Additionally, in our phase I/II clinical trial, 2 mg/kg of PRX-102 demonstrated approximately a 40 times higher circulatory half-life compared with other enzyme replacement therapies, and, as demonstrated in a Fabry mice model, with materially higher active enzyme reaching target organs affected by Fabry disease. Pharmacokinetic (PK) analysis and modeling from the phase I/II clinical trial indicate that PRX-102 levels at the second week after infusion remain 10 times higher than published Fabrazyme levels at the day of infusion. Moreover, the amount of PRX-102 in the circulation at weeks three and four, are higher than those of Fabrazyme during the two-week treatments. These results provide strong rationale for the clinical evaluation of a once-monthly dosing.

We plan to enroll up to 30 Fabry patients currently treated with an approved enzyme replacement therapy in this study. A safety and efficacy evaluation will occur at 12 months with additional long term follow-up.

Phase I/II Clinical Data

Our phase I/II clinical trial of PRX-102, which we completed in 2015, was a worldwide, multi-center, open label, dose ranging study to evaluate the safety, tolerability, pharmacokinetics, immunogenicity and efficacy parameters of PRX-102 in adult Fabry patients. Sixteen adult naive Fabry patients (9 male and 7 female) completed the trial, each in one of three dosing groups, 0.2 mg/kg, 1mg/kg and 2mg/kg. Each patient received intravenous infusions of PRX-102 every two weeks for 12 weeks, with efficacy follow-up after six-month and twelve-month periods. All patients that completed the trial opted to continue to receive 1 mg/kg of PRX-102 in an open-label, 60-month extension study under which all patients have been switched to receive 1 mg/kg of the drug, the selected dose for our phase III studies of PRX-102.

The data set forth below was recorded at 24 months from 11 patients enrolled and treated in the long-term open-label extension trial. Patients who did not continue in the extension trial included female patients who became or planned to become pregnant, and therefore were unable to continue in accordance with the study protocol, and patients that relocated to a location where treatment was not available under the clinical study.

Efficacy

- Lyso Gb3 levels decreased approximately 90% from baseline (see Figure 1);
- Renal function remained stable with mean eGRF levels of 108.02 and 107.20 at baseline and 24 months, respectively with a modest annual eGFR slope of -2.1; (see Figure 2)
- An improvement across all the gastrointestinal symptoms evaluated, including severity and frequency of abdominal pain and frequency of diarrhea, were noted (see Figure 1);
- Cardiac parameters, including LVM, LVMI and EF, remained stable with no cardiac fibrosis development detected;
- In conclusion, an improvement of over 40% in disease severity was shown as measured by the Mainz Severity Score Index (MSSI), a score compiling the different elements of the disease severity including neurological, renal and cardiovascular parameters; and
- An improvement was noted in each of the individual parameters of the MSSI.

Figure 1. Continuous reductions observed over 24 months

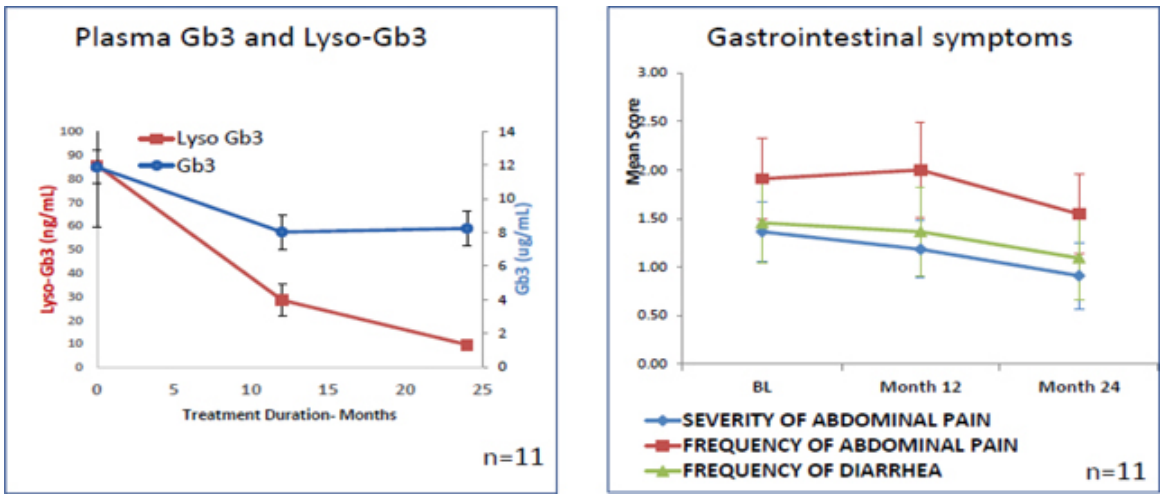
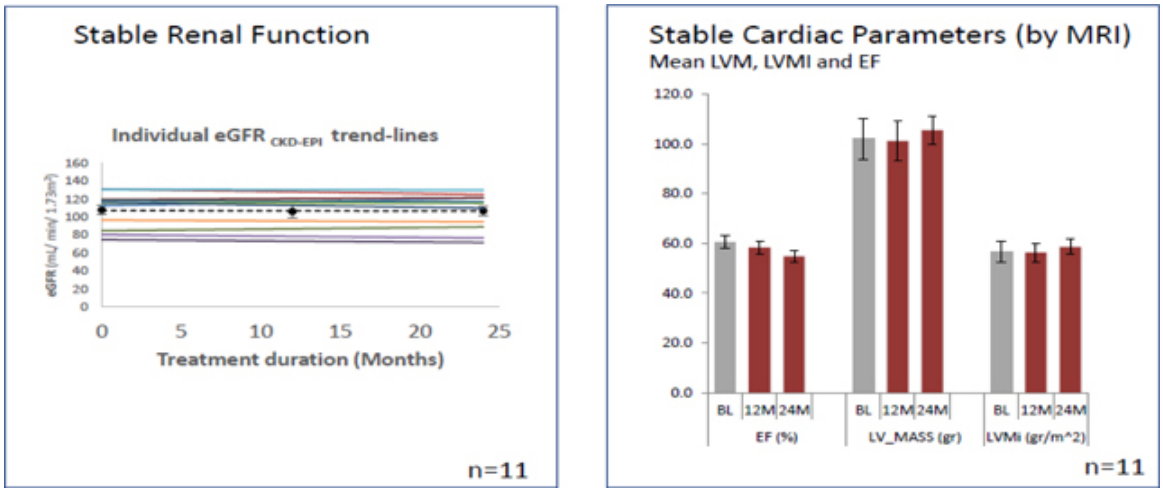


Figure 2. Continuous clinical stability observed over 24 months



Safety

- The majority of adverse events were mild to moderate in severity, and transient in nature;
- During the first 12 months of treatment, only three of 16 patients (less than 19%) formed anti-drug antibodies (ADA), of which two of these patients (less than 13%) had neutralizing antibodies;
- Importantly, however, the ADAs turned negative for all three of these patients following 12 months of treatment; and
- The ADA positivity effect had no observed impact on the safety, efficacy or continuous biomarker reduction of PRX-102.

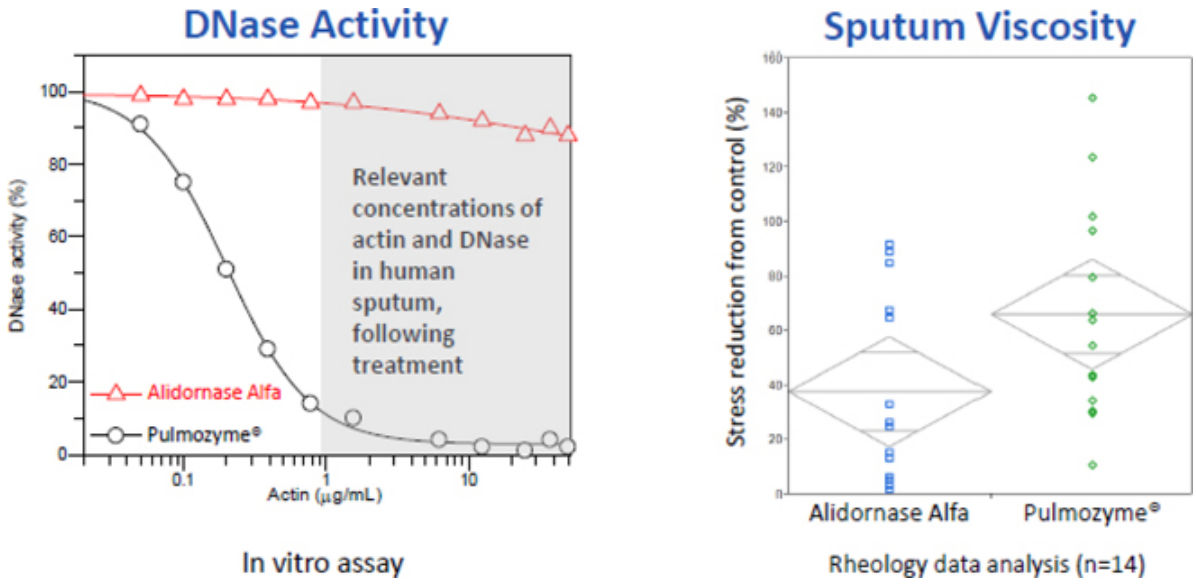
alidornase Alfa (PRX-110) for the Treatment of Cystic Fibrosis

alidornase alfa is our proprietary plant cell recombinant form of human deoxyribonuclease I (DNase I) that we are developing for the treatment of CF, to be administered by inhalation. DNase I cleaves extracellular DNA and thins the thick mucus that accumulates in the lungs of CF patients. Currently, Pulmozyme® is the only DNase I commercially available, with annual sales of approximately CHF 730 million (approximately $748 million) in sales for 2017 according to public reports by F. Hoffman-La Roche Ltd.

In vitro studies with PRX-110 demonstrated improved enzyme kinetics, significantly reduced sensitivity to inhibition by actin and improved ex vivo efficacy when compared to Pulmozyme. Preclinical studies of alidornase alfa administered by inhalation showed substantial enzymatic activity in lungs.

We designed alidornase alfa, through chemical modification, to be resistant to inhibition by actin so as to improve lung function and lower the incidence of recurrent infections by enhancing the enzyme's efficacy in patients' sputa. Actin, a potent inhibitor of DNase, is found in high concentration in CF patients' sputum. As demonstrated in Figure 3, the activity of alidornase alfa, as demonstrated in in vitro studies, remains almost with no change in the relevant actin concentration found in CF patients while Pulmozyme is degraded significantly.

Figure 3. Actin and DNase concentrations in human sputum tested in *in vitro* assays; Rheology Data Analysis in in human sputum samples



In addition, alidornase alfa has demonstrated improved disease parameters in human models sputum testing when compared to the currently marketed product. In particular, alidornase alfa has demonstrated a reduction in mucus viscosity in human sputum samples when compared to the currently marketed product. See Figure 3.

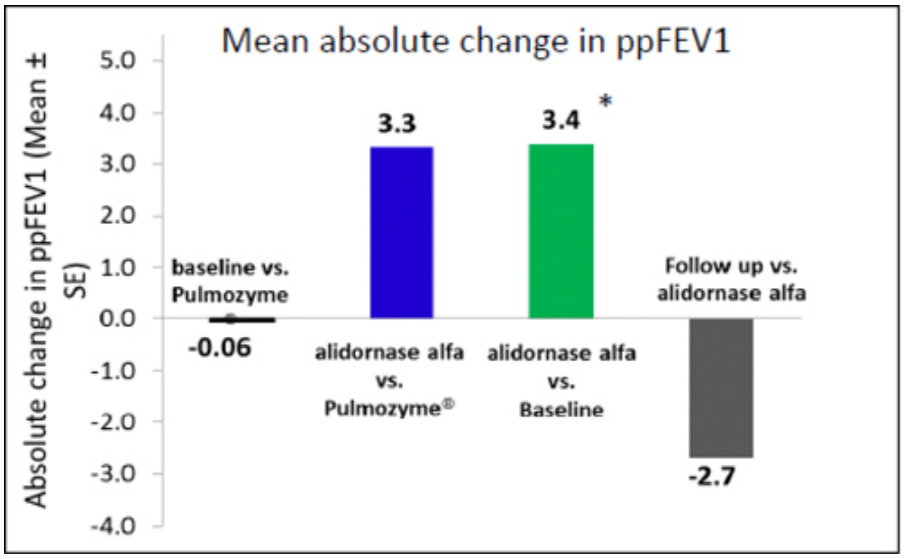
alidornase alfa Development Program

We completed a phase I clinical trial of alidornase alfa with 18 healthy volunteers in which alidornase alfa was found to be safe and tolerable.

In July 2016 we commenced a phase IIa clinical trial of alidornase alfa for the treatment of CF, and we released the final results of the study in April 2017. Sixteen patients were enrolled in the study, all of whom completed the study. The phase II trial was a 28-day switchover study to evaluate the safety and efficacy of alidornase alfa in CF patients previously treated with Pulmozyme (currently the only commercially available DNase therapy). Participation in the trial was preceded by a two-week washout period from Pulmozyme before treatment with alidornase alfa via inhalation.

The primary efficacy results show that treatment with alidornase alfa resulted in clinically meaningful lung function improvement, as demonstrated by a mean absolute increase in the percent predicted forced expiratory volume in one second (ppFEV1) of 3.4 points from baseline. Moreover, a mean absolute increase in ppFEV1 of 2.8 points was also observed in patients participating in the trial when compared to measurements taken from patients at initiation before the switch from Pulmozyme to alidornase alfa. See Figure 4.

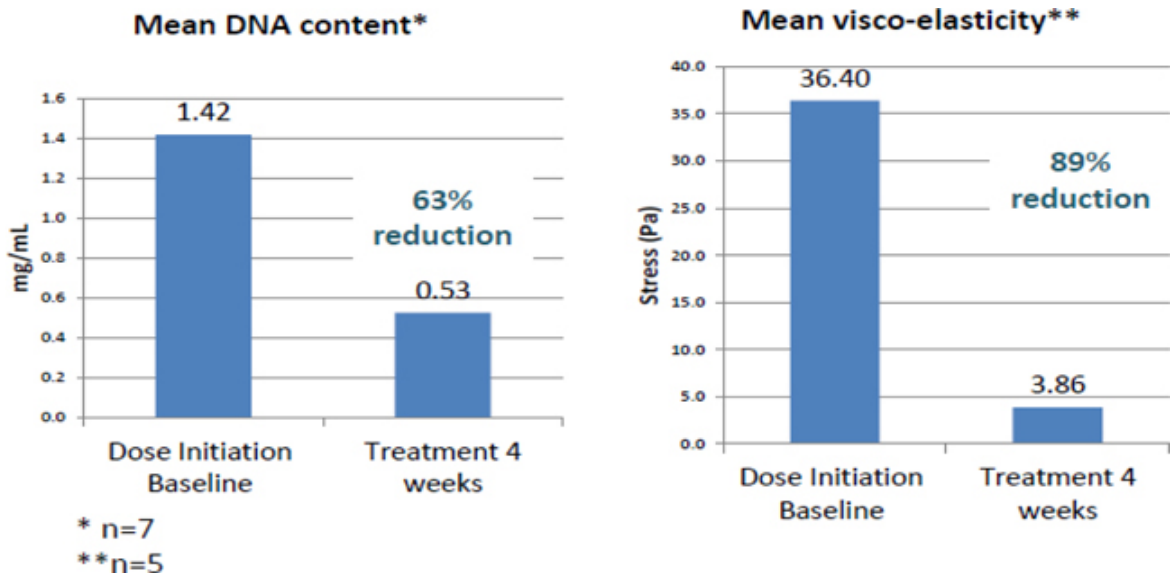
Figure 4. Phase II trial demonstrates clinically meaningful lung function improvement



A commercially available small molecule CFTR modulator for the treatment of CF has reported a mean absolute increase in ppFEV1 of 2.5 from baseline in its registration clinical study. This score was achieved while 74% of the patients participating in the trial of the CFTR modulator were also treated with the modulator on top of Pulmozyme. While this marketed CFTR addresses a certain mutation applicable to less than 50% of CF patients, alidornase alfa is being developed to treat all CF patients.

Sputa available DNA samples were analyzed for approximately half of the patients. A mean reduction of over 70% in DNA content from baseline was observed, and a mean reduction of over 90% from baseline was observed for sputa visco-elasticity. Correlation between improvement in sputa parameters and pulmonary function was observed. See Figure 5.

Figure 5. Decrease in sputum DNA content and sputum viscosity upon alidornase alfa treatment initiation



In addition, an in vitro study of alidornase alfa demonstrated a significant inhibition of Pseudomonas Aeruginosa, with alidornase alfa treated colonies reduced by over 50%, compared to baseline. Pseudomonas, strains of bacteria that are widely found in the environment, are a major cause of lung infections in CF patients. Chronic pulmonary infection is a leading cause of morbidity and mortality in CF patients, despite the aggressive use of antibiotics, and Pseudomonas is the most prevalent organism in the airway colonization of CF patients.

PK analysis performed indicated alidornase alfa is not absorbed into a patient's circulatory system, suggesting higher levels of alidornase alfa remains available in the patient's lungs. This provides further support for the potential that alidornase alfa may offer additional efficacy to CF patients.

The above-mentioned material decrease in visco-elasticity and DNA presence in CF patients' sputa, coupled with the significant inhibition of Pseudomonas and higher levels of alidornase alfa available in the patients' lungs, provides further supportive evidence of improved lung function after treatment with alidornase alfa, as demonstrated by the increase in FEV1.

alidornase alfa was well tolerated with no serious adverse events reported.

OPRX-106; Oral antiTNF for the treatment of inflammatory diseases

OPRX-106, our oral antiTNF product candidate, is a recombinant antiTNF (Tumor, Necrosis Factor) protein that we are expressing through ProCellEx. Auto-immune-mediated inflammatory disorders are conditions that are characterized by common pathways that lead to inflammation and are caused or triggered by a compromised or dysregulation of the normal immune response. Immune-mediated inflammatory disorders can cause organ damage, and are associated with increased morbidity. Common auto-immune diseases include rheumatoid arthritis, inflammatory bowel disease (IBD) such as ulcerative colitis and crohn's disease, psoriasis, and others. Some of the major treatments are antiTNF drugs, administered as subcutaneous injections or as intravenous infusions. Sales of anti-TNF drugs exceeded $30 billion annually. Well-known antiTNF drugs include Humira, Remicade and Enbrel.

OPRX-106 is a plant cell-expressed form of the fused protein that is naturally encapsulated within BY-2 cells genetically engineered to express the enzyme. Plant cells have the unique attribute of a cellulose cell wall which makes them resistant to enzyme degradation when passing through the digestive tract. The plant cell itself serves as a delivery vehicle, once released and absorbed, to transport the enzyme in active form to the bloodstream. If proven effective, our experimental oral antiTNF would be the first protein to be administered orally rather than through injection. We believe that our oral delivery mechanism could be applied to additional proteins and has the potential to change the method of protein administration in certain indications.

OPRX-106 Development Program

OPRX-102 for the treatment of ulcerative colitis is currently the subject of a phase IIa clinical trial. The first patient was enrolled in the trial in November 2016. The phase II clinical trial is a randomized, open label, 2-arm study of OPRX-106 in patients with active mild to moderate ulcerative colitis. A total of 24 patients were enrolled and randomized to receive 2 mg or 8 mg of OPRX-106, administered orally, once daily, for 8 weeks. Currently, the first 14 patients have completed the study, and four patients are currently in treatment and follow-up. The trial evaluated key efficacy endpoints including clinical response and remission utilizing the Mayo score, as well as safety and pharmacokinetics. Interim data generated from the first 14 patients that completed the trial was released in January 2018. The interim data demonstrates that 57% of the patients achieved clinical response and 36% achieved clinical remission at week 8. In the rectal bleeding analysis, a sub category of the Mayo score, 79% of those patients show an improvement. In addition, the majority of those patients show improvement in the study's additional efficacy endpoints, with 86% of the patients achieved an improvement in calprotectin, a protein biomarker present in the feces indicating intestinal inflammation, and 64% have an improved Geboes score, a histopathological scoring for the assessment of disease activity in ulcerative colitis. We except to release complete results by the end of March, 2018.

For purposes of the study, clinical response at week 8 is defined as a decrease in the Mayo score of at least 3 points and either a decrease in the sub-score for rectal bleeding of at least 1 point from baseline, or rectal bleeding sub-score of 0 or 1. Clinical remission at week 8 is defined as clinically symptom free, a Mayo score ≤ 2, with no individual sub-score exceeding 1 point after treatment.

Treatment was well tolerated and the majority of adverse events have been mild to moderate and transient in nature, with headaches being the most common. No immunosuppression was evident.

The results from our phase I clinical trial of OPRX-106 demonstrated that the drug was safe and well tolerated, and showed biological activity in the gut. The phase I clinical trial was a randomized, parallel-design, open-label study designed to evaluate the safety and pharmacokinetics of OPRX-106 in healthy volunteers. The trial enrolled 14 subjects that were randomized to one of three dosing cohorts receiving OPRX-106 doses equivalent to 2mg, 8mg or 16mg Tumor Necrosis Factor receptor-Fc fusion protein. Subjects received once daily oral administrations for five consecutive days. The results demonstrated that oral administration of OPRX-106 is safe and well tolerated. No major side effects were noted, and no suppression of the immune system was observed. Regulatory T cell activation showing biological activity in the gut was observed. Fluorescence-activated cell sorting analysis (FACS) was performed using various antibodies for surface markers, and it was observed that all three dosages of OPRX-106 promoted the induction of various subsets of T cells, some of which are correlated with anti-inflammatory response.

Commercialization Agreement with Chiesi Farmaceutici

On October 19, 2017, Protalix Ltd. and Chiesi entered into the Chiesi Agreement pursuant to which Chiesi was granted an exclusive, license for all markets outside of the United States to develop and commercialize pegunigalsidase alfa. Protalix Ltd. retained the right to commercialize pegunigalsidase alfa in the United States. Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to $25 million in development costs, capped at $10 million per year. Protalix Ltd. is also eligible to receive an additional up to $320 million, in the aggregate, in regulatory and commercial milestone payments. Protalix Ltd. and Chiesi have agreed to a specific allocation of the responsibilities for the continued development efforts for pegunigalsidase alfa. Protalix Ltd. agreed to manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi is required to make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa. The Chiesi Agreement also provides for reimbursement by Chiesi of certain costs to be incurred by Protalix Ltd.

We are required to pay a royalty equal to 3% of the PRX-102-related revenues Chiesi records under the Chiesi Agreement to the National Authority for Technological Innovation, or NATI.

Technology Transfer Agreement with Fiocruz

Our Brazil Agreement became effective in January 2014. The technology transfer is designed to be completed in four stages and is intended to transfer to Fiocruz the capacity and skills required for the Brazilian government to construct its own manufacturing facility, at its sole expense, and to produce a sustainable, high-quality, and cost-effective supply of taliglucerase alfa. The initial term of the technology transfer is seven years. The agreement contains certain purchase commitments by Fiocruz. If Fiocruz fails to comply with the purchase commitments, we may terminate the agreement, and all of our rights to the technology will be returned.

In 2017, we received a purchase order from the Brazilian MoH for the purchase of approximately $24.3 million of alfataliglicerase for the treatment of Gaucher patients in Brazil. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in the best interest of our company.

The Brazil Agreement may be extended for an additional five-year term, as needed, to complete the technology transfer. All of the terms of the arrangement, including the minimum annual purchases, will apply during the additional term. Upon completion of the technology transfer, and subject to Fiocruz receiving approval from ANVISA to manufacture taliglucerase alfa in its facility in Brazil, the agreement will enter into the final term and will remain in effect until our last patent in Brazil expires. During such period, Fiocruz will be the sole provider of this important treatment option for Gaucher patients in Brazil and shall pay us a single-digit royalty on net sales.

Intellectual Property

We maintain a proactive intellectual property strategy which includes patent filings in multiple jurisdictions, including the United States and other commercially significant markets. As of December 31, 2017, we held, or had license rights to, 69 patents and 58 pending patent applications with respect to various compositions, methods of production and methods of use relating to our ProCellEx protein expression system and our proprietary product pipeline. Of the above, one is a joint patent, eight are joint patent applications, and one is a licensed patent application.

Our competitive position and future success depend in part on our ability, and that of our licensees, to obtain and leverage the intellectual property covering our product candidates, know-how, methods, processes and other technologies, to protect our trade secrets, to prevent others from using our intellectual property and to operate without infringing the intellectual property of third parties. We seek to protect our competitive position by filing United States, European Union, Israeli and other foreign patent applications covering our technology, including both new technology and improvements to existing technology. Our patent strategy includes obtaining patents, where possible, on methods of production, compositions of matter and methods of use. We also rely on know-how, continuing technological innovation, licensing and partnership opportunities to develop and maintain our competitive position.

We issued a series of 7.5% convertible notes in December 2016 and July 2017, which are guaranteed by our subsidiaries and secured by perfected liens on all of our material assets, primarily consisting of our intellectual property assets, including a stock pledge of our foreign subsidiaries in favor of the holders of outstanding 7.5% convertible notes.

As of December 31, 2017, our patent portfolio consisted of several patent families (consisting of patents and/or patent applications) covering our technology, protein expression methodologies and system and product candidates, as follows:

- With respect to our ProCellEx protein expression system, we held nine issued patents and seven patent applications relating to the large scale production of proteins in cultured plant cells. The issued patents and any patents to issue in the future based on pending patent applications in this patent family, if at all, are expected to expire in 2028. One patent relating to a separate family, covering methods for culturing and harvesting plant cells and/or tissues in consecutive cycles is expected to expire in 2025.

- We held a patent family containing 24 issued patents and one patent application in India, South Africa, Russian Federation, Australia, China, the United States, Ukraine, Singapore, Japan, Europe, Hong Kong, Mexico, Korea, Canada, Brazil and Israel relating to the production of recombinant glycosylated lysosomal proteins in our plant culture platform, including taliglucerase alfa, and uses of these proteins and cells containing these proteins for the treatment of lysosomal disorders. The issued patents and any patents to issue in the future based on pending patent applications in this patent family, if at all, are expected to expire in 2024.

- We held a patent family containing three granted patents relating to a system and method for production of antibodies in a plant cell culture, and antibodies produced in such a system. The issued patents in this patent family are expected to expire in 2025.

- We held a patent family containing four issued patents in Europe, South Africa, Australia and Israel, and one pending patent application relating to a new method for delivering active recombinant proteins systemically through oral administration of transgenic plant cells. The issued patents and any patents to issue in the future based on patent applications in this patent family, if at all, are expected to expire in 2026.

- We held a patent family containing five granted patents in the United States, Europe, South Africa, Israel and Australia, relating to saccharide containing protein conjugates. The issued patents and any patents to issue in the future based on the patent applications in this patent family, if at all, are expected to expire in 2028.

- We held a patent family containing four granted patents in Japan, United States, Europe and China, and six pending patent applications relating to Nucleic Acid construct for expression of alpha-galactosidase enzyme in plants and plant cells. The patents to issue in the future based on the patent applications in this patent family, if at all, are expected to expire in 2031.

- We held a patent family containing 16 granted patents in Europe, United States, Australia, Japan, Russian Federation, China, Hong Kong, Singapore, New Zealand and South Africa, and eight pending patent applications relating to multimeric protein structures of α-galactosidase and to uses thereof in treating Fabry disease. The issued patents and any patents to issue in the future based on the patent applications in this patent family, if at all, are expected to expire in 2031.

- We held three patent families containing two granted patents in the United States and six pending applications relating to plant recombinant human DNase I and uses in therapy. The patents to issue in the future based on these patent applications, if at all, are expected to expire in 2033.

- We held a a patent family containing 11 patent applications relating to chemically modified plant recombinant human DNase I and uses in therapy. The patents to issue in the future based on this patent application, if at all, are expected to expire in 2036.

- We held three families containing 10 patent applications relating to plant recombinant TNF alpha inhibitor polypeptides. The patents to issue in the future based on these patent applications, if at all, are expected to expire in 2034/2035.

- Our patent portfolio includes a patent that we co-own that covers human glycoprotein hormone and chain splice variants, including isolated nucleic acids encoding these variants. More specifically, this patent covers a new splice variant of human FSH. This patent was issued in the United States and is expected to expire in 2024.

- We co-own and have an exclusive license to a patent family, containing eight pending applications, that covers use of plant cells expressing a TNF alpha polypeptide inhibitor in therapy. The patents to issue in the future based on these patent applications, if at all, are expected to expire in 2034.

- We have licensed the rights to a United States patent application covering oral composition comprising a TNF antagonist. The patents to issue in the future based on this application, if at all, are expected to expire in 2034.

We are aware of U.S. patents, and corresponding international counterparts of such patents, owned by third parties that contain claims covering methods of producing GCD. We do not believe that, if any claim of infringement were to be asserted against us based upon such patents, taliglucerase alfa would be found to infringe any valid claim under such patents. However, there can be no assurance that a court would find in our favor or that, if we choose or are required to seek a license to any one or more of such patents, a license would be available to us on acceptable terms or at all.

In April 2005, Protalix Ltd. entered into a license agreement with Icon Genetics AG, or Icon, pursuant to which we received an exclusive worldwide license to develop, test, use and commercialize Icon's technology to express certain proteins in our ProCellEx protein expression system. We are also entitled to a non-exclusive worldwide license to make and have made other proteins expressed by using Icon's technology in our technology. As consideration for the license, we are obligated to make royalty payments equal to varying low, single-digit percentages of net sales of products by us, our affiliates, or any sublicensees under the agreement. In addition, we are obligated to make milestone payments equal to $350,000, in the aggregate, for each product developed under the license, upon the achievement of certain milestones.

Our license agreement with Icon remains in effect until the earlier of the expiration of the last patent under the agreement or, if all of the patents under the agreement expire, 20 years after the first commercial sale of any product under the agreement. Icon may terminate the agreement upon written notice to us that we are in material breach of our obligations under the agreement and we are unable to remedy such material breach within 30 days after we receive such notice. Further, Icon may terminate the agreement in connection with certain events relating to a wind up or bankruptcy, if we make a general assignment for the benefit of our creditors, or if we cease to conduct operations for a certain period. Icon may also terminate the exclusivity granted to us by written notice if we fail to reach certain milestones within a designated period of time. Notwithstanding the termination date of the agreement, our obligation to pay royalties to Icon under the agreement may expire prior to the termination of the agreement, subject to certain conditions.

Manufacturing

We use our current facility, which has approximately 20,000 sq/ft of clean rooms built according to industry standards, to develop, process and manufacture pegunigalsidase alfa, taliglucerase alfa and other recombinant proteins. Pegunigalsidase alfa and our other drug product candidates, as well as taliglucerase alfa, must be manufactured in a sterile environment and in compliance with cGMPs set by the FDA and other relevant foreign regulatory authorities. We are currently producing Fabry drug substance for our phase III and other clinical trials, as well as the manufacture of the taliglucerase alfa we need in the near future, included the taliglucerase alfa to be purchased by Pfizer under the Pfizer Agreement. In addition, we intend to use our manufacturing space to produce all of the drug substance needed in connection with the clinical trials for our product candidates.

In 2017, the FDA approved the Supplemental New Drug Application (sNDA) we submitted to allow us to convert our manufacturing facility from a single dedicated product facility to a multi-product facility. We expect that the conversion will allow us to realize potentially significant operational savings. Our facility's current capacity can serve all of our current and expected commercial and clinical needs, and we believe it will be sufficient to serve our production needs for the anticipated commercialization of PRX-102.

Our manufacturing facilities in Carmiel, Israel, have undergone successful audits by the Israeli MOH, the FDA, ANVISA, and the European Union under the European Union's centralized marketing authorization procedure, the Australian TGA and Health Canada.

Our current facility in Israel has been granted “Approved Enterprise” status, and we have elected to participate in the alternative benefits program. Our facility is located in a Zone A location, and, therefore, our income from the Approved Enterprise will be tax exempt in Israel for a 10-year period commencing with the year in which we first generate taxable income from the relevant Approved Enterprise and after we use our net operating loss carryforwards, or “NOLs.” We expect to be entitled to similar tax benefits for a number of years thereafter. To remain eligible for these tax benefits, we must continue to meet certain conditions, and if we increase our activities outside of Israel, for example, by future acquisitions, such increased activities generally may not be eligible for inclusion in Israeli tax benefit programs. In addition, our technology is subject to certain restrictions with respect to the transfer of technology and manufacturing rights. “See Risk Factors—The manufacture of our products is an exacting and complex process, and if we or one of our materials suppliers encounter problems manufacturing our products, it will have a material adverse effect on our business and results of operations.”

Raw Materials and Suppliers

We believe that the raw materials that we require throughout the manufacturing process of Elelyso, PRX-102, alidornase alfa and OPRX-106 and our other current and potential drug product candidates are widely available from numerous suppliers and are generally considered to be generic industrial biological supplies. We rely on a single approved supplier for certain materials relating to the current expression of our proprietary biotherapeutic proteins through ProCellEx. We have identified additional suppliers for most of the materials required for the production of our product candidates.

Development and regulatory approval of our pharmaceutical products are dependent upon our ability to procure active ingredients and certain packaging materials from sources approved by the FDA and other regulatory authorities. Since the FDA and other regulatory approval processes require manufacturers to specify their proposed suppliers of active ingredients and certain packaging materials in their applications, FDA approval of a supplemental application to use a new supplier in connection with any drug candidate or approved product, if any, would be required if active ingredients or such packaging materials were no longer available from the specified supplier, which could result in manufacturing delays. From time to time, we intend to continue to identify alternative FDA-approved suppliers to ensure the continued supply of necessary raw materials.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly evolving technology and significant competition. Competition from numerous existing companies and others entering the fields in which we operate is intense and expected to increase. Most of these companies have substantially greater research and development, manufacturing, marketing, financial, technological personnel and managerial resources than we do. In addition, many specialized biotechnology companies have formed collaborations with large, established companies to support research, development and commercialization of products that may be competitive with our current and future product candidates and technologies. Acquisitions of competing companies by large pharmaceutical or biotechnology companies could further enhance such competitors’ financial, marketing and other resources. Academic institutions, governmental agencies and other public and private research organizations are also conducting research activities and seeking patent protection and may commercialize competitive products or technologies on their own or through collaborations with pharmaceutical and biotechnology companies.

There are two approved ERTs for the treatment of Fabry disease; Fabrazyme which is marketed by Genzyme and Replagal, which is marketed by Shire. Fabrazyme is available in the United States and the European Union. Replagal is available in the European Union and certain other territories outside the United States. In addition, we are aware of other late clinical stage, early clinical stage and experimental drugs which are being developed for the treatment of Fabry disease by Amicus Therapeutics, Inc. and other companies. In addition, in May 2016, Galafold™ (migalastat), an oral small molecule pharmacological chaperone marketed by Amicus was approved in the European Union and other countries, but not in the United States, as a first line therapy for long-term treatment of adults and adolescents aged 16 years and older with a confirmed diagnosis of Fabry disease and who have an amenable mutation.

With respect to alidornase alfa, we face competition from Genentech Inc., a member of the Roche Group, which markets Pulmozyme.

With respect to PRX-106, we face competition from AbbVie Inc. (Humira), Johnson & Johnson and Merck & Co. (Remicade) and Pfizer and Amgen Inc. (Enbrel). In addition, we are aware of other clinical stage, early clinical stage and experimental antiTNF drugs.

We also face competition from companies that are developing other platforms for the expression of recombinant therapeutic pharmaceuticals. We are aware of companies that are developing alternative technologies to develop and produce therapeutic proteins in anticipation of the expiration of certain patent claims covering marketed proteins. Competitors developing alternative expression technologies include Crucell N.V. (which was acquired by Johnson & Johnson during 2010), Shire and GlycoFi, Inc. (which was acquired by Merck & Co. Inc.). Other companies are developing alternate plant-based technologies, include, among others, iBio, Inc., Medicago Inc., and Greenovation Biotech GmbH, none of which are cell-based. Rather, such companies base their product development on transgenic plants or whole plants. See "Risk Factors—Developments by competitors may render our products or technologies obsolete or non-competitive which would have a material adverse effect on our business, results of operations and financial condition."

Scientific Advisory Board

We have reorganized our scientific advisory board by establishing a core team of advisors. The scientific advisory board may invite additional experts to attend meetings on a case-by-case basis. Members of our scientific advisory board consult with our management within their professional areas of expertise; exchange strategic and business development ideas with our management; attend scientific, medical and business meetings with our management, such as meetings with the FDA and comparable foreign regulatory authorities, meetings with strategic or potential strategic partners and other meetings relevant to their areas of expertise; and attend meetings of our scientific advisory board. We expect our scientific advisory board to convene at least twice annually, and we frequently consult with the individual members of our scientific advisory board. Our scientific advisory board currently includes the following people:

Name	Affiliations (selected)
Roger D. Kornberg, Ph.D. (Chairman)	Laureate of the Nobel Prize in Chemistry
	Member, U.S. National Academy of Sciences
	Winzer Professor of Medicine, Department of Structural Biology at Stanford University
	2001 Welch Prize (highest award granted in the field of chemistry in the United States)
	2002 Leopold Mayer Prize (the highest award granted in the field of biomedical sciences from the French Academy of Sciences)
Professor Aaron Ciechanover, M.D., D.Sc.	Laureate of the Nobel Prize in Chemistry
	Distinguished research Professor at the Cancer and Vascular Biology Research Center of the Rappaport Research Institute and Faculty of Medicine at the Technion, Israel's Institute of Technology
	American Academy of Arts and Sciences, Member
Alexander Levitzki, Ph.D.	Wolfson Family Professor of Biochemistry in the Department of Biological Chemistry of The Alexander Silberman Institute of Life Sciences, Hebrew University of Jerusalem
	American Association for Cancer Research, 2013 Award for Outstanding Achievement in Chemistry in Cancer Research.
	1990 Israel Prize in Biochemistry
	1990 Rothschild Prize in Biology

	2002 Hamilton-Fairley Award, European Society of Medical Oncology
	2005 Wolf Prize for Medicine
	2012 Nauta Award in Pharmacochemistry, The European Federation of Medicinal Chemistry (EFMC) (the highest award from the European Federation for Medicinal Chemistry)
Charles J. Arntzen, Ph.D.	Regent's Profession and Florence Ely Nelson Presidential Chair
	Biodesign Institute, CIDV, Arizona State University
	Member, National Academy of Sciences, USA
	American Society of Plant Biology Leadership in Science Public Service Award (2004)
	Botanical Society of America Centennial Award (2006)
	Fellow of American Society of Plant Biologists (2007)
	Doctor of Science *honoris causa.*, Hebrew University of Jerusalem
	Chair, Section O "Agriculture, Food, and Renewable Resources," American Association for the Advancement of Science (AAAS) (2011-2012)

Government Regulation

The testing, manufacture, distribution, advertising and marketing of drug products are subject to extensive regulation by federal, state and local governmental authorities in the United States, including the FDA, and by similar authorities in other countries. Any product that we develop must receive all relevant regulatory approvals or clearances, as the case may be, before it may be marketed in a particular country.

The regulatory process, which includes overseeing preclinical studies and clinical trials of each pharmaceutical compound to establish its safety and efficacy and confirmation by the FDA that good laboratory, clinical and manufacturing practices were maintained during testing and manufacturing, can take many years, requires the expenditure of substantial resources and gives larger companies with greater financial resources a competitive advantage over us. Delays or terminations of clinical trials that we undertake would likely impair our development of product candidates. Delays or terminations could result from a number of factors, including stringent enrollment criteria, slow rate of enrollment, size of patient population, having to compete with other clinical trials for eligible patients, geographical considerations and others.

The FDA review process can be lengthy and unpredictable, and we may encounter delays or rejections of our applications when submitted. Generally, in order to gain FDA approval, we must first conduct preclinical studies in a laboratory and in animal models to obtain preliminary information on a compound and to identify any potential safety problems. The results of these studies are submitted as part of an IND application that the FDA must review before human clinical trials of an investigational drug can commence. Clinical trials may be terminated by the clinical trial site, sponsor or the FDA if toxicities appear that are either worse than expected or unexpected.

Clinical trials are normally performed in three sequential phases and generally take two to five years, or longer, to complete. Phase I consists of testing the drug product in a small number of humans, normally healthy volunteers, to determine preliminary safety and tolerable dose range. Phase II usually involves studies in a limited patient population to evaluate the effectiveness of the drug product in humans having the disease or medical condition for which the product is indicated, determine dosage tolerance and optimal dosage and identify possible common adverse effects and safety risks. Phase III consists of additional controlled testing at multiple clinical sites to establish clinical safety and effectiveness in an expanded patient population of geographically dispersed test sites to evaluate the overall benefit-risk relationship for administering the product and to provide an adequate basis for product labeling. Phase IV clinical trials may be conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication.

After completion of clinical trials of a new drug product, FDA and foreign regulatory authority marketing approval must be obtained. Assuming that the clinical data support the product's safety and effectiveness for its intended use, a new drug application, or NDA, or a BLA is submitted to the FDA for review. Generally, it takes one to three years to obtain approval. If questions arise during the FDA review process, approval may take a significantly longer period of time. The testing and approval processes require substantial time and effort and approval on a timely basis, if at all, or the approval that we receive may be for a narrower indication than we had originally sought, potentially undermining the commercial viability of the product. Even if regulatory approvals are obtained, approved products are subject to continual review and holders of an approved product are required, for example, to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain requirements concerning advertising and promotional labeling for the product. Also, quality control and manufacturing procedures relating to a product must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to comply with cGMP and other aspects of regulatory compliance. The later discovery of previously unknown problems or failure to comply with the applicable regulatory requirements with respect to any product may result in restrictions on the marketing of the product or withdrawal of the product from the market as well as possible civil or criminal sanctions. See also "—International Regulation."

Under the Orphan Drug Act of 1983, the FDA may grant orphan drug designation to drugs and biological products intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. The FDA grants orphan drug designation to drugs that may provide a significant therapeutic advantage over existing treatments and target conditions affecting 200,000 or fewer U.S. patients per year. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. Among the other benefits of orphan drug designation are possible funding and tax savings to support clinical trials and for other financial incentives and a waiver of the marketing application user fee and most likely priority review. If a significant therapeutic advantage over existing treatments is shown in the marketing application, the FDA may grant orphan drug approval and provide a seven-year period of marketing exclusivity.

The FDA has a fast track program that is is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need, the purpose being to make important new drugs available to patients earlier. A drug candidate that receives Fast Track designation from the FDA is eligible for some or all of the following: more frequent meetings with the FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval; more frequent written communication from the FDA about such things as the design of the proposed clinical trials; eligibility for the FDA's Accelerated Approval and Priority Review, if relevant criteria are met; and eligibility for Rolling Review, which allows a drug company to submit completed sections of its BLA or NDA for review by the FDA, rather than waiting until every section of the BLA or NDA is completed before the entire application can be reviewed. BLA or NDA review usually does not begin until the drug company has submitted the entire application to the FDA. We used the Rolling Review option for our taliglucerase alfa NDA, which we completed in April 2010.

The United States federal government regulates healthcare through various agencies, including but not limited to the following: (i) the FDA, which administers the Federal Food, Drug, and Cosmetic Act (FDCA), as well as other relevant laws; (ii) the Center for Medicare & Medicaid Services (CMS), which administers the Medicare and Medicaid programs; (iii) the Office of Inspector General (OIG) which enforces various laws aimed at curtailing fraudulent or abusive practices, including by way of example, the Anti-Kickback Law, the Anti-Physician Referral Law, commonly referred to as Stark, the Anti-Inducement Law, the Civil Money Penalty Law and the laws that authorize the OIG to exclude healthcare providers and others from participating in federal healthcare programs; and (iv) the Office of Civil Rights, which administers the privacy aspects of the Health Insurance Portability and Accountability Act of 1996, or HIPAA. All of the aforementioned are agencies within the Department of Health and Human Services (HHS). Healthcare is also provided or regulated, as the case may be, by the Department of Defense through its TriCare program, the Department of Veterans Affairs, especially through the Veterans Health Care Act of 1992, the Public Health Service within HHS under Public Health Service Act § 340B (42 U.S.C. § 256b), the Department of Justice through the Federal False Claims Act and various criminal statutes, and state governments under the Medicaid and other state sponsored or funded programs and their internal laws regulating all healthcare activities. Many states also have anti-kickback and anti-physician referral laws that are similar to the federal laws, but may be applicable in situations where federal laws do not apply.

Medicare is the federal healthcare program for those who are (i) over 65 years of age, (ii) disabled, (iii) suffering from end-stage renal disease or (iv) suffering from Lou Gehrig's disease. Medicare consists of part A, which covers inpatient costs, part B, which covers services by physicians and laboratories, durable medical equipment and certain drugs, primarily those administered by physicians, and part D, which provides drug coverage for most prescription drugs other than those covered under part B. Medicare also offers a managed care option under part C. Medicare is administered by CMS. In contrast, Medicaid is a state-federal healthcare program for the poor and is administered by the states pursuant to an agreement with the Secretary of Health and Human Services. Most state Medicaid programs cover most outpatient prescription drugs.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, PPACA, became law in the United States. PPACA substantially changes the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Key provisions of PPACA specific to the pharmaceutical industry, among others, include the following:

- An annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents into the United States, apportioned among these entities according to their market share in certain federal government healthcare programs (excluding sales of any drug or biologic product marketed for an orphan indication), beginning in 2011;

- An increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;

- A new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D, beginning in 2011;

- Extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, effective March 23, 2010;

- Expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in April 2010 and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;

- Expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective January 2010;

- New requirements to report certain financial arrangements with physicians and others, including reporting any "transfer of value" made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2012, with reporting starting in 2013;

- A new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;

- A licensure framework for follow-on biologic products; and

- A new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

International Regulation

We are subject to regulations and product registration requirements in many foreign countries in which we may sell our products, including in the areas of product standards, packaging requirements, labeling requirements, import and export restrictions and tariff regulations, duties and tax requirements. The time required to obtain clearance required by foreign countries may be longer or shorter than that required for FDA clearance, and requirements for licensing a product in a foreign country may differ significantly from FDA requirements.

Pharmaceutical products may not be imported into, or manufactured or marketed in, the State of Israel absent drug registration. The three basic criteria for the registration of pharmaceuticals in Israel is quality, safety and efficacy of the pharmaceutical product and the Israeli MOH requires pharmaceutical companies to conform to international developments and standards. Regulatory requirements are constantly changing in accordance with scientific advances as well as social and ethical values.

The relevant legislation of the European Union requires that medicinal products, including generic versions of previously approved products, and new strengths, dosage forms and formulations, of previously approved products, shall have a marketing authorization before they are placed on the market in the European Union. Authorizations are granted after the assessment of quality, safety and efficacy by the respective health authorities. In order to obtain an authorization, an application must be made to the competent authority of the member state concerned or in a centralized procedure to the EMA. Besides various formal requirements, the application must contain the results of pharmaceutical (physico-chemical, biological or microbiological) tests, of preclinical (toxicological and pharmacological) tests as well as of clinical trials. All of these tests must have been conducted in accordance with relevant EU regulations and must allow the reviewer to evaluate the quality, safety and efficacy of the medicinal product. Orphan drug designation in the European Union is granted to medicinal products intended for the diagnosis, prevention and treatment of life-threatening diseases and very serious conditions that affect not more than five in 10,000 people in the European Union. Orphan drug designation is generally given to medicinal products that treat conditions for which no current therapy exists or are expected to bring a significant benefit to patients over existing therapies.

Israeli Government Programs

The following is a summary of the current principal Israeli tax laws applicable to us and Protalix Ltd., and of the Israeli Government programs from which Protalix Ltd. benefits. Some parts of this discussion are based on new tax legislation that has not been subject to judicial or administrative interpretation. Therefore, the views expressed in the discussion may not be accepted by the tax authorities in question. The discussion should not be construed as legal or professional tax advice and does not cover all possible tax considerations.

General Corporate Tax Structure in Israel

The income of Protalix Ltd., other than income from “Approved Enterprises,” is taxed in Israel at the regular rates which were 26.5% for fiscal year 2015, 25% in 2016 and 24% in 2017.

In January 2016, the Law for the Amendment of the Income Tax Ordinance (No. 216) was published, enacting a reduction of corporate tax rate beginning in 2016 and thereafter, from 26.5% to 25%. In December 2016, the Economic Efficiency Law (Legislative Amendments for Implementing the Economic Policy for the 2017 and 2018 Budget Year), 2016 was published, introducing a gradual reduction in corporate tax rate from 25% to 23%. However, the law also included a temporary provision setting the corporate tax rate in 2017 at 24%. As a result, the corporate tax rate was 24% in 2017 and will be 23% in 2018 and thereafter.

Capital gains on the sale of assets are subject to capital gains tax according to the corporate tax rate in effect in the year which the assets are sold.

Law for the Encouragement of Capital Investments, 1959

The Law for the Encouragement of Capital Investments, 1959, as amended, or the Investment Law, provides certain incentives for capital investments in a production facility (or other eligible assets). Generally, an investment program that is implemented in accordance with the provisions of the Investment Law, referred to as an “Approved Enterprise,” is entitled to benefits. These benefits may include cash grants from the Israeli government and tax benefits, based upon, among other things, the location of the facility in which the investment is made and specific elections made by the grantee.

Protalix Ltd. will continue to enjoy the tax benefits under the pre-revision provisions of the Investment Law. If any new benefits are granted to Protalix Ltd. in the future, Protalix Ltd. will be subject to the provisions of the amended Investment Law with respect to these new benefits. Therefore, the following discussion is a summary of the Investment Law prior to its amendment as well as the relevant changes contained in the new legislation.

Under the Investment Law prior to its amendment, a company that wished to receive benefits had to receive approval from the Authority for the Investment and Development of the Industry and Economy, or the Authority. Each certificate of approval for an Approved Enterprise relates to a specific investment program in the Approved Enterprise, delineated both by the financial scope of the investment and by the physical characteristics of the facility or the asset, e.g., the equipment to be purchased and utilized pursuant to the program.

An Approved Enterprise may elect to forego any entitlement to the grants otherwise available under the Investment Law and, instead, participate in an alternative benefits program under which the undistributed income from the Approved Enterprise is fully exempt from corporate tax for a defined period of time. Under the alternative package of benefits, a company's undistributed income derived from an Approved Enterprise will be exempt from corporate tax for a period of between two and 10 years from the first year of taxable income, depending upon the geographic location within Israel of the Approved Enterprise. Upon expiration of the exemption period, the Approved Enterprise is eligible for the reduced tax rates otherwise applicable under the Investment Law for any remainder of the otherwise applicable benefits period (up to an aggregate benefits period of either seven or 10 years, depending on the location of the company or its definition as a foreign investors' company). If a company has more than one Approved Enterprise program or if only a portion of its capital investments are approved, its effective tax rate is the result of a weighted combination of the applicable rates. The tax benefits from any certificate of approval relate only to taxable profits attributable to the specific Approved Enterprise. Income from activity that is derived from different Approved Enterprises does not enjoy these tax benefits.

A company that has an Approved Enterprise program is eligible for further tax benefits if it qualifies as a foreign investors' company. A foreign investors' company eligible for benefits is essentially a company in which more than 25% of the share capital (in terms of shares, rights to profit, voting and appointment of directors) is owned (measured by both share capital and combined share and loan capital) by non-Israeli residents. A company that qualifies as a foreign investors' company and has an Approved Enterprise program is eligible for tax benefits for a 10-year benefit period and may enjoy a reduced corporate tax rate of 10% to 25%, depending on the amount of the company's shares held by non-Israeli shareholders.

If a company that has an Approved Enterprise program is a wholly owned subsidiary of another company, the percentage of foreign investments is determined based on the percentage of foreign investment in the parent company. The tax rates and related levels of foreign investments are set forth in the following table:

Percent of Foreign Ownership	**Rate of Reduced Tax**
0-49%	25%
49-74%	20%
74-90%	15%
90-100%	10%

Our original facility in Israel has been granted "Approved Enterprise" status, and it has elected to participate in the alternative benefits program. Under the terms of its Approved Enterprise program, the facility is located in a top priority location, or "Zone A," and, therefore, the income from that Approved Enterprise will be tax exempt in Israel for a period of 10 years, commencing with the year in which taxable income is first generated from the relevant Approved Enterprise. The current benefits program may not continue to be available and Protalix Ltd. may not continue to qualify for its benefits.

A company that has elected to participate in the alternative benefits program and that subsequently pays a dividend out of the income derived from the Approved Enterprise during the tax exemption period will be subject to corporate tax in respect of the amount distributed at the rate that would have been applicable had the company not elected the alternative benefits program (generally 10% to 25%, depending on the extent to which non-Israeli shareholders hold such company's shares). If the dividend is distributed within 12 years after the commencement of the benefits period (or, in the case of a foreign investor's company, without time limitation), the dividend recipient is taxed at the reduced withholding tax rate of 15% applicable to dividends from approved enterprises, or at the lower rate under an applicable tax treaty. After this period, the withholding tax rate is 25%, or at the lower rate under an applicable tax treaty. In the case of a company with a foreign investment level (as defined by the Investment Law) of 25% or more, the 12-year limitation on reduced withholding tax on dividends does not apply. The company must withhold this tax at its source, regardless of whether the dividend is converted into foreign currency.

The Investment Law also provides that an Approved Enterprise is entitled to accelerated depreciation on its property and equipment that are included in an approved investment program. This benefit is an incentive granted by the Israeli government regardless of whether the alternative benefits program is elected.

The benefits available to an Approved Enterprise are conditioned upon terms stipulated in the Investment Law and regulations and the criteria set forth in the applicable certificate of approval. If Protalix Ltd. does not fulfill these conditions in whole or in part, the benefits can be canceled and Protalix Ltd. may be required to refund the received benefits, linked to the Israeli consumer price index with the addition of interest or alternatively with an additional penalty payment. We believe that Protalix Ltd. currently operates in compliance with all applicable conditions and criteria, but there can be no assurance that Protalix Ltd. will continue to do so. Furthermore, there can be no assurance that any Approved Enterprise status granted to Protalix Ltd.'s facilities will entitle Protalix Ltd. to the same benefits to which it is currently entitled.

Under the Investment Law, the approval of the Authority is required only for Approved Enterprises that receive cash grants. Approved Enterprises that do not receive benefits in the form of governmental cash grants, but only tax benefits, are no longer required to obtain this approval. Instead, these Approved Enterprises are required to make certain investments as specified in the Investment Law.

The amended Investment Law specifies certain conditions for an Approved Enterprise to be entitled to benefits. These conditions include:

- the Approved Enterprise's revenues from any single country or a separate customs territory may not exceed 75% of the Approved Enterprise's total revenues; or

- at least 25% of the Approved Enterprise's revenues during the benefits period must be derived from sales into a single country or a separate customs territory with a population of at least 14 million.

There can be no assurance that Protalix Ltd. will comply with the above conditions in the future or that Protalix Ltd. will be entitled to any additional benefits under the Investment Law. In addition, it is possible that Protalix Ltd. may not be able to operate in a manner that maximizes utilization of the potential benefits available under the Investment Law.

From time to time, the Israeli Government has considered reducing the benefits available to companies under the Investment Law. The termination or substantial reduction of any of the benefits available under the Investment Law could materially impact the cost of our future investments.

Encouragement of Industrial Research, Development and Technology Innovation Law, 1984

To date, Protalix Ltd. has received grants from the OCS under the Israeli Law for the Encouragement of Industrial Research, Development and Technology Innovation, 1984, and related regulations, or the Research Law. On January 1, 2016, the Israeli government established NATI which replaced many of the functions of the Office of the Chief Scientist of the Israeli Department of Labor, or the OCS. For purposes of clarity, references to NATI will include the OCS. NATI grants are made available to finance of a portion of Protalix Ltd.'s research and development expenditures in Israel. As of December 31, 2017, NATI approved grants in respect of Protalix Ltd.'s continuing operations totaling approximately $50.9 million, measured from inception. Protalix Ltd. is required to repay up to 100% of grants actually received (plus interest at the LIBOR rate applied to the grants received on or after January 1, 1999) to NATI through payments of royalties at a rate of 3% to 6% of the revenues generated from NATI-funded project, depending on the period in which revenues were generated. As of December 31, 2017, Protalix Ltd. either paid or accrued royalties payable of $8.7 million and Protalix Ltd.'s contingent liability to NATI with respect to grants received was approximately $42.2 million.

Under the Research Law, recipients of grants from NATI are prohibited from manufacturing products developed using these grants outside of the State of Israel without special approvals, although the Research Law does enable companies to seek prior approval for conducting manufacturing activities outside of Israel without being subject to increased royalties. If Protalix Ltd. receives approval to manufacture the products developed with government grants outside of Israel, it will be required to pay an increased total amount of royalties (possibly up to 300% of the grant amounts plus interest), depending on the manufacturing volume that is performed outside of Israel, as well as at a possibly increased royalty rate.

Additionally, under the Research Law, Protalix Ltd. is prohibited from transferring NATI-financed technologies and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the approval of NATI Council or the Research Committee. Protalix Ltd. may not receive the required approvals for any proposed transfer and, if received, Protalix Ltd. may be required to pay NATI a portion of the consideration that it receives upon any sale of such technology by a non-Israeli entity. The scope of the support received, the royalties that Protalix Ltd. has already paid to NATI, the amount of time that has elapsed between the date on which the know-how was transferred and the date on which NATI grants were received and the sale price and the form of transaction will be taken into account in order to calculate the amount of the payment to NATI. Approval of the transfer of technology to residents of the State of Israel is required, and may be granted in specific circumstances only if the recipient abides by the provisions of applicable laws, including the restrictions on the transfer of know-how and the obligation to pay royalties. No assurance can be made that approval to any such transfer, if requested, will be granted.

Under the Research Law and the regulations promulgated thereunder, NATI Council may allow the transfer outside of Israel of know-how derived from an approved program and the related manufacturing rights in limited circumstances which are currently as follows:

- in the event of a sale of know-how itself to a non-affiliated third party, provided that upon such sale the owner of the know-how pays to NATI an amount, in cash, as set forth in the Research Law (and the regulations promulgated thereunder). In addition, the amendment provides that if the purchaser of the know-how gives the selling Israeli company the right to exploit the know-how by way of an exclusive, irrevocable and unlimited license, the research committee may approve such transfer in special cases without requiring a cash payment.

- in the event of a sale of a company which is the owner of know-how, pursuant to which the company ceases to be an Israeli company, provided that upon such sale, the owner of the know-how makes a cash payment to NATI as set forth in the Research Law (and the regulations promulgated thereunder).

- in the event of an exchange of know-how such that in exchange for the transfer of know-how outside of Israel, the recipient of the know-how transfers other know-how to the company in Israel in a manner in which NATI is convinced that the Israeli economy realizes a greater, overall benefit from the exchange of know-how.

The Research Committee may, in special cases, approve the transfer of manufacture or of manufacturing rights of a product developed within the framework of the approved program or which results therefrom, outside of Israel.

The State of Israel does not own intellectual property rights in technology developed with NATI funding and there is no restriction on the export of products manufactured using technology developed with NATI funding. The technology is, however, subject to transfer of technology and manufacturing rights restrictions as described above. For a description of such restrictions, please see “Risk Factors—Risks Relating to Our Operations in Israel.” NATI approval is not required for the export of any products resulting from the research or development or for the licensing of any technology in the ordinary course of business.

Law for the Encouragement of Industry (Taxes), 1969

We believe that Protalix Ltd. currently qualifies as an “Industrial Company” within the meaning of the Law for the Encouragement of Industry (Taxes), 1969, or the Industry Encouragement Law. The Industry Encouragement Law defines “Industrial Company” as a company resident in Israel and incorporated in Israel, that derives 90% or more of its income in any tax year (other than specified kinds of passive income such as capital gains, interest and dividends) from an “Industrial Enterprise” operating in Israel (including Judea & Samaria territories and the Gaza strip), that it owns. An “Industrial Enterprise” is defined as an enterprise whose major activity in a given tax year is industrial production.

The following corporate tax benefits, among others, are available to Industrial Companies:

- amortization of the cost of purchased know-how and patents over an eight-year period for tax purposes;
- accelerated depreciation rates on equipment and buildings;
- under specified conditions, an election to file consolidated tax returns with other related Israeli Industrial Companies; and
- expenses related to a public offering are deductible in equal amounts over three years.

Eligibility for the benefits under the Industry Encouragement Law is not subject to receipt of prior approval from any governmental authority. It is possible that Protalix Ltd. may fail to qualify or may not continue to qualify as an "Industrial Company" or that the benefits described above will not be available in the future.

Tax Benefits for Research and Development

Under specified conditions, Israeli tax laws allow a tax deduction by a company for research and development expenditures, including capital expenditures, for the year in which such expenditures are incurred. These expenditures must relate to scientific research and development projects and must be approved by NATI. Furthermore, the research and development projects must be for the promotion of the company and carried out by or on behalf of the company seeking such tax deduction. However, the amount of such deductible expenditures is reduced by the sum of any funds received through government grants for the finance of such scientific research and development projects. Expenditures not so approved are deductible over a three-year period.

Employees

As of December 31, 2017, we had 190 employees, of whom 21 have a Ph.D. or an M.D.in their respective scientific fields. We believe that our relations with these employees are good. We believe that our success will greatly depend on our ability to identify, attract and retain capable employees. The Israeli Ministry of Labor and Welfare is authorized to make certain industry-wide collective bargaining agreements, or Expansion Orders, that apply to types of industries or employees including ours. These agreements affect matters such as cost of living adjustments to salaries, length of working hours and week, recuperation, travel expenses, and pension rights. Otherwise, our employees are not represented by a labor union or represented under a collective bargaining agreement. See "Risk Factors—We depend upon key employees and consultants in a competitive market for skilled personnel. If we are unable to attract and retain key personnel, it could adversely affect our ability to develop and market our products."

Company Background

Our principal business address is set forth below. Our executive offices and our main research manufacturing facility are located at that address. Our telephone number is +972-4-988-9488. We were originally incorporated in the State of Florida in April 1992, and reincorporated in the State of Delaware in March 2016. Protalix Ltd., our wholly-owned subsidiary and sole operating unit, is an Israeli company and was originally incorporated in Israel on December 27, 1993. During 1999, Protalix Ltd. changed its focus from plant secondary metabolites to the expression of recombinant therapeutic proteins in plant cells, and in April 2004 changed its name to Protalix Ltd.

ProCellEx® is our registered trademark. Each of the other trademarks, trade names or service marks appearing in this Annual Report on Form 10-K belongs to its respective holder.

Available Information

Our corporate website is www.protalix.com. We make available on our website, free of charge, our Commission filings, including our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports, as soon as reasonably practicable after we electronically file these documents with, or furnish them to, the Commission. Additionally, from time to time, we provide notifications of material news including press releases and conferences on our website. Webcasts of presentations made by our company at certain conferences may also be available from time to time on our website, to the extent the webcasts are available. The content of our website is not intended to be incorporated by reference into this report or in any other report or document we file and any references to these websites are intended to be inactive textual references only.

We are also listed on the Tel Aviv Stock Exchange, or the TASE, and, accordingly, we submit copies of all our filings with the Commission to the Israeli Securities Authority and the TASE. Such copies can be retrieved electronically through the TASE's internet messaging system (www.maya.tase.co.il) and through the MAGNA distribution site of the Israeli Securities Authority (www.magna.isa.gov.il).

Our website also includes printable versions of our Code of Business Conduct and Ethics and the charters for each of the Audit, Compensation and Nominating Committees of our Board of Directors. Each of these documents is also available in print, free of charge, to any shareholder who requests a copy by addressing a request to:

Protalix BioTherapeutics, Inc.
2 Snunit Street, Science Park
P.O. Box 455
Carmiel 20100, Israel
Attn: Mr. Yossi Maimon, Chief Financial Officer

Item 1A. Risk Factors

You should carefully consider the risks described below together with the other information included in this Annual Report on Form 10-K. Our business, financial condition or results of operations could be adversely affected by any of these risks. If any of these risks occur, the value of our common stock could decline.

Risks Related to Clinical Trials and Regulatory Matters

Clinical trials are very expensive, time-consuming and difficult to design and implement and may result in unforeseen costs which may have a material adverse effect on our business, results of operations and financial condition.

Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time-consuming. Other than taliglucerase alfa, all of our other drug candidates, including pegunigalsidase alfa, are in the clinical, preclinical or research stages and will take at least several years to complete. Preliminary and initial results from a clinical trial do not necessarily predict final results, and failure can occur at any stage of the trial. We may encounter problems that cause us to abandon or repeat preclinical studies or clinical trials. Failure or delay in the commencement or completion of our clinical trials may be caused by several factors, including:

- slower than expected rates of patient recruitment, particularly with respect to trials of rare diseases such as Fabry disease;
- determination of dosing issues;
- unforeseen safety issues;
- lack of effectiveness during clinical trials;
- disagreement by applicable regulatory bodies over our trial protocols, our the interpretation of data from preclinical studies or clinical trials or conduct and control of clinical trials;
- determination that the patient population participating in a clinical trial may not be sufficiently broad or representative to assess efficacy and safety for our target population;
- inability to monitor patients adequately during or after treatment;
- inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; and
- lack of sufficient funding to finance the clinical trials.

Any failure or delay in commencement or completion of any clinical trials of pegunigalsidase alfa or our other product candidates will have a material adverse effect on our business, results of operations and financial condition. In addition, we or the FDA or other regulatory authorities may suspend any clinical trial at any time if it appears that we are exposing participants in the trial to unacceptable safety or health risks or if the FDA or such other regulatory authorities, as applicable, find deficiencies in our IND submissions or the conduct of the trial. Any suspension of a clinical trial may have a material adverse effect on our business, results of operations and financial condition.

We may find it difficult to enroll patients in our clinical trials, which could cause significant delays in the completion of such trials or may cause us to abandon one or more clinical trials.

Some of the diseases or disorders that our drug candidates are intended to treat, such as Fabry disease, are relatively rare and we expect only a subset of the patients with these diseases to be eligible for our clinical trials. Our clinical trials generally mandate that a patient cannot be involved in another clinical trial for the same indication. Therefore, subjects that participate in ongoing clinical trials for products that are competitive with our drug candidates are not available for our clinical trials. An inability to enroll a sufficient number of patients for our ongoing phase III clinical trials of pegunigalsidase alfa, or for any of our other current or future clinical trials, would result in significant delays or may require us to abandon one or more clinical trials altogether, which will have a material adverse effect on our business, results of operations and financial condition.

If the results of our clinical trials do not support our claims relating to a drug candidate, or if serious side effects are identified, the completion of development of such drug candidate may be significantly delayed or we may be forced to abandon development altogether, which will significantly impair our ability to generate product revenues.

The results of our clinical trials with respect to any drug candidate might not support our claims of superiority, safety or efficacy, the effects of our drug candidates may not be the desired effects or may include undesirable side effects or the drug candidates may have other unexpected characteristics. Further, success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and the results of later clinical trials may not replicate the results of prior clinical trials and preclinical testing. Data obtained from tests are susceptible to varying interpretations which may delay, limit or prevent regulatory approval. The clinical trial process may fail to demonstrate that our drug candidates are safe for humans and effective for indicated uses. In addition, our clinical trials, particularly with respect to pegunigalsidase alfa, may involve specific and small patient populations. Results of early clinical trials conducted on a small patient population may not be indicative of future results. Adverse or inconclusive results may cause us to abandon a drug candidate and may delay development of other drug candidates. Any delay in, or termination of, our clinical trials will delay the filing of NDAs and BLAs with the FDA, or other filings with other foreign regulatory authorities, and, ultimately, significantly impair our ability to commercialize our drug candidates and generate product revenues which would have a material adverse effect on our business, results of operations and financial condition.

Patients may discontinue their participation in our clinical trials which may negatively impact the results of these studies and extend the timeline for completion of our development programs.

Patients enrolled in our clinical trials may discontinue their participation at any time during the study as a result of a number of factors, including withdrawing their consent, experiencing adverse clinical events, which may or may not be judged related to our drug candidates under evaluation, or due to planned or actual pregnancies. The discontinuation of patients in any one of our studies may delay the completion of the study or cause the results from the study not to be positive or to not support a filing for regulatory approval of the applicable drug candidate, which would have a material adverse effect on our business, results of operations and financial condition.

Because our clinical trials depend upon third-party researchers, the results of our clinical trials and such research activities are subject to delays and other risks which are, to a certain extent, beyond our control, which could impair our clinical development programs and our competitive position.

We depend upon independent investigators and collaborators, such as universities and medical institutions, to conduct our preclinical and clinical trials. These collaborators are not our employees, and we cannot control the amount or timing of resources that they devote to our clinical development programs. The investigators may not assign as great a priority to our clinical development programs or pursue them as diligently as we would if we were undertaking such programs directly. If outside collaborators fail to devote sufficient time and resources to our clinical development programs, or if their performance is substandard, the approval of anticipated NDAs, BLAs and other marketing applications, and our introduction of new drugs, if any, may be delayed which could impair our clinical development programs and would have a material adverse effect on our business and results of operations. The collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators also assist our competitors, our competitive position could be harmed.

We are subject to extensive governmental regulation including the requirements of the FDA and other comparable regulatory authorities before our drug candidates may be marketed.

Both before and after marketing approval of our drug candidates, if at all, we, our drug candidates, our suppliers, our contract manufacturers and our contract testing laboratories are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. Failure to comply with applicable requirements of the FDA or comparable foreign regulatory authorities could result in, among other things, any of the following actions:

- warning letters;
- fines and other monetary penalties;
- unanticipated expenditures;
- delays in the FDA's or other foreign regulatory authorities' approving, or the refusal of any regulatory authority to approve, any drug candidate;

- product recall or seizure;
- interruption of manufacturing or clinical trials;
- operating restrictions;
- injunctions; and
- criminal prosecutions.

In addition to the approval requirements, other numerous and pervasive regulatory requirements apply, both before and after approval, to us, our drug candidates, and our suppliers, contract manufacturers, and contract laboratories. These include requirements related to:

- testing;
- manufacturing;
- quality control;
- labeling;
- advertising;
- promotion;
- distribution;
- export;
- reporting to the FDA certain adverse experiences associated with use of the drug candidate; and
- obtaining additional approvals for certain modifications to the drug candidate or its labeling or claims.

We also are subject to inspection by the FDA and comparable foreign regulatory authorities, to determine our compliance with regulatory requirements, as are our suppliers, contract manufacturers, and contract testing laboratories, and there can be no assurance that the FDA or any other comparable foreign regulatory authority, will not identify compliance issues that may disrupt production or distribution, or require substantial resources to correct. We may be required to make modifications to our manufacturing operations in response to these inspections which may require significant resources and may have a material adverse effect upon our business, results of operations and financial condition.

The approval process for any drug candidate may also be delayed by changes in government regulation, future legislation or administrative action or changes in policy of the FDA and comparable foreign authorities that occur prior to or during their respective regulatory reviews of such drug candidate. Delays in obtaining regulatory approvals with respect to any drug candidate may:

- delay commercialization of, and our ability to derive product revenues from, such drug candidate;
- delay any regulatory-related milestone payments payable under outstanding collaboration agreements;
- require us to perform costly procedures with respect to such drug candidate; or
- otherwise diminish any competitive advantages that we may have with respect to such drug candidate.

Delays in the approval process for any drug candidate may have a material adverse effect upon our business, results of operations and financial condition.

We may not obtain the necessary U.S., EMA or other worldwide regulatory approvals to commercialize our drug candidates in a timely manner, if at all, which would have a material adverse effect on our business, results of operations and financial condition.

We need FDA approval to commercialize our drug candidates in the United States, EMA approval to commercialize our drug candidates in the European Union and approvals from other foreign regulators to commercialize our drug candidates elsewhere. In order to obtain FDA approval of any of our drug candidates, we must submit to the FDA an NDA or a BLA demonstrating that the drug candidate is safe for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials. In the European Union, we must submit an MAA to the EMA. Satisfaction of the regulatory requirements of the FDA, EMA and other foreign regulatory authorities typically takes many years, depends upon the type, complexity and novelty of the drug candidate and requires substantial resources for research, development and testing. Even if we comply with all the requests of regulatory authorities, the authorities may ultimately reject any marketing application that we file for a product candidate in the future, if any, or we might not obtain regulatory clearance in a timely manner. Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced or late-stage clinical trials, even after obtaining promising earlier trial results or in preliminary findings or other comparable authorities for such clinical trials. Further, even if favorable testing data is generated by the clinical trials of a drug candidate, the applicable regulatory authority may not accept or approve the marketing application filed by a pharmaceutical or biotechnology company for the drug candidate. Failure to obtain approval of the FDA, EMA or comparable foreign authorities of any of our drug candidates in a timely manner, if at all, will severely undermine our business, financial condition and results of operation by reducing our potential marketable products and our ability to generate corresponding product revenues.

Our research and clinical efforts may not result in drugs that the FDA, EMA or foreign regulatory authorities consider safe for humans and effective for indicated uses, which would have a material adverse effect on our business, results of operations and financial condition. After clinical trials are completed for any drug candidate, if at all, the FDA, EMA and foreign regulatory authorities have substantial discretion in the drug approval process of the drug candidate in their respective jurisdictions and may require us to conduct additional clinical testing or perform post-marketing studies which would cause us to incur additional costs. Incurring such costs may have a material adverse effect on our business, results of operations and financial condition.

We have only limited experience in regulatory affairs, and some of our drug candidates may be based on new technologies. These factors may affect our ability or the time we require to obtain necessary regulatory approvals.

We have only limited experience in filing and prosecuting the applications necessary to gain regulatory approvals for medical devices and drug candidates. Moreover, some of the drug candidates that are likely to result from our development programs may be based on new technologies that have not been extensively tested in humans. The regulatory requirements governing these types of drug candidates may be less well defined or more rigorous than for conventional products. As a result, we may experience a longer regulatory process in connection with obtaining regulatory approvals of any products that we develop.

Orphan drug designation may not ensure that we will enjoy market exclusivity in any jurisdiction. If any of our other competitors are able to obtain orphan drug exclusivity for any products that are competitive with our products, we may be precluded from selling or obtaining approval of our competing products by the applicable regulatory authorities for a significant period of time.

In the United States, the European Union and other countries, a drug may be designated as having orphan drug status, subject to certain conditions. There can be no assurance that a drug candidate that receives orphan drug designation will receive orphan drug marketing exclusivity and more than one drug can have orphan designation for the same indication. In addition, the orphan drug designation granted to pegunigalsidase alfa by the EMA does not affect Fabry disease treatments that preexist the approval of pegunigalsidase alfa, if at all.

Foreign regulations regarding orphan drugs are similar to those in the United States but there are several differences. For example, the exclusivity period in the European Union is generally 10 years. From time to time, we may apply to the FDA or any comparable foreign regulatory authority for orphan drug designation for any one or more of our drug candidates. Other than pegunigalsidase alfa which was granted orphan drug designation by the EMA, none of our drug candidates have been designated as an orphan drug and there is no guarantee that the FDA or any other regulatory authority will grant such designation in the future. In addition, neither orphan drug designation nor orphan drug exclusivity prevents competitors from developing or marketing different drugs for the relevant indication. Even if we obtain orphan drug exclusivity for one or more indications for one of our drug candidates, we may not be able to maintain the exclusivity. For example, if a competitive product that is the same drug or biologic as one of our drug candidates is shown to be clinically superior to the drug candidate, any orphan drug exclusivity granted to the drug candidate will not block the approval of the competitive product.

If any drug receives orphan drug exclusivity in any jurisdiction for the same indication of any of our drug candidates, we may be prevented from attaining a similar designation with respect to our drug candidate or from marketing the drug candidate in the jurisdiction during the applicable exclusivity period, which will have a material adverse effect on our business, results of operations and financial condition.

The fast track designation for pegunigalsidase alfa for the treatment of Fabry disease may not lead to a faster development or regulatory review or approval process or increase the likelihood that pegunigalsidase alfa will receive regulatory approval for the treatment of Fabry disease.

In January 2018, the FDA granted Fast Track designation to pegunigalsidase alfa for the treatment of Fabry disease. A drug that receives Fast Track designation from the FDA is eligible for certain benefits. However, fast track designation does not increase the likelihood that pegunigalsidase alfa will receive regulatory approval for the treatment of Fabry disease. Further, despite the designation, we may not experience a faster development process, review or approval compared to applications considered for approval under conventional FDA procedures. In addition, the FDA is entitled to withdraw the Fast Track designation of a drug candidate at any time. Any failure to realize the benefits of fast track designation may have a material adverse effect on our business, results of operations and financial condition.

Risks Related to Our Business

We have a limited operating history which may limit the ability of investors to make an informed investment decision.

Taliglucerase alfa is our only product with commercial approvals. The successful commercialization of our other drug candidates will require us to perform a variety of functions, including:

- continuing to perform preclinical development and clinical trials;
- participating in regulatory approval processes;
- formulating and manufacturing products; and
- conducting sales and marketing activities.

Our operations have been limited to organizing and staffing our company, acquiring, developing and securing our proprietary technology and undertaking, through third parties, preclinical trials and clinical trials of our principal drug candidates. To date, our phase III clinical trial of taliglucerase alfa is the only phase III study we have completed. These operations provide a limited basis for investors to assess our ability to commercialize our drug candidates and whether to invest in our company.

We currently depend heavily on the success of pegunigalsidase alfa. Any failure to commercialize pegunigalsidase alfa, or the experience of significant delays in doing so, will have a material adverse effect on our business, results of operations and financial condition.

We are investing a significant portion of our efforts and financial resources in the development of pegunigalsidase alfa and our ability to generate significant product revenues in the future, will depend heavily on the successful development and commercialization of pegunigalsidase alfa. The successful commercialization of pegunigalsidase alfa will depend on several factors, including the following:

- successful completion of our ongoing studies of pegunigalsidase alfa;
- Chiesi's efforts under the Chiesi Agreement;
- obtaining marketing approvals from the FDA, the EMA and other foreign regulatory authorities;
- maintaining the cGMP compliance of our manufacturing facility or establishing manufacturing arrangements with third parties;
- the successful audit of our facilities by the FDA and other foreign regulatory authorities;
- our development of a successful sales and marketing organization for pegunigalsidase in the United States;
- the availability of reimbursement to patients from healthcare payors for pegunigalsidase alfa, if approved;
- a continued acceptable safety and efficacy profile of pegunigalsidase alfa following approval; and
- other risks described in these Risk Factors.

Any failure to commercialize pegunigalsidase alfa or the experience of significant delays in doing so will have a material adverse effect on our business, results of operations and financial condition.

Any failure by us to supply drug substance to Pfizer may have a material adverse effect on our business, results of operations and financial condition.

Under the Amended Pfizer Agreement, we have agreed, for the first 10-year period after the execution of the agreement, to sell drug substance to Pfizer for the production of Elelyso, and Pfizer maintains the right to extend the supply period for up to two additional 30-month periods subject to certain terms and conditions. As part of that obligation, we agreed to substantial financial penalties in case we fail to comply with the supply commitments, or are delayed in doing so. The amounts of the penalties depend on when any such failure occurs and for how long it persists, if at all, and other considerations. Any failure to comply with the supply commitments under the Amended Pfizer Agreement may have a material adverse effect on our business, results of operations and financial condition.

Our strategy, in certain cases, is to enter into collaboration agreements with third parties to leverage our ProCellEx system to develop product candidates. If we fail to enter into these agreements or if we or the third parties do not perform under such agreements or terminate or elect to discontinue the collaboration, it could have a material adverse effect on our revenues.

Our strategy, in certain cases, is to enter into arrangements with pharmaceutical companies to leverage our ProCellEx system to develop additional product candidates. Under these arrangements, we may grant to our partners rights to license and commercialize pharmaceutical products developed under the applicable agreements, as we have done with pegunigalsidase alfa. Our partners may control key decisions relating to the development of the products and we may depend on our partners' expertise and dedication of sufficient resources to develop and commercialize our product candidates. The rights of our partners limit our flexibility in considering alternatives for the commercialization of our product candidates. If we or any of our current or future partners breach or terminate the agreements that make up such arrangements, our partners otherwise fail to conduct their obligations under such arrangements in a timely manner, there is a dispute about their obligations or if either party terminates the applicable agreement or elects not to continue the arrangement, we may not enjoy the benefits of the agreements or receive a sufficient amount of royalty or milestone payments from them, if any, which may have a material adverse effect on our business, results of operations and financial condition.

If we are unable to develop and commercialize our product candidates, our business will be adversely affected.

A key element of our strategy is to develop and commercialize a portfolio of new products in addition to taliglucerase alfa. We seek to do so through our internal research programs and strategic collaborations for the development of new products. Research programs to identify new product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- a product candidate is not capable of being produced in commercial quantities at an acceptable cost, or at all;
- a product candidate may not be accepted by patients, the medical community or third-party payors;
- competitors may develop alternatives that render our product candidates obsolete;
- the research methodology used may not be successful in identifying potential product candidates; or
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory approval.

Any failure to develop or commercialize any of our other product candidates may have a material adverse effect on our business, results of operations and financial condition.

Our ProCellEx protein expression system is based on our proprietary plant cell-based expression technology which has a limited history and any material problems with the system, which may be unforeseen, may have a material adverse effect on our business, results of operations and financial condition.

Our ProCellEx protein expression system is based on our proprietary plant cell-based expression technology. The success of our business is dependent upon the successful development and approval of our product and product candidates produced through this technology. Although taliglucerase alfa and all of our product candidates are produced through ProCellEx, the technology remains novel. Accordingly, the technology remains subject to certain risks. Mammalian cell-based protein expression systems have been used in connection with recombinant therapeutic protein expression for more than 30 years and are the subject of a wealth of data; in contrast, there is not a significant amount of data generated regarding plant cell-based protein expression and, accordingly, plant cell-based protein expression systems may be subject to unknown risks. In addition, the protein glycosilation pattern created by our protein expression system is not identical to the natural human glycosilation pattern and, although to date clinical data for up to five years, and commercial data for an additional five years, on taliglucerase alfa has not demonstrated any sign of any effect, the longer term effect of the protein glycosilation pattern created by our protein expression system on human patients, if any, is still unknown. Lastly, as our protein expression system is a new technology, we cannot always rely on existing equipment; rather, there is a need to design custom-made equipment and to generate specific growth media for the plant cells which may not be available at favorable prices, if at all. Any material problems with the technology underlying our plant cell-based protein expression system may have a material adverse effect on our business, results of operations and financial condition.

The manufacture of our products is an exacting and complex process, and if we or one of our materials suppliers encounter problems manufacturing our products, it will have a material adverse effect on our business and results of operations.

The FDA and foreign regulators require manufacturers to register manufacturing facilities. The FDA and foreign regulators also inspect these facilities to confirm compliance with cGMP or similar requirements that the FDA or foreign regulators establish. We or our materials suppliers may face manufacturing or quality control problems causing product production and shipment delays or a situation where we or the supplier may not be able to maintain compliance with the FDA's cGMP requirements, or those of foreign regulators, necessary to continue manufacturing our drug candidates. Any failure to comply with cGMP requirements or other FDA or foreign regulatory requirements could adversely affect our clinical research activities and our ability to market and develop our products. To date, our current facility has passed audits by the FDA and a number of other regulatory authorities but remains subject to audit by other foreign regulatory authorities. There can be no assurance that we will be able to comply with FDA or foreign regulatory manufacturing requirements for our current facility or any facility we may establish in the future, and the failure to so comply will have a material adverse effect on our business, results of operations and financial condition.

We rely on third parties for final processing of taliglucerase alfa, pegunigalsidase alfa and our product candidates, which exposes us to a number of risks that may delay development, regulatory approval and commercialization of taliglucerase alfa and our other product candidates or result in higher product costs.

We have no experience in the final filling and freeze drying steps of the drug manufacturing process. We have engaged a European contract manufacturer to act as an additional source of fill and finish activities for taliglucerase alfa and pegunigalsidase alfa, and have engaged other parties for our product candidates. We currently rely primarily on other third-party contractors to perform the final manufacturing steps for taliglucerase alfa on a commercial scale. We may be unable to identify manufacturers and/or replacement manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA and other regulatory authorities, as applicable, must approve any manufacturer and/or replacement manufacturer, including us, and we or any such third party manufacturer might be unable to formulate and manufacture our drug products in the volume and of the quality required to meet our clinical and commercial needs. If we engage any contract manufacturers, such manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical or commercial needs. In addition, contract manufacturers are subject to the rules and regulations of the FDA and comparable foreign regulatory authorities and face the risk that any of those authorities may find that they are not in compliance with applicable regulations. Each of these risks, if realized, could delay our clinical trials, the approval, if any, of taliglucerase alfa and our other potential drug candidates by the FDA and other regulatory authorities, or the commercialization of taliglucerase alfa and our other drug candidates or could result in higher product costs or otherwise deprive us of potential product revenues.

Developments by competitors may render our products or technologies obsolete or non-competitive which would have a material adverse effect on our business, results of operations and financial condition.

We compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Our drug candidates will have to compete with existing therapies and therapies under development by our competitors. In addition, our commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective or safer than our drug products. Other companies have drug candidates in various stages of preclinical or clinical development to treat diseases for which we are also seeking to develop drug products. Some of these potential competing drugs are further advanced in development than our drug candidates and may be commercialized earlier. Even if we are successful in developing effective drugs, our products may not compete successfully with products produced by our competitors. See Business – Competition.

Most of our competitors, either alone or together with their collaborative partners, operate larger research and development programs, staff and facilities and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- undertaking preclinical testing and human clinical trials;
- obtaining marketing approvals from the FDA and other regulatory authorities;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

These organizations also compete with us to attract qualified personnel, acquisitions and joint ventures candidates and for other collaborations. Activities of our competitors may impose unanticipated costs on our business which would have a material adverse effect on our business, results of operations and financial condition.

If we in-license drug candidates, we may delay or otherwise adversely affect the development of our existing drug candidates, which may negatively impact our business, results of operations and financial condition.

In addition to our own internally developed drug candidates, we proactively seek opportunities to in-license and advance other drug candidates that are strategic and have value-creating potential to take advantage of our development know-how and technology. If we in-license any additional drug candidate, our capital requirements may increase significantly. In addition, in-licensing additional drug candidates may place a strain on the time of our existing personnel, which may delay or otherwise adversely affect the development of our existing drug candidates or cause us to re-prioritize our drug pipeline if we do not have the necessary capital resources to develop all of our drug candidates, which may delay the development of our drug candidates and materially and adversely impact our business, results of operations and financial condition.

If we are unable to manage future growth successfully, there could be a material adverse impact on our business, results of operations and financial condition.

To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability on the part of our management to manage growth could delay the execution of our business plans or disrupt our operations. If we are unable to manage our growth effectively, we may not use our resources in an efficient manner, which may delay the development of our drug candidates and materially and adversely impact our business, results of operations and financial condition.

If we acquire companies, products or technologies, we may face integration risks and costs associated with those acquisitions that could negatively impact our business, results of operations and financial condition.

If we are presented with appropriate opportunities, we may acquire or make investments in complementary companies, products or technologies. We may not realize the anticipated benefit of any acquisition or investment. If we acquire companies or technologies, we will face risks, uncertainties and disruptions associated with the integration process, including difficulties in the integration of the operations of an acquired company, integration of acquired technology with our products, diversion of our management's attention from other business concerns, the potential loss of key employees or customers of the acquired business and impairment charges if future acquisitions are not as successful as we originally anticipate. In addition, our operating results may suffer because of acquisition-related costs or amortization expenses or charges relating to acquired intangible assets. Any failure to successfully integrate other companies, products or technologies that we may acquire may have a material adverse effect on our business and results of operations. Furthermore, we may have to incur debt or issue equity securities to pay for any additional future acquisitions or investments, the issuance of which could be dilutive to our existing stockholders.

We depend upon key employees and consultants in a competitive market for skilled personnel. If we are unable to attract and retain key personnel, it could adversely affect our ability to develop and market our products.

We are highly dependent upon the principal members of our management team, especially our President and Chief Executive Officer, Moshe Manor, as well as the Chairman of our Board of Directors, Shlomo Yanai, our other directors, our scientific advisory board members, consultants and collaborating scientists. Many of these people have been involved with us for many years and have played integral roles in our progress, and we believe that they will continue to provide value to us. A loss of any of these personnel may have a material adverse effect on aspects of our business, clinical development and regulatory programs. We have employment agreements with Moshe Manor and our other executive officers that may be terminated by us or the applicable officer at any time with varying notice periods of 60 to 90 days. Although these employment agreements generally include non-competition covenants, the applicable noncompetition provisions can be difficult and costly to monitor and enforce. The loss of any of these persons' services may adversely affect our ability to develop and market our products and obtain necessary regulatory approvals. Further, we do not maintain key-man life insurance.

We also depend in part on the continued service of our key scientific personnel and our ability to identify, hire and retain additional personnel, including marketing and sales staff. We experience intense competition for qualified personnel, and the existence of non-competition agreements between prospective employees and their former employers may prevent us from hiring those individuals or subject us to suit from their former employers. While we attempt to provide competitive compensation packages to attract and retain key personnel, many of our competitors are likely to have greater resources and more experience than we have, making it difficult for us to compete successfully for key personnel.

Our collaborations with outside scientists and consultants may be subject to restriction and change.

We work with medical experts, biologists, chemists and other scientists at academic and other institutions, and consultants who assist us in our research, development, regulatory and commercial efforts, including the members of our scientific advisory board. These scientists and consultants have provided, and we expect that they will continue to provide, valuable advice regarding our programs. These scientists and consultants are not our employees, may have other commitments that would limit their future availability to us and typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, we will be unable to prevent them from establishing competing businesses or developing competing products. For example, if a key scientist acting as a principal investigator in any of our clinical trials identifies a potential product or compound that is more scientifically interesting to his or her professional or academic interests, his or her availability to remain involved in our clinical trials could be restricted or eliminated, which may have a material adverse effect on our business, results of operations and financial condition.

Under current U.S. and Israeli law, we may not be able to enforce employees' covenants not to compete and therefore may be unable to prevent our competitors from benefiting from the expertise of some of our former employees.

We have entered into non-competition agreements with substantially all of our employees. These agreements prohibit our employees, if they cease working for us, from competing directly with us or working for our competitors for a limited period. Under current U.S. and Israeli law, we may be unable to enforce these agreements against most of our employees and it may be difficult for us to restrict our competitors from gaining the expertise our former employees gained while working for us. If we cannot enforce our employees' non-compete agreements, we may be unable to prevent our competitors from benefiting from the expertise of our former employees, which may have a material adverse effect on our business, results of operations and financial condition.

Our internal computer systems, or those used by our third-party contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our present and future contractors and consultants are vulnerable to damage from computer viruses and unauthorized access. Although to our knowledge we have not experienced any material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

If product liability claims are brought against us, it may result in reduced demand for our products and product candidates or damages that exceed our insurance coverage.

The clinical testing, marketing and use of our products and product candidates exposes us to product liability claims if the use or misuse of those products or product candidates cause injury or disease, or results in adverse effects. Use of our products or product candidates, whether in clinical trials or post approval, could result in product liability claims. We presently carry clinical trial liability insurance with coverages of up to $10.0 million per occurrence and $10.0 million in the aggregate, an amount we consider reasonable and customary. However, this insurance coverage includes various deductibles, limitations and exclusions from coverage, and in any event might not fully cover any potential claims. We may need to obtain additional clinical trial liability coverage prior to initiating additional clinical trials. We expect to obtain product liability insurance coverage before commercialization of our product candidates; however, such insurance is expensive and insurance companies may not issue this type of insurance when we need it. We may not be able to obtain adequate insurance in the future at an acceptable cost. Any product liability claim, even one that was not in excess of our insurance coverage or one that is meritless and/or unsuccessful, may adversely affect our cash available for other purposes, such as research and development, which may have a material adverse effect on our business, results of operations and financial condition. Product liability claims, even if without merit, may result in reduced demand for our products, if approved, which would have a material adverse effect on our business, results of operations and financial condition. In addition, the existence of a product liability claim could affect the market price of our common stock.

Reforms in the healthcare industry and the uncertainty associated with pharmaceutical pricing, reimbursement and related matters could adversely affect the marketing, pricing and demand for our products, if approved.

Increasing healthcare expenditures have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would result in changes in the U.S. healthcare system have been introduced or proposed in the U.S. Congress and in some state legislatures within the United States, including reductions in the pricing of prescription products and changes in the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products. Legislation passed in recent years has imposed certain changes to the way in which drugs, including our product candidates, are covered and reimbursed in the United States. For example, federal legislation and regulations have implemented new reimbursement methodologies for certain drugs, created a voluntary prescription drug benefit, Medicare Part D, and have imposed significant revisions to the Medicaid Drug Rebate Program. The PPACA imposes yet additional changes to these programs. We believe that legislation that reduces reimbursement for our product candidates could adversely impact how much or under what circumstances healthcare providers will prescribe or administer our product candidates, if approved. This could materially and adversely impact our business by reducing our ability to generate revenue, raise capital, obtain additional collaborators and market our products, if approved. In addition, we believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of pharmaceutical products, which may adversely impact product sales, upon approval, if at all.

Governments outside the United States tend to impose strict price controls and reimbursement approval policies, which may adversely affect our prospects for generating revenue.

In some countries, particularly European Union member states, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time (six to 12 months or longer) after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries with respect to any product candidate that achieves regulatory approval, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products upon approval, if at all, is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our prospects for generating revenue, if any, could be adversely affected which would have a material adverse effect on our business, results of operations and financial condition. Further, if we achieve regulatory approval of any product, we must successfully negotiate product pricing for such product in individual countries. As a result, the pricing of our product candidates, if approved, in different countries may vary widely, thus creating the potential for third-party trade in our products in an attempt to exploit price differences between countries. This third-party trade of our products could undermine our sales in markets with higher prices which could have a material adverse effect on our business, results of operations and financial condition.

Our ability to utilize net operating loss carryforwards may be limited.

Our NOLs, as of December 31, 2017, are equal to approximately $207 million, of which approximately $23 million may be restricted under Section 382 of the Internal Revenue Code of 1986, as amended, or the "Code." Section 382 of the Code imposes limitations on a corporation's ability to utilize NOLs to offset taxable income if the corporation experiences an "ownership change." In general terms, an "ownership change" may result from transactions increasing the ownership of certain stockholders in the stock of a corporation by more than 50% over a three-year period. In the event that an ownership change has occurred (including as a result of conversion of our outstanding convertible notes into shares of our common stock), or were to occur, utilization of our NOLs would be subject to an annual limitation under Section 382, which is generally the fair market value of the pre-change entity multiplied by the long-term tax exempt rate, which is published monthly by the U.S. Internal Revenue Service.

Our corporate structure may create U.S. federal income tax inefficiencies

Protalix Ltd. is our wholly-owned subsidiary and thus a controlled foreign corporation of our company for U.S. federal income tax purposes. This organizational structure may create inefficiencies, as certain types of income and investments of Protalix Ltd. that otherwise would not be currently taxable under general U.S. federal income tax principles may become taxable. These inefficiencies may require us to use more of our NOLs than we otherwise might and may result in a tax liability without a corresponding distribution from our subsidiary.

We are a holding company with no operations of our own.

We are a holding company with no operations of our own. Accordingly, our ability to conduct our operations, service any debt that we may incur in the future and pay dividends, if any, is dependent upon the earnings from the business conducted by Protalix Ltd. The distribution of those earnings or advances or other distributions of funds by our subsidiary to us, as well as our receipt of such funds, are contingent upon the earnings of Protalix Ltd. and are subject to various business considerations and U.S. and Israeli law. If Protalix Ltd. is unable to make sufficient distributions or advances to us, or if there are limitations on our ability to receive such distributions or advances, we may not have the cash resources necessary to conduct our corporate operations or service our debt which would have a material adverse effect on our business, results of operations and financial condition.

Risks Related to Our Financial Condition and Capital Requirements

Servicing our debt and settling conversion requests may require a significant amount of cash, and we may not have sufficient cash flow from our business to pay our debt. Furthermore, restrictive covenants governing our indebtedness may restrict our ability to raise additional capital.

Our ability to pay interest on, or to make any scheduled or otherwise required payment of the principal of, and settle conversion requests on our outstanding convertible notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt and make necessary expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. If we raise additional debt, it would increase our interest expense, leverage and operating and financial costs. In addition, the terms of the indentures governing our outstanding convertible notes, which are secured by certain of our material assets, including all of our intellectual property, and the agreements governing future indebtedness may restrict us from adopting any of these alternatives. We may be able to obtain amendments and waivers of such restrictions, subject to such restrictions under the terms of the applicable indenture or any subsequent indebtedness. In the event of any such default, the holders of the indebtedness could, among other things, elect to declare all amounts owed immediately due and payable, which could cause all or a large portion of our available cash flow to be used to pay such amounts and thereby reduce the amount of cash available to pursue our business plans or force us into bankruptcy or liquidation, or, with respect to our indebtedness that is secured, result in the foreclosure on the assets that secure the debt, which would force us to relinquish rights to assets that we may believe are critical to our business. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Any default on our debt will have a material adverse effect on our business, results of operations and financial condition.

A substantial majority of our authorized shares of common stock under our certificate of incorporation are either outstanding or reserved for issuance.

Our certificate of incorporation currently authorizes the issuance of 250,000,000 shares of common stock and 100,000,000 shares of preferred stock, par value $0.0001 per share, for a total of 350,000,000 shares of capital stock. As of December 31, 2017, a total of approximately 4.9 million shares of common stock are reserved for issuance upon the exercise of outstanding stock options under our 2006 Stock Incentive Plan, as amended, and a total of 2,554,075 shares of common stock are reserved for issuance in connection with future grants of stock options and/or future issuances of shares under the plan. In addition, approximately 81.6 million shares of common stock are reserved for issuance upon the conversion of our outstanding convertible notes. After taking into account the total number of shares of common stock issued and outstanding, in addition to the aggregate number of shares of common stock reserved for future issuance as described above, approximately 6.9% of our authorized shares of common stock remain available to be issued or reserved for issuance as of the date of this report.

We currently intend to solicit the approval of our stockholders at our upcoming 2018 annual meeting of stockholders to increase the number of authorized shares. Absent the approval, we are left without sufficient, authorized shares of common stock to pursue a variety of other business and financial objectives without further action of the stockholders (except when required by applicable law or regulation). As a result, a delay in securing, or a failure to secure, stockholder approval to amend our certificate of incorporation would seriously jeopardize the financial viability of the Company. Unless and until we attain the approval of our stockholders to increase the number of authorized shares, our ability to manage our capital needs is restricted which may have a material adverse effect on our business, results of operations and financial condition.

Our significant level of indebtedness could adversely affect our business, results of operations and financial condition and prevent us from fulfilling our obligations under our convertible notes and our other indebtedness.

Our outstanding convertible notes represent a significant amount of indebtedness with substantial debt service requirements. We may also incur additional indebtedness to meet future financing needs. Our substantial indebtedness could have material adverse effects on our business, results of operations and financial condition. For example, it could:

- make it more difficult for us to satisfy our financial obligations, including with respect to the convertible notes;
- result in an event of default under our outstanding convertible notes if we fail to comply with the financial and other restrictive covenants contained in agreements governing any future indebtedness, which event of default could result in all of our debt becoming immediately due and payable;
- increase our vulnerability to general adverse economic, industry and competitive conditions;
- reduce the availability of our cash flow to fund working capital, capital expenditures, acquisitions and other general corporate purposes because we will be required to dedicate a substantial portion of our cash flow from operations to the payment of principal and interest on our indebtedness;

- limit our flexibility in planning for, or reacting to, and increasing our vulnerability to changes in our business, the industry in which we operate and the general economy;
- prevent us from raising funds necessary to purchase convertible notes surrendered to us by holders upon a fundamental change (as described in the indentures governing the two series of convertible notes), which failure would result in an event of default with respect to the convertible notes;
- place us at a competitive disadvantage compared to our competitors that have less indebtedness or are less highly leveraged and that, therefore, may be able to take advantage of opportunities that our debt levels or leverage prevent us from exploiting; and
- limit our ability to obtain additional financing.

Each of these factors may have a material and adverse effect on our business, results of operations and financial condition and our ability to meet our payment obligations under the convertible notes and our other indebtedness. Our ability to make payments with respect to the convertible notes and to satisfy any other debt obligations depends on our future operating performance and our ability to generate significant cash flow in the future, which will be affected by prevailing economic conditions and financial, business, competitive, legislative and regulatory factors as well as other factors affecting our company and industry, many of which are beyond our control.

If we are unable to refinance or otherwise defease the remaining outstanding 4.5% convertible notes on or prior to June 16, 2018, we may face liquidity constraints.

If we are not able to refinance or otherwise defease all of our outstanding 4.5% convertible notes by June 16, 2018, the maturity date of the 7.5% convertible notes will be accelerated to June 15, 2018. Our ability to refinance or retire our outstanding 4.5% convertible notes will depend on our cash balance, the capital markets environment and our financial condition as well as the terms of the indenture governing the 7.5% convertible notes. The indenture governing the 7.5% convertible notes includes certain payment restrictions that may limit our ability to defease the 4.5% convertible notes. If the maturity of the 7.5% convertible notes is accelerated, we may be unable to obtain financing to pay the principal amount thereof, which will have a material adverse effect on our business, results of operations and financial condition.

We are required to comply with a number of covenants under the indenture governing our outstanding 7.5% convertible notes that could hinder our growth.

The indenture governing our 7.5% convertible notes contains a number of restrictive affirmative and negative covenants, which limit our ability to incur additional debt; exceed certain limits; pay dividends or distributions; or merge, consolidate or dispose of substantially all of our assets, including all of our intellectual property assets and other material assets securing such convertible notes. A breach of these covenants could result in default, and if such default is not cured or waived, the holders of the indebtedness could, among other things, elect to declare all amounts owed immediately due and payable, which could cause all or a large portion of our available cash flow to be used to pay such amounts and thereby reduce the amount of cash available to pursue our business plans or force us into bankruptcy or liquidation, or, result in the foreclosure on the assets that secure the debt, including all of our intellectual property assets, which would force us to relinquish rights to such assets that we may believe are critical to our business. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Any default on our debt will have a material adverse effect on our business, results of operations and financial condition.

Any conversion of our outstanding convertible notes into common stock will dilute the ownership interest of our existing stockholders, including holders who had previously converted their notes.

The conversion of some or all of our convertible notes into shares of our common stock will dilute the ownership interests of our existing stockholders. Any sales in the public market of our common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of our outstanding convertible notes may encourage short selling by market participants because the conversion of convertible notes could depress the market price of our common stock.

The fundamental change purchase feature of our outstanding convertible notes may delay or prevent an otherwise beneficial attempt to take over our company.

The terms of our outstanding convertible notes require us to offer to purchase the notes for cash in the event of a fundamental change. A non-stock takeover of our company may trigger the requirement that we purchase the notes. This feature may have the effect of delaying or preventing a takeover of our company that would otherwise be beneficial to our stockholders.

We may fail to meet the continued market capitalization-based listing requirement or other continued listing requirements of The NYSE American.

The stock market in general, and the market for life sciences companies in particular, have experienced extreme price and volume fluctuations that may have been unrelated or disproportionate to the operating performance of the listed companies. There have been dramatic fluctuations in the market prices of securities of biotechnology companies. These price fluctuations may be rapid and severe and may leave investors little time to react. Broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. Sharp drops in the market price of our common stock expose us to securities class-action litigation. The trading price of our common stock has been volatile and has been subject to wide price fluctuations in response to various factors, many of which are beyond our control. The volatility of our stock price has from time to time in recent periods affected our market capitalization. Stock price fluctuations that adversely affect our market capitalization may result in a failure to meet the continued market capitalization-based listing requirement for The NYSE American, which would require us to take steps to gain compliance with alternate listing standards or take remedial steps to bring us into compliance. A failure to maintain or regain compliance with applicable listing standards could adversely affect the liquidity of our common stock.

We currently have no significant product revenues and may need to raise additional capital to operate our business, which may not be available on favorable terms, or at all, and which will have a dilutive effect on our stockholders.

To date, we have not generated significant revenues from product sales and only minimal revenues from research and development services and other fees, other than the milestone and other payments we have received in connection with our agreements with Pfizer and Chiesi. For the years ended December 31, 2017, 2016 and 2015, we had net losses from continuing operations of $47.3 million, excluding a one-time, non-cash net charge of $38 million in connection with the remeasurement of a derivative, $29.2 million and $27.3 million, respectively, primarily as a result of expenses incurred through a combination of research and development activities and expenses supporting those activities, which includes share-based compensation expense. Drug development and commercialization is very capital intensive. We fund all of our operations and capital expenditures from the revenues we generate from licensing fees and grants, the net proceeds of equity and debt offerings and other sources. Based on our current plans, expectations and capital resources, we believe that our cash and cash equivalents will be sufficient to enable us to meet our planned operating needs for at least 12 months. However, changes may occur that could consume our existing capital at a faster rate than projected, including, among others, the cost and timing of regulatory approvals, changes in the progress of our research and development efforts and the costs of protecting our intellectual property rights.

We may need to finance our future cash needs through corporate collaboration, licensing or similar arrangements, public or private equity offerings or debt financings. If we are unable to secure additional financing in the future on acceptable terms, or at all, we may be unable to commence or complete planned preclinical and clinical trials or obtain approval of our drug candidates from the FDA and other regulatory authorities. In addition, we may be forced to reduce or discontinue product development or product licensing, reduce or forego sales and marketing efforts and other commercialization activities or forego attractive business opportunities in order to improve our liquidity and to enable us to continue operations which would have a material adverse effect on our business and results of operations. Furthermore, any additional source of financing will likely involve the issuance of our equity securities, which will have a dilutive effect on our stockholders. See also “—A substantial majority of our authorized shares of common stock under our certificate of incorporation are either outstanding or reserved for issuance.”

We are not currently profitable and delays in achieving profitability, if at all, will have a material adverse effect on our business and results of operations and could negatively impact the value of our common stock.

We may incur losses for the foreseeable future. We expect to continue to incur significant operating expenditures, and we anticipate that our expenses will increase in the foreseeable future as we:

- continue to undertake preclinical development and clinical trials for our current and new drug candidates;
- seek regulatory approvals for our drug candidates; and
- seek to license-in additional technologies.

We also may continue to experience negative cash flow for the foreseeable future as we fund our operating losses and capital expenditures. As a result, we will need to generate significant revenues in order to achieve and maintain profitability. We may not be able to generate these revenues or achieve profitability in the foreseeable future, if at all. Delays in achieving profitability, or subsequent failures to maintain profitability, will have a material adverse effect on our business and results of operations and could negatively impact the value of our common stock.

Risks Related to Investing in our Common Stock

The market price of our common stock may fluctuate significantly.

The market price of our common stock may fluctuate significantly in response to numerous factors, some of which are beyond our control, such as:

- the progress and results of our ongoing studies regarding pegunigalsidase alfa and our other product candidates;
- announcements regarding partnerships or collaborations by us or our competitors;
- purchases of alfataliglicerase in Brazil;
- developments concerning intellectual property rights and regulatory approvals;
- the announcement of new products or product enhancements by us or our competitors;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts;
- developments in the biotechnology industry; and
- general market conditions and other factors, including factors unrelated to our operating performance.

Further, stock markets in general, and the market for biotechnology companies in particular, have recently experienced price and volume fluctuations. Continued market fluctuations could result in extreme volatility in the price of our common stock, which could cause a decline in the value of our common stock. Price volatility of our common stock may be worse if the trading volume of our common stock is low. We have not paid, and do not expect to pay, any cash dividends on our common stock as any earnings generated from future operations will be used to finance our operations. As a result, investors will not realize any income from an investment in our common stock until and unless their shares are sold at a profit.

Future sales of our common stock could reduce our stock price.

If our existing stockholders or their distributees sell substantial amounts of our common stock in the public market, including shares of our common stock issuable upon conversion of our outstanding convertible notes, the market price of our common stock could decrease significantly. The perception in the public market that our existing stockholders might sell shares of common stock could also depress the trading price of our common stock. Any such sales of our common stock in the public market may affect the price of our common stock.

A substantial majority of our outstanding shares of our common stock are freely tradable without restriction or further registration under the federal securities laws, unless owned by our affiliates. In addition, we may sell additional shares of our common stock in the future to raise capital and a substantial number of shares of our common stock are reserved for issuance upon the exercise of stock options and upon conversion of our outstanding convertible notes. We cannot predict the size of future issuances, if any. At December 31, 2017, there were outstanding options to purchase common stock issued covering approximately 4.9 million shares of our common stock with a weighted average exercise price of $3.59 per share. Also at December 31, 2017, there were approximately 2.6 million shares of common stock available for future for issuance in connection with future grants of incentives under our amended 2006 stock incentive plan and approximately 81.1 million shares of common stock reserved for issuance upon conversion of our outstanding convertible notes. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities.

If securities analysts stop publishing research or reports about us or our business or if they downgrade our common stock, the market price of our common stock could decline.

The market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. We do not control these analysts. If any analyst who covers us downgrades our stock or lowers its future stock price targets or estimates of our operating results, the market price for our common stock could decline rapidly. Furthermore, if any analyst ceases to cover us, we could lose visibility in the market, which in turn could cause the market price of our common stock to decline.

Our common stock is listed to trade on more than one stock exchange, and this may result in price variations.

Our common stock is listed for trade on both the NYSE American and the TASE. Dual-listing may result in price variations between the exchanges due to a number of factors. First, our common stock is traded in U.S. dollars on the NYSE American and in NIS on the TASE. In addition, the exchanges are open for trade at different times of the day and on different days. For example, the TASE opens generally during Israeli business hours, Sunday through Thursday, while the NYSE American opens generally during U.S. business hours, Monday through Friday. The two exchanges also have differing vacation schedules. Differences in the trading schedules, as well as volatility in the exchange rate of the two currencies, among other factors, may result different trading prices for our common stock on the two exchanges. Other external influences may have different effects on the trading price of our common stock on the two exchanges.

Directors and executive officers own a significant percentage of our capital stock, and they may make decisions that an investor may not consider to be in the best interests of our stockholders.

Our directors and executive officers, principal stockholders and affiliated entities beneficially own, in the aggregate, approximately 4.0% of our common stock, as of February 15, 2018, giving effect to stock options that are held by such persons that are exercisable within such 60 days from such date. As a result, if some or all of them acted together, they would have the ability to exert substantial influence over the election of our Board of Directors and the outcome of issues requiring approval by our stockholders. This concentration of ownership may have the effect of delaying or preventing a change in control of our company that may be favored by other stockholders. This could prevent the consummation of transactions favorable to other stockholders, such as a transaction in which stockholders might otherwise receive a premium for their shares over current market prices.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and operating results. In addition, current and potential stockholders could lose confidence in our financial reporting, which could have a material adverse effect on the price of our common stock.

Effective internal controls are necessary for us to provide reliable financial reports and effectively prevent fraud. If we cannot provide reliable financial reports or prevent fraud, our results of operation could be harmed.

Section 404 of the Sarbanes-Oxley Act of 2002 requires annual management assessments of the effectiveness of our internal controls over financial reporting and a report by our independent registered public accounting firm addressing these assessments. We continuously monitor our existing internal controls over financial reporting systems to confirm that they are compliant with Section 404, and we may identify deficiencies that we may not be able to remediate in time to meet the deadlines imposed by the Sarbanes-Oxley Act. This process may divert internal resources and will take a significant amount of time and effort to complete.

If, at any time, it is determined that we are not in compliance with Section 404, we may be required to implement new internal control procedures and reevaluate our financial reporting. We may experience higher than anticipated operating expenses as well as increased independent auditor fees during the implementation of these changes and thereafter. Further, we may need to hire additional qualified personnel. If we fail to maintain the adequacy of our internal controls, as such standards are modified, supplemented or amended from time to time, we may not be able to conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act, which could result in our being unable to obtain an unqualified report on internal controls from our independent auditors. Failure to maintain an effective internal control environment could also cause investors to lose confidence in our reported financial information, which could have a material adverse effect on the price of our common stock.

Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses, divert management's attention from operating our business which could have a material adverse effect on our business.

There have been other changing laws, regulations and standards relating to corporate governance and public disclosure in addition to the Sarbanes-Oxley Act, as well as new regulations promulgated by the Commission and rules promulgated by the national securities exchanges, including the NYSE American and the NASDAQ. These new or changed laws, regulations and standards are subject to varying interpretations in many cases due to their lack of specificity, and as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. As a result, our efforts to comply with evolving laws, regulations and standards are likely to continue to result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities. Our board members, Chief Executive Officer and Chief Financial Officer could face an increased risk of personal liability in connection with the performance of their duties. As a result, we may have difficulty attracting and retaining qualified board members and executive officers, which could have a material adverse effect on our business. If our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, we may incur additional expenses to comply with standards set by regulatory authorities or governing bodies which would have a material adverse effect on our business, results of operations and financial condition.

The issuance of preferred stock or additional shares of common stock could adversely affect the rights of the holders of shares of our common stock.

Our Board of Directors is authorized to issue up to 100,000,000 shares of preferred stock without any further action on the part of our stockholders. Our Board of Directors has the authority to fix and determine the voting rights, rights of redemption and other rights and preferences of preferred stock. Currently, we have no shares of preferred stock outstanding.

Our Board of Directors may, at any time, authorize the issuance of a series of preferred stock that would grant to holders the preferred right to our assets upon liquidation, the right to receive dividend payments before dividends are distributed to the holders of common stock and the right to the redemption of the shares, together with a premium, before the redemption of our common stock, which may have a material adverse effect on the rights of the holders of our common stock. In addition, our Board of Directors, without further stockholder approval, may, at any time, issue large blocks of preferred stock. In addition, the ability of our Board of Directors to issue shares of preferred stock without any further action on the part of our stockholders may impede a takeover of our company and may prevent a transaction that is favorable to our stockholders.

Under the rules of the TASE, other than incentives under our amended 2006 stock incentive plan, we were prohibited from issuing any securities of any class or series different than the common stock that is listed on the TASE for the 12-month period immediately succeeding our initial listing, which occurred on September 6, 2010. As of the date hereof, the rules of the TASE allow us to issue securities with preferential rights with respect to dividends but such other securities may not include voting rights. The foregoing does not limit our liability to issue and grant options and warrants for the purchase of shares of our common stock.

Risks Related to the Commercialization of Drug Products

Fiocruz may not comply with the terms and conditions of the Supply and Technology Transfer Agreement.

We do not control and may not be able to effectively influence Fiocruz's ability to distribute alfataliglicerase in Brazil. If Fiocruz fails to comply with the purchase requirements of the Supply and Technology Transfer Agreement, we may terminate the agreement and market alfataliglicerase in Brazil on our own. Any failure by Fiocruz to comply with the purchase requirements of the Supply and Technology Transfer Agreement, or any other material breach by Fiocruz of the agreement, may have a material adverse effect on our business, results of operations and financial condition.

In 2017, we received a purchase order from the Brazilian MoH for the purchase of approximately $24.3 million of alfataliglicerase for the treatment of Gaucher patients in Brazil. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in the best interest of our company.

We face the risk that the Brazilian MoH may ultimately fail to purchase the amounts of alfataliglicerase for which it has already stated its intentions. In addition, we may fail to supply the intended amounts on time, if at all. We also cannot accurately predict the amount of revenues we will generate under our Supply and Technology Transfer with Fiocruz in future periods, if any. Any failure by the Brazilian MoH to purchase alfataliglicerase, by us, to supply alfataliglicerase for purchase or by Fiocruz to distribute alfataliglicerase in Brazil, or the experience of significant delays in any of the foregoing, may have a material adverse effect on our business, results of operations and financial condition.

We have limited experience in selling, marketing or distributing products and limited internal capability to do so.

We currently have very limited sales, marketing or distribution capabilities and no experience in building a sales force and distribution capabilities. We retained the marketing rights to alfataliglicerase in Brazil and, under the Chiesi Agreement, we retained the rights to market pegunigalsidase alfa in the United States, if approved. We have not licensed the marketing or commercialization rights to any of our other product candidates to any party. The commercialization of a drug product requires that we commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and with supporting distribution capabilities. Factors that may inhibit our efforts to commercialize our products directly and without strategic partners include:

- the inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to an adequate numbers of physicians or to pursuance them to prescribe our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating and sustaining an independent sales and marketing organization.

We may not be successful in recruiting or retaining the sales and marketing personnel necessary to sell alfataliglicerase or any of our products upon approval, if at all, which would have a material adverse effect on our business, results of operations and financial condition.

We may enter into distribution arrangements and marketing alliances for certain products and any failure to successfully identify and implement these arrangements on favorable terms, if at all, may impair our ability to commercialize our product candidates.

We may need to establish a sales force to market alfataliglicerase or our our product candidates, if approved. We do not anticipate having the resources in the foreseeable future to develop global sales and marketing capabilities for all of the products we are developing. We may elect to pursue arrangements regarding the sales and marketing and distribution of alfataliglicerase or one or more of our product candidates, and our future revenues may depend, in part, on our ability to enter into and maintain arrangements with other companies having sales, marketing and distribution capabilities and the ability of such companies to successfully market and sell any such products. Any failure to enter into such arrangements and marketing alliances on favorable terms, if at all, could delay or impair our ability to commercialize our product candidates and could increase our costs of commercialization. Any use of distribution arrangements and marketing alliances to commercialize our product candidates will subject us to a number of risks, including the following:

- we may be required to relinquish important rights to our products or product candidates;
- we may not be able to control the amount and timing of resources that our distributors or collaborators may devote to the commercialization of our product candidates;
- our distributors or collaborators may experience financial difficulties;
- our distributors or collaborators may not devote sufficient time to the marketing and sales of our products; and
- business combinations or significant changes in a collaborator's business strategy may adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement.

We may need to enter into additional co-promotion arrangements with third parties where our own sales force is neither well situated nor large enough to achieve maximum penetration in the market. We may not be successful in entering into any co-promotion arrangements, and the terms of any co-promotion arrangements we enter into may not be favorable to us.

If physicians, patients, third party payors and others in the medical community do not accept and use taliglucerase alfa, or any of our other product candidates, if approved, our ability to generate revenue from product sales will be materially impaired.

Physicians and patients, and other healthcare providers, may not accept and use any of our products or any product candidates, if approved, for marketing. Future acceptance and use of any of our products or any product candidates, if approved, will depend upon a number of factors including:

- perceptions by physicians, patients, third party payors and others in the medical community about the safety and effectiveness of taliglucerase alfa or our other drug candidates;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the prevalence and severity of any side effects, including any limitations or warnings contained in our products' approved labeling;
- pharmacological benefits of taliglucerase alfa or our other drug candidates relative to competing products and products under development;
- the efficacy and potential advantages relative to competing products and products under development;
- relative convenience and ease of administration;
- effectiveness of education, marketing and distribution efforts by us and our licensees and distributors, if any;
- publicity concerning taliglucerase alfa or our other drug candidates or competing products and treatments;
- coverage and reimbursement of our products by third party payors; and
- the price for our products and competing products.

A lack of market acceptance of taliglucerase alfa in Brazil, or globally for any of our other products candidates, if approved, would have a material adverse effect on our business, results of operations and financial condition.

If the market opportunities for other product candidates, and for taliglucerase alfa in Brazil, are smaller than we believe they are, our revenues may be adversely affected and our business may suffer.

To date, our development efforts have focused mainly on relatively rare disorders with small patient populations, in particular Gaucher disease and Fabry disease. Currently, most reported estimates of the prevalence of these diseases are based on studies of small subsets of the population of specific geographic areas, which are then extrapolated to estimate the prevalence of the diseases in the broader world population. As new studies are performed, the estimated prevalence of these diseases may change. There can be no assurance that the prevalence of Gaucher disease or Fabry disease in the study populations, particularly in these newer studies, accurately reflect the prevalence of these diseases in the broader world population. If the market opportunities for our current product candidates are smaller than we believe they are, our revenues may be adversely affected and our business may suffer.

Coverage and reimbursement may not be available for alfataliglicerase or any of our other product candidates, if approved, in all territories which could diminish our sales or affect our ability to sell alfataliglicerase or any other products profitably.

Market acceptance and sales of alfataliglicerase in Brazil, or for any of our other product candidates globally, if approved, will depend on coverage and reimbursement policies in the countries in which they are approved for sale. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Obtaining reimbursement approval for an approved product from governments and other third party payors is a time consuming and costly process that requires our collaborators or us, as the case may be, to provide supporting scientific, clinical and cost-effectiveness data for the use of our products, if and when approved, to every payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement or we might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of approved products, if any, to such payors' satisfaction. Such studies might require our collaborators or us to commit a significant amount of management time and financial and other resources. Even if a payor determines that an approved product is eligible for reimbursement, the payor may impose coverage limitations that preclude payment for some uses that are approved by the FDA or other regulatory authorities. In addition, full reimbursement may not be available for high priced products. Moreover, eligibility for coverage does not imply that any approved product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Also, limited reimbursement amounts may reduce the demand for, or the price of, our product candidates. Except with respect to taliglucerase alfa, we have not commenced efforts to have our product candidates covered and reimbursed by government or third-party payors. If coverage and reimbursement are not available or are available only to limited levels, the sales of our products, if approved may be diminished or we may not be able to sell such products profitably.

We and our collaborating partners may be subject, directly or indirectly, to federal and state healthcare fraud and abuse and false claims laws and regulations. If we or our collaborating partners are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

All marketing activities associated with drug products that are approved for sale in the United States, if any, will be, directly or indirectly through our customers, subject to numerous federal and state laws governing the marketing and promotion of pharmaceutical products in the United States, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act and HIPAA. These laws may adversely impact, among other things, our proposed sales, marketing and education programs.

The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of co-payments and deductibles, ownership interests and providing anything at less than its fair market value. The reach of the Anti-Kickback Statute was also broadened by the PPACA which, among other things, amends the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b, effective March 23, 2010. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. The federal Anti-Kickback Statute is broad, and despite a series of narrow safe harbors, prohibits many arrangements and practices that are lawful in businesses outside of the healthcare industry. Penalties for violations of the federal Anti-Kickback Statute include criminal penalties and civil sanctions such as fines, imprisonment and possible exclusion from Medicare, Medicaid and other state or federal healthcare programs. Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs, and do not contain identical safe harbors.

The federal False Claims Act imposes liability on any person who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The "qui tam" provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payer and not merely a federal healthcare program. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties of $5,500 to $11,000 for each separate false claim.

HIPAA created several new federal crimes, including health care fraud, and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private third-party payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services.

We are unable to predict whether we could be subject to actions under any of these or other fraud and abuse laws, or the impact of such actions. Moreover, to the extent that taliglucerase alfa, or any of our products, if approved for marketing, will be sold in a foreign country, we and our future collaborators, may be subject to similar foreign laws and regulations. If we or any of our future collaborators are found to be in violation of any of the laws described above and other applicable state and federal fraud and abuse laws, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare reimbursement programs and the curtailment or restructuring or our operations, any of which could have a material adverse effect on our business, results of operations and financial condition.

Risks Related to Intellectual Property Matters

The intellectual property and assets owned by our subsidiaries are subject to security agreements that secure our payment and other obligations under our 7.5% convertible notes, and our subsidiaries have guaranteed all of those obligations.

In connection with the issuance of our 7.5% convertible notes, we entered into security agreements pursuant to which our subsidiaries provided first priority security interests in all of their assets, which consist of all of our intellectual property and other material assets. The security agreements secure certain payment, indemnification and other obligations under the 7.5% convertible notes. If we were to default on certain of ours obligations, or in certain other circumstances generally related to a bankruptcy or insolvency, holders of our outstanding 7.5% convertible notes could seek to foreclose on the collateral under the security agreements to obtain satisfaction our obligations, and our business could be materially and adversely impacted, which would in turn materially and adversely impact our business, results of operations and financial condition.

Furthermore, in connection with the issuance of the 7.5% convertible notes, our subsidiaries guaranteed all of our obligations under the indenture governing such convertible notes. If we were to default on our obligations under the indenture, the holders could require our subsidiaries to satisfy all of those obligations under the guarantees.

If we fail to adequately protect or enforce our intellectual property rights or secure rights to third party patents, the value of our intellectual property rights would diminish and our business, competitive position and results of operations would suffer.

As of December 31, 2017, we had 58 pending patent applications of which eight are joint pending patent applications with a third party and one is an-in licensed application. However, the filing of a patent application does not mean that we will be issued a patent, or that any patent eventually issued will be as broad as requested in the patent application or sufficient to protect our technology. Any modification required to a current patent application may delay the approval of such patent application which would have a material adverse effect on our business, results of operations and financial condition. In addition, there are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications to not be granted, including known or unknown prior art, deficiencies in the patent application or the lack of originality of the technology. Our competitive position and future revenues will depend in part on our ability and the ability of our licensors and collaborators to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing the proprietary rights of third parties. We have filed U.S. and international patent applications for process patents, as well as composition of matter patents, for taliglucerase alfa and other product candidates. However, we cannot predict:

- the degree and range of protection any patents will afford us against competitors and those who infringe upon our patents, including whether third parties will find ways to invalidate or otherwise circumvent our licensed patents;
- if and when patents will issue;
- whether or not others will obtain patents claiming aspects similar to those covered by our licensed patents and patent applications; or
- whether we will need to initiate litigation or administrative proceedings, which may be costly, and whether we win or lose.

As of December 31, 2017, we held, or had license rights to, 69 patents. If patent rights covering our products or technologies are not sufficiently broad, they may not provide us with sufficient proprietary protection or competitive advantages against competitors with similar products and technologies. Furthermore, if the U.S. Patent and Trademark Office or foreign patent offices issue patents to us or our licensors, others may challenge the patents or circumvent the patents, or the patent office or the courts may invalidate the patents. Thus, any patents we own or license from or to third parties may not provide any protection against our competitors and those who infringe upon our patents.

Furthermore, the life of our patents is limited. The patents we hold, and the patents that may be issued in the future based on patent applications from the patent families, relating to our ProCellEx protein expression system are expected to expire between 2017 and 2025.

We rely on confidentiality agreements that could be breached and may be difficult to enforce which could have a material adverse effect on our business and competitive position.

Our policy is to enter agreements relating to the non-disclosure of confidential information with third parties, including our contractors, consultants, advisors and research collaborators, as well as agreements that purport to require the disclosure and assignment to us of the rights to the ideas, developments, discoveries and inventions of our employees and consultants while we employ them. However, these agreements can be difficult and costly to enforce. Moreover, to the extent that our contractors, consultants, advisors and research collaborators apply or independently develop intellectual property in connection with any of our projects, disputes may arise as to the proprietary rights to the intellectual property. If a dispute arises, a court may determine that the right belongs to a third party, and enforcement of our rights can be costly and unpredictable. In addition, we rely on trade secrets and proprietary know-how that we seek to protect in part by confidentiality agreements with our employees, contractors, consultants, advisors and others. Despite the protective measures we employ, we still face the risk that:

- these agreements may be breached;
- these agreements may not provide adequate remedies for the applicable type of breach; or
- our trade secrets or proprietary know-how will otherwise become known.

Any breach of our confidentiality agreements or our failure to effectively enforce such agreements may have a material adverse effect on our business and competitive position.

If we infringe the rights of third parties we could be prevented from selling products, forced to pay damages and required to defend against litigation which could result in substantial costs and may have a material adverse effect on our business, results of operations and financial condition.

We have not received to date any claims of infringement by any third parties. However, as our drug candidates progress into clinical trials and commercialization, if at all, our public profile and that of our drug candidates may be raised and generate such claims. Defending against such claims, and occurrence of a judgment adverse to us, could result in unanticipated costs and may have a material adverse effect on our business and competitive position. If our products, methods, processes and other technologies infringe the proprietary rights of other parties, we may incur substantial costs and we may have to:

- obtain licenses, which may not be available on commercially reasonable terms, if at all;
- redesign our products or processes to avoid infringement;
- stop using the subject matter claimed in the patents held by others, which could cause us to lose the use of one or more of our drug candidates;
- defend litigation or administrative proceedings that may be costly whether we win or lose, and which could result in a substantial diversion of management resources; or
- pay damages.

Any costs incurred in connection with such events or the inability to sell our products may have a material adverse effect on our business, results of operations and financial condition.

If we cannot meet requirements under our license agreements, we could lose the rights to our products, which could have a material adverse effect on our business.

We depend on licensing agreements with third parties to maintain the intellectual property rights to certain of our product candidates. Our license agreements require us to make payments and satisfy performance obligations in order to maintain our rights under these agreements. All of these agreements last either throughout the life of the patents that are the subject of the agreements, or with respect to other licensed technology, for a number of years after the first commercial sale of the relevant product.

In addition, we are responsible for the cost of filing and prosecuting certain patent applications and maintaining certain issued patents licensed to us. If we do not meet our obligations under our license agreements in a timely manner, we could lose the rights to our proprietary technology which could have a material adverse effect on our business, results of operations and financial condition.

Risks Relating to Our Operations in Israel

Potential political, economic and military instability in the State of Israel, where the majority of our senior management and our research and development facilities are located, may adversely affect our results of operations.

Our executive office and operations are located in the State of Israel. Accordingly, political, economic and military conditions in Israel directly affect our business. Since the State of Israel was established in 1948, a number of armed conflicts have occurred between Israel and its Arab neighbors. Any hostilities involving Israel or the interruption or curtailment of trade between Israel and its present trading partners, or a significant downturn in the economic or financial condition of Israel, could affect adversely our operations and product development. Although Israel has entered into various agreements with Egypt, Jordan and the Palestinian Authority, there have been times since October 2000 when Israel has experienced an increase in unrest and terrorist activity. The establishment in 2006 of a government in the Gaza Strip by representatives of the Hamas militant group has created additional unrest and uncertainty in the region. Starting in December 2008, for approximately three weeks, Israel engaged in an armed conflict with Hamas in the Gaza Strip. Armed conflicts have taken place between Israel and Hamas in the Gaza Strip in 2008, 2012 and 2014. Our facilities in northern Israel are in range of rockets that were fired from Lebanon into Israel during a 2006 war with the Hizbollah in Lebanon, and suffered minimal damages during one of the rocket attacks. Our insurance policies do not cover us for the damages incurred in connection with these conflicts or for any resulting disruption in our operations. The Israeli government, as a matter of law, provides coverage for the reinstatement value of direct damages that are caused by terrorist attacks or acts of war; however, the government may cease providing such coverage or the coverage might not be enough to cover potential damages. If our facilities are damaged as a result of hostile action, our operations may be materially adversely affected.

In addition to the foregoing, since the end of 2010, numerous acts of protest and civil unrest have taken place in several countries in the Middle East and North Africa, many of which involved significant violence. Civil unrest in Egypt, which borders Israel, has resulted in significant changes to the country’s government. There is currently a civil war in Syria, also bordering Israel, and Israel has been hit by rockets and mortars originating from Syria. The ultimate effect of these developments on the political and security situation in the Middle East and on Israel’s position within the region is not clear at this time.

Our operations may be disrupted by the obligations of our personnel to perform military service which could have a material adverse effect on our business.

Many of our male employees in Israel, including members of senior management, are obligated to perform up to one month (in some cases more) of annual military reserve duty until they reach the age of 45 and, in the event of a military conflict, could be called to active duty. Our operations could be disrupted by the absence of a significant number of our employees related to military service or the absence for extended periods of military service of one or more of our key employees. A disruption could have a material adverse effect on our business.

Because a certain portion of our expenses is incurred in New Israeli Shekels, our results of operations may be seriously harmed by currency fluctuations and inflation.

We report our financial statements in U.S. dollars, our functional currency. Although most of our expenses are incurred in U.S. dollars, we pay a portion of our expenses in New Israeli Shekels, or NIS, and as a result, we are exposed to risk to the extent that the inflation rate in Israel exceeds the rate of devaluation of the NIS in relation to the U.S. dollar or if the timing of these devaluations lags behind inflation in Israel. In that event, the U.S. dollar cost of our operations in Israel will increase and our U.S. dollar-measured results of operations will be adversely affected. To the extent that the value of the NIS increases against the dollar, our expenses on a dollar cost basis increase. Our operations also could be adversely affected if we are unable to guard against currency fluctuations in the future. To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rate of the U.S. dollar against the NIS. These measures, however, may not adequately protect us from material adverse effects.

The tax benefits available to us require that we meet several conditions and may be terminated or reduced in the future, which would increase our taxes.

We are able to take advantage of tax exemptions and reductions resulting from the "Approved Enterprise" status of our facilities in Israel. To remain eligible for these tax benefits, we must continue to meet certain conditions, including making specified investments in property and equipment, and financing at least 30% of such investments with share capital. If we fail to meet these conditions in the future, the tax benefits would be canceled and we may be required to refund any tax benefits we already have enjoyed. These tax benefits are subject to investment policy by the Investment Center and may not be continued in the future at their current levels or at any level. In recent years the Israeli government has reduced the benefits available and has indicated that it may further reduce or eliminate some of these benefits in the future. The termination or reduction of these tax benefits or our inability to qualify for additional "Approved Enterprise" approvals may increase our tax expenses in the future, which would reduce our expected profits and adversely affect our business and results of operations. Additionally, if we increase our activities outside of Israel, for example, by future acquisitions, such increased activities generally may not be eligible for inclusion in Israeli tax benefit programs.

The Israeli government grants we have received for certain research and development expenditures restrict our ability to manufacture products and transfer technologies outside of Israel and require us to satisfy specified conditions. If we fail to satisfy these conditions, we may be required to refund grants previously received together with interest and penalties which could have a material adverse effect on our business and results of operations.

Our research and development efforts have been financed, in part, through grants that we have received from NATI. We, therefore, must comply with the requirements of the Research Law. Under the Research Law we are prohibited from manufacturing products developed using these grants outside of the State of Israel without special approvals, although the Research Law does enable companies to seek prior approval for conducting manufacturing activities outside of Israel without being subject to increased royalties. We may not receive the required approvals for any proposed transfer of manufacturing activities. Even if we do receive approval to manufacture products developed with government grants outside of Israel, we may be required to pay an increased total amount of royalties (possibly up to 300% of the grant amounts plus interest), depending on the manufacturing volume that is performed outside of Israel, as well as at a possibly increased royalty rate. This restriction may impair our ability to outsource manufacturing or engage in similar arrangements for those products or technologies.

Additionally, under the Research Law, Protalix Ltd. is prohibited from transferring NATI-financed technologies and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the approval of NATI Council or the Research Committee. Protalix Ltd. may not receive the required approvals for any proposed transfer and, if received, Protalix Ltd. may be required to pay NATI a portion of the consideration that it receives upon any sale of such technology by a non-Israeli entity. The scope of the support received, the royalties that Protalix Ltd. has already paid to NATI, the amount of time that has elapsed between the date on which the know-how was transferred and the date on which NATI grants were received and the sale price and the form of transaction will be taken into account in order to calculate the amount of the payment to NATI. Approval of the transfer of technology to residents of the State of Israel is required, and may be granted in specific circumstances only if the recipient abides by the provisions of applicable laws, including the restrictions on the transfer of know-how and the obligation to pay royalties. No assurance can be made that approval to any such transfer, if requested, will be granted.

These restrictions may impair our ability to sell our technology assets or to outsource manufacturing outside of Israel. The restrictions will continue to apply for a certain period of time even after we have repaid the full amount of royalties payable for the grants. For the years ended December 31, 2015, 2016 and 2017, we recorded grants totaling $4.9 million, $5.8 million and $3.3 million from NATI, respectively. The grants represent 19.5%, 19.1% and 10.4%, respectively, of our gross research and development expenditures for the years ended December 31, 2015, 2016 and 2017. If we fail to satisfy the conditions of the Research Law, we may be required to refund certain grants previously received together with interest and penalties, and may become subject to criminal charges, any of which could have a material adverse effect on our business, results of operations and financial condition.

Investors may have difficulties enforcing a U.S. judgment, including judgments based upon the civil liability provisions of the U.S. federal securities laws against us, our executive officers and most of our directors or asserting U.S. securities laws claims in Israel.

All of our directors and executive officers are residents of Israel, and accordingly, most of their assets and our assets are located outside the United States. Service of process upon our non-U.S. resident directors and officers and enforcement of judgments obtained in the United States against us, some of our directors and executive officers may be difficult to obtain within the United States. We have been informed by our legal counsel in Israel that investors may find it difficult to assert claims under U.S. securities laws in original actions instituted in Israel or obtain a judgment based on the civil liability provisions of U.S. federal securities laws against us, our officers and our directors. Israeli courts may refuse to hear a claim based on a violation of U.S. securities laws against us or our officers and directors because Israel is not the most appropriate forum to bring such a claim. In addition, even if an Israeli court agrees to hear a claim, it may determine that Israeli law and not U.S. law is applicable to the claim. If U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact which can be a time-consuming and costly process. Certain matters of procedure will also be governed by Israeli law. There is little binding case law in Israel addressing the matters described above.

Israeli courts might not enforce judgments rendered outside Israel which may make it difficult to collect on judgments rendered against us. Subject to certain time limitations, an Israeli court may declare a foreign civil judgment enforceable only if it finds that:

- the judgment was rendered by a court which was, according to the laws of the state of the court, competent to render the judgment;
- the judgment may no longer be appealed;
- the obligation imposed by the judgment is enforceable according to the rules relating to the enforceability of judgments in Israel and the substance of the judgment is not contrary to public policy; and
- the judgment is executory in the state in which it was given.

Even if these conditions are satisfied, an Israeli court will not enforce a foreign judgment if it was given in a state whose laws do not provide for the enforcement of judgments of Israeli courts (subject to exceptional cases) or if its enforcement is likely to prejudice the sovereignty or security of the State of Israel. An Israeli court also will not declare a foreign judgment enforceable if:

- the judgment was obtained by fraud;
- there is a finding of lack of due process;
- the judgment was rendered by a court not competent to render it according to the laws of private international law in Israel;
- the judgment is at variance with another judgment that was given in the same matter between the same parties and that is still valid; or
- at the time the action was brought in the foreign court, a suit in the same matter and between the same parties was pending before a court or tribunal in Israel.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our manufacturing facility and executive offices are located in Carmiel, Israel. The facilities currently contain approximately 20,000 sq/ft of manufacturing space and additional 48,000 sq/ft of laboratory, warehouse and office space and are leased at a rate of approximately $65,000 per month. In addition, we are entitled to use an additional 13,000 sq/ft in the same facility, which we intend to utilize in connection with an anticipated expansion of our manufacturing facilities. Our facilities are equipped with the requisite laboratory services required to conduct our business, and we believe that the existing facilities are adequate to meet our needs for the foreseeable future. Our original lease for the facility was in effect until 2016, at which time we extended the term until 2021. We retain two addition options to extend the term for a five-year period, for an aggregate of 10 additional years. Upon the exercise of each remaining option to extend the term of the lease, if any, the then current base rent shall be increased by 10%.

Item 3. Legal Proceedings

We are not involved in any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is traded on the NYSE American under the symbol "PLX." Our common stock is also listed on the TASE under the symbol "PLX." The following table sets forth the quarterly high and low closing prices for our common stock on the NYSE American.

	Price Range	
	High	Low
Fourth Quarter 2017	$ 0.83	$ 0.57
Third Quarter 2017	$ 0.84	$ 0.49
Second Quarter 2017	$ 1.34	$ 0.78
First Quarter 2017	$ 1.44	$ 0.41
Fourth Quarter 2016	$ 0.57	$ 0.29
Third Quarter 2016	$ 0.67	$ 0.56
Second Quarter 2016	$ 0.90	$ 0.64
First Quarter 2016	$ 1.02	$ 0.76

These quotations reflect prices between dealers and do not include retained mark-ups, mark-downs and commissions and may not necessarily represent actual transactions. There were approximately 80 holders of record of our common stock at March 1, 2018. A substantially greater number of holders of our common stock are "street name" or beneficial holders, whose shares are held of record by banks, brokers and other financial institutions. To date, we have not declared or paid any cash dividends on our common stock. We do not anticipate paying any dividends on our common stock in the foreseeable future.

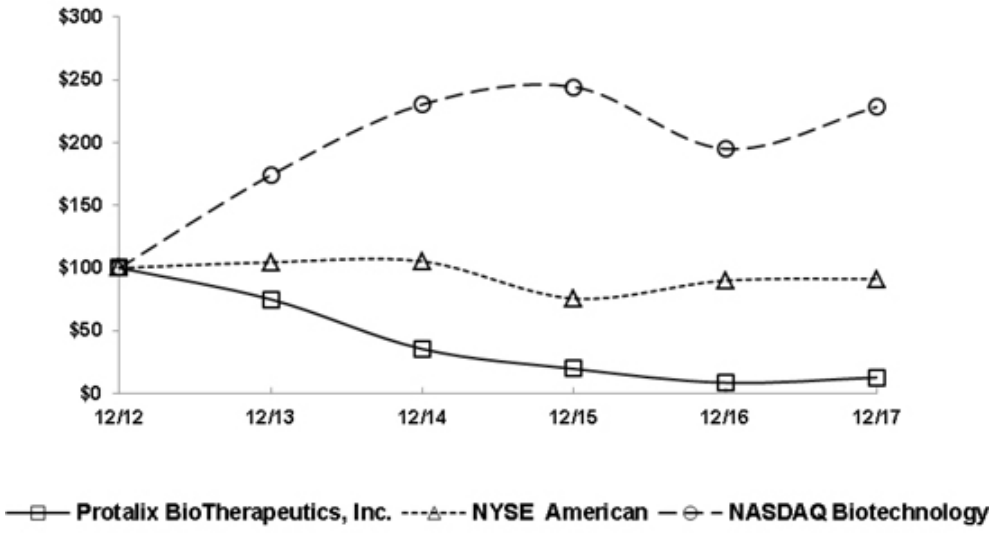
STOCK PERFORMANCE GRAPH

The following graph compares the cumulative total shareholder return data for our common stock from December 31, 2012 through December 31, 2017 to the cumulative return over such time period of (i) The NYSE American Index and (ii) The Nasdaq Biotechnology Index. The graph assumes an investment of $100 on December 31, 2012 in each of our common stock, the stocks comprising the NYSE American Index and the stocks comprising the Nasdaq Biotechnology Index, including dividend reinvestment, if any.

The stock price performance shown on the graph below represents historical price performance and is not necessarily indicative of any future stock price performance. Notwithstanding anything to the contrary set forth in any of our previous filings under the Securities Act or the Exchange Act, which might incorporate future filings made by us under those statutes, this Stock Performance Graph will not be incorporated by reference into any of those prior filings, nor will such report or graph be incorporated by reference into any future filings made by us under those Acts.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

Among Protalix BioTherapeutics, Inc., the NYSE American Index
and the NASDAQ Biotechnology Index



*$100 invested on 12/31/12 in stock or index, including reinvestment of dividends. Fiscal year ending December 31.

Item 6. Selected Financial Data

The selected consolidated financial data below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. The selected consolidated statements of operations data for the years ended December 31, 2017, 2016 and 2015 and the selected consolidated balance sheet data as of December 31, 2017 and 2016, are derived from the audited consolidated financial statements included elsewhere in this Annual Report. The statement of operations data for the years ended December 31, 2014 and 2013 and the balance sheet data as of December 31, 2015, 2014 and 2013 are derived from audited financial statements not included in this Annual Report. We adopted, retrospectively, ASU 2014-08 during 2015 regarding discontinued operations which resulted in the reclassification of prior year amounts. The historical results presented below are not necessarily indicative of future results.

	Year Ended December 31,				
	2013	**2014**	**2015**	**2016**	**2017**
	(in thousands, except share and per share amounts)				
Consolidated Statement of Operations Data:					
Revenues	$ -	$ 3,523	$ 4,364	$ 9,199	$ 19,242
Cost of revenues	-	630	730	8,398	15,231
Gross profit	-	2,893	3,634	801	4,011
Research and development expenses, net	26,012	22,224	20,025	24,608	28,834
Selling, general and administrative expenses	8,051	9,228	7,279	9,356	11,530
Financial income (expenses), net	(674)	(4,739)	(3,612)	3,987	(48,923)
Loss from continuing operations	$ 34,737	$ 33,298	$ 27,282	$ 29,176	$ (85,276)
(Loss) income from discontinued operations	6,947	3,355	85,319	(189)	
Net income (loss) for the year	(27,790)	(29,943)	58,037	(29,365)	(85,276)
Net income (loss) per share of common stock, basic and diluted:					
Loss from continuing operations	$ (0.38)	$ (0.36)	$ (0.29)	$ (0.29)	$ (0.65)
(Loss) income from discontinued operations	0.08	0.04	0.90	(0.00)	
Net (loss) income per share of common stock	(0.30)	(0.32)	0.61	(0.29)	(0.65)
Weighted average number of shares of common stock used in computing net loss per share of common stock	92,368,138	92,891,846	94,922,390	101,387,704	131,085,958
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 86,398	$ 54,767	$ 76,374	$ 63,281	$ 51,163
All other assets	26,935	23,590	20,879	18,966	21,051
Total assets	113,192	78,357	97,253	82,247	72,214
Current liabilities	26,696	64,354	11,235	66,212	22,752
Long term convertible notes	67,048	67,351	67,796	19,343	46,267
Total liabilities	140,138	133,958	86,380	92,204	103,507
Total stockholders' equity (capital deficiency)	(26,946)	(55,601)	10,873	(9,957)	(31,293)

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis, particularly with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read "Risk Factors" in Item 1A of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins based on our proprietary ProCellEx® protein expression system. We developed our first commercial drug product, Elelyso®, using our ProCellEx system and we are now focused on utilizing the system to develop a pipeline of proprietary, clinically superior versions of recombinant therapeutic proteins that primarily target large, established pharmaceutical markets and that in most cases rely upon known biological mechanisms of action. With our experience to date, we believe ProCellEx will enable us to develop additional proprietary recombinant proteins that are therapeutically superior to existing recombinant proteins currently marketed for the same indications including applying the unique properties of our ProCellEx system for the oral delivery of therapeutic proteins.

On October 19, 2017, Protalix Ltd., our wholly-owned subsidiary, and Chiesi entered into the Chiesi Agreement pursuant to which Chiesi was granted an exclusive, license for all markets outside of the United States to commercialize pegunigalsidase alfa. Pegunigalsidase alfa is our chemically modified version of the recombinant protein alpha-Galactosidase-A protein that is currently being evaluated in phase III clinical trials for the treatment of Fabry disease. Under the terms and conditions of the Chiesi Agreement, Protalix Ltd. retained the right to commercialize pegunigalsidase alfa in the United States. Under the Chiesi Agreement, Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to $25 million in development costs, capped at $10 million per year. Protalix Ltd. is also eligible to receive an additional up to $320 million, in the aggregate, in regulatory and commercial milestone payments. Protalix Ltd. agreed to manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi is required to make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa. The Chiesi Agreement also provides for reimbursement by Chiesi of certain costs to be incurred by Protalix Ltd.

In December 2017, the European Commission granted Orphan Drug Designation for pegunigalsidase alfa for the treatment of Fabry disease. The designation was granted after the COMP issued a positive opinion supporting the designation noting that we had established that there was medically plausible evidence that pegunigalsidase alfa will provide a significant benefit over existing approved therapies in the European Union for the treatment of Fabry disease. The COMP cited clinical and non-clinical justifications we provided to establish the significant benefit of pegunigalsidase alfa, noting that the COMP considered the justifications to constitute a clinically relevant advantage. Orphan Drug Designation for pegunigalsidase alfa qualifies Protalix Ltd. for access to a centralized marketing authorization procedure, including applications for inspections and for protocol assistance. If the orphan drug designation is maintained at the time pegunigalsidase alfa is approved for marketing in the European Union, if at all, we expect that PRX-102 will benefit from 10 years of market exclusivity within the European Union. The market exclusivity will not have any effect on Fabry disease treatments already approved at that time.

In January 2018, the FDA granted Fast Track designation to PRX-102. Fast Track designation is a process designed to facilitate the development and expedite the review of drugs and vaccines for serious conditions that fill an unmet medical need.

On May 1, 2012, the FDA approved for sale our first commercial product, taliglucerase alfa for injection, an ERT for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease. Subsequently, taliglucerase alfa was approved for marketing by the regulatory authorities of other countries. Taliglucerase alfa is called alfataliglicerase in Brazil and certain other Latin American countries, where it is marketed under the name alfataliglicerase. Taliglucerase alfa is marketed under the name Elelyso in other territories.

Since its approval by the FDA, taliglucerase alfa has been marketed by Pfizer, as provided in the Pfizer Agreement. In October 2015, we entered into the Amended Pfizer Agreement which amends and restates the Pfizer Agreement in its entirety. Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso in exchange for a cash payment equal to $36.0 million. As part of the sale, we agreed to transfer our rights to Elelyso in Israel to Pfizer, while gaining full rights to Elelyso in Brazil. We will continue to manufacture drug substance for Pfizer, subject to certain terms and conditions. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all revenues globally for Elelyso, excluding Brazil, where we are responsible for all expenses and retain all revenues.

For the first 10-year period after the execution of the Amended Pfizer Agreement, we have agreed to sell drug substance to Pfizer for the production of Elelyso, and Pfizer maintains the right to extend the supply period for up to two additional 30-month periods subject to certain terms and conditions. Any failure to comply with our supply commitments may subject us to substantial financial penalties, which will have a material adverse effect on our business, results of operations and financial condition. The Amended Pfizer Agreement also includes customary provisions regarding cooperation for regulatory matters, patent enforcement, termination, indemnification and insurance requirements.

On June 18, 2013, we entered into the Brazil Agreement with Fiocruz, an arm of the Brazilian MoH, for taliglucerase alfa.

In 2017, we received a purchase order from the Brazilian MoH for the purchase of approximately $24.3 million of alfataliglicerase for the treatment of Gaucher patients in Brazil. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in the best interest of our company.

We are developing an innovative product pipeline using our ProCellEx protein expression system. Our product pipeline currently includes, among other candidates:

(1) pegunigalsidase alfa, or PRX-102, a therapeutic protein candidate for the treatment of Fabry disease, a rare, genetic lysosomal disorder in humans, currently in an ongoing phase III clinical trial.

(2) alidornase alfa, or PRX-110, a proprietary plant cell recombinant human Deoxyribonuclease 1 under development for the treatment of CF, to be administered by inhalation. We recently completed a phase IIa efficacy and safety study of alidornase alfa for the treatment of CF.

(3) OPRX-106, our oral antiTNF product candidate which is being developed as an orally-delivered anti-inflammatory treatment using plant cells as a natural capsule for the expressed protein. We expect to release final data generated in our phase II clinical trial of OPRX-106 for the treatment of ulcerative colitis by the end of March, 2018.

Except for the rights to commercialize taliglucerase alfa worldwide (other than Brazil), which we licensed to Pfizer, and the rights to pegunigalsidase alfa Chiesi outside the United States, which we licensed to Chiesi, we hold the worldwide commercialization rights to all of our proprietary development candidates. In addition, we continuously evaluate potential strategic marketing partnerships as well as collaboration programs with biotechnology and pharmaceutical companies and academic research institutes.

Critical Accounting Policies

Our significant accounting policies are more fully described in Note 1 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K. We believe that the accounting policies below are critical for one to fully understand and evaluate our financial condition and results of operations.

The discussion and analysis of our financial condition and results of operations is based on our financial statements, which we prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate such estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Functional Currency

The currency of the primary economic environment in which our operations are conducted is the U.S. dollar. All of our revenues are derived in dollars. In addition, most of our expenses and capital expenditures are incurred in dollars, and the major source of our financing has been provided in dollars.

Revenues

Our primary sources of revenues include our sales of taliglucerase alfa in Brazil and of drug substance to Pfizer under our Amended Pfizer Agreement. We recognize revenue when the earnings process is complete, which is when revenue is realized or realizable and earned, there is persuasive evidence a revenue arrangement exists, delivery of goods or services has occurred, the sales price is fixed or determinable and collectability is reasonably assured.

We also generate revenues from the Chiesi Agreement. As Chiesi is obligated to acquire pegunigalsidase alfa from us, and has limited, immaterial rights until then, the development services performed under the agreement are not considered to have a stand-alone value, and will be viewed as one unit of account - manufacturing and supply of the drug. Therefore payments received from Chiesi prior to the fulfillment of the one unit of account will be deferred until the commencement of the commercial manufacturing. We will recognize revenues after the commencement of drug supply over the period of the product's sales according to our best estimate of sale price.

Discontinued Operations

Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso. As part of the sale, we agreed to transfer our rights to Elelyso in Israel to Pfizer while gaining full rights to Elelyso in Brazil. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all of the revenues, globally, for Elelyso, excluding Brazil where we are responsible for all expenses and retain all revenues. The Amended Pfizer Agreement eliminated Pfizer's entitlement to annual payments of up to $12.5 million in relation to commercialization of Elelyso in Brazil. For further details please see notes 2 and 12 to the financial statements.

We accounted for the sale of our share in the collaboration created under the initial Pfizer Agreement, including the transfer of our rights to Elelyso in Israel, in accordance with ASU No. 2014-08.

Certain of our assets and liabilities associated with our share in the former collaboration, including our rights to Elelyso in Israel, have been segregated and classified as assets and liabilities of discontinued operations, as appropriate, in our consolidated balance sheets as of December 31, 2016 and 2017. In addition, certain financial information related to our share in the former collaboration, including our rights to Elelyso in Israel, have been segregated from continuing operations and have been reported as discontinued operations in our consolidated statements of operations. See note 12 to the financial statements.

Research and Development Expense

We expect our research and development expense to remain our primary expense in the near future as we continue to develop our product candidates. Research and development expense consists of:

- internal costs associated with research and development activities;
- payments made to third party contract research organizations, investigative/clinical sites and consultants;

- manufacturing development costs;
- personnel-related expenses, including salaries, benefits, travel, and related costs for the personnel involved in research and development;
- activities relating to the advancement of product candidates through preclinical studies and clinical trials; and
- facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, as well as laboratory and other supplies.

The following table identifies our current major research and development projects:

Project	Status	Expected Near Term Milestones
PRX-102 – pegunigalsidase alfa	Phase III clinical trial, ongoing	Completion of enrollment in trial and interim data analysis
PRX-110 – alidornase alfa	Phase IIa completed	Design of next clinical trial
OPRX-106 – Oral antiTNF	Phase IIa completed	Full results for the study

We anticipate incurring increasing costs in connection with the continued development of all of the product candidates in our pipeline. Our internal resources, employees and infrastructure are not tied to any individual research project and are typically deployed across all of our projects. We currently do not record and maintain research and development costs per project.

The costs and expenses of our projects are partially funded by grants we have received from NATI. Each grant is deducted from the related research and development expenses as the costs are incurred. For additional information regarding the grant process, see “Business—Israeli Government Programs—Encouragement of Industrial Research, Development and Technology Innovation, 1984” in Item 1 of this Annual Report. There can be no assurance that we will continue to receive grants from NATI in amounts sufficient for our operations, if at all. In addition, under the Chiesi Agreement, Protalix Ltd. is entitled to payments of up to $25 million to cover development costs for pegunigalsidase alfa, capped at $10 million per year.

At this time, due to the inherently unpredictable nature of preclinical and clinical development processes and given the early stage of our preclinical product development programs, we are unable to estimate with any certainty the costs we will incur in the continued development of the product candidates in our pipeline for potential commercialization. Clinical development timelines, the probability of success and development costs can differ materially from expectations. The current focus of our product development efforts are on pegunigalsidase alfa. Our future research and development expenses for pegunigalsidase alfa and the other product candidates will depend on the clinical success of each product candidate, as well as ongoing assessments of each product candidate’s commercial potential. In addition, we cannot forecast with any degree of certainty which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements. See “Risk Factors—If we are unable to develop and commercialize our product candidates, our business will be adversely affected” and “—We may not obtain the necessary U.S., EMA or other worldwide regulatory approvals to commercialize our drug candidates in a timely manner, if at all, which would have a material adverse effect on our business, results of operations and financial condition.”

We expect our research and development expenses to continue to be our primary expense in the future as we continue the advancement of our clinical trials and preclinical product development programs for our product candidates, particularly with respect to the development of pegunigalsidase alfa. The lengthy process of completing clinical trials and seeking regulatory approvals for our product candidates requires expenditure of substantial resources. Any failure or delay in completing clinical trials, or in obtaining regulatory approvals, could cause a delay in generating product revenue and cause our research and development expense to increase and, in turn, have a material adverse effect on our operations. Due to the factors set forth above, we are not able to estimate with any certainty when we would recognize any net cash inflows from our projects. See “Risk Factors—Clinical trials are very expensive, time-consuming and difficult to design and implement and may result in unforeseen costs which may have a material adverse effect on our business, results of operations and financial condition.”

Share-Based Compensation

The discussion below regarding share-based compensation relates to our share-based compensation.

In accordance with the guidance, we record the benefit of any grant to a non-employee and remeasure the benefit in any future vesting period for the unvested portion of the grants, as applicable. In addition, we use the straight-line accounting method for recording the benefit of the entire grant, unlike the graded method we use to record grants made to employees.

We measure share-based compensation cost for all share-based awards at the fair value on the grant date and recognition of share-based compensation over the service period for awards that we expect will vest. The fair value of stock options is determined based on the number of shares granted and the price of our ordinary shares, and calculated based on the Black-Scholes valuation model. We recognize such value as expense over the service period, net of estimated forfeitures, using the accelerated method.

The guidance requires companies to estimate the expected term of the option rather than simply using the contractual term of an option. Because of lack of data on past option exercises by employees, the expected term of the options could not be based on historic exercise patterns. Accordingly, we adopted the simplified method, according to which companies may calculate the expected term as the average between the vesting date and the expiration date, assuming the option was granted as a “plain vanilla” option.

In performing the valuation, we assumed an expected 0% dividend yield in the previous years and in the next years. We do not have a dividend policy and given the lack of profitability, dividends are not expected in the foreseeable future, if at all. The guidance stipulates a number of factors that should be considered when estimating the expected volatility, including the implied volatility of traded options, historical volatility and the period that the shares of the company are being publicly traded.

The risk-free interest rate used in the valuation of the options is based on the implied yield of U.S. federal reserve zero–coupon government bonds. The remaining term of the bonds used for each valuation was equal to the expected term of the grant. This methodology has been applied to all grants valued by us. The guidance requires the use of a risk–free interest rate based on the implied yield currently available on zero–coupon government issues of the country in whose currency the exercise price is expressed, with a remaining term equal to the expected life of the option being valued. This requirement has been applied for all grants valued as part of this report.

Convertible Notes

All outstanding convertible notes are accounted for using the guidance set forth in the Financial Accounting Standards Board, or FASB, Accounting Standards Codification (ASC) 815 requiring that we determine whether the embedded conversion option must be separated and accounted for separately. ASC 470-20 regarding debt with conversion and other options requires the issuer of a convertible debt instrument that may be settled in cash upon conversion to separately account for the liability (debt) and equity (conversion option) components of the instrument in a manner that reflects the issuer’s nonconvertible debt borrowing rate. We account for the 4.5% convertible notes as liability, on an aggregated basis, in their entirety. The conversion feature for our 7.5% convertible notes is accounted for as a derivative which is bifurcated from the debt host contract and is measured at fair value through the statement of operations.

Issuance costs regarding the issuance of our 7.5% convertible notes were allocated to the liability, equity component, derivative and shares of common stock based on their relative fair values. Issuance costs that were allocated to liability will be amortized using the effective interest rate, other than issuance costs that were allocated to derivative, which were expensed immediately.

The debt discount and debt issuance costs regarding the issuance of 4.5% convertible notes are deferred and amortized over the applicable convertible period (5 years).

Year Ended December 31, 2017 Compared to the Year Ended December 31, 2016

Revenues

We recorded revenues of $19.2 million for the year ended December 31, 2017, an increase of approximately $10.0 million, or 109%, compared to revenues of $9.2 million for the year ended December 31, 2016. Revenues include $7.1 million of products sold in Brazil and $12.1 million of drug substance sold to Pfizer The increase resulted from an increase in the amount of $3.1 million of product sold to Brazil and $7.0 million of drug substance sold to Pfizer.

Cost of Revenues

Cost of revenues was $15.2 million for the year ended December 31, 2017, an increase of $6.8 million or 81%, compared to the cost of revenues of $8.4 million for the year ended December 31, 2016. The increase resulted primarily from costs related to the production of drug substance for sale to Pfizer, and of drug product for sale to Brazil.

Research and Development Expenses

Research and development expenses were $32.2 million for the year ended December 31, 2017, an increase of $1.8 million, or 6% from $30.4 million for the year ended December 31, 2016. The increase resulted primarily from an increase of $2.4 million in clinical trial related costs, which was partially offset by a decrease of $0.7 million in materials.

We expect research and development expenses to continue to be our primary expense as we enter into a more advanced stage of preclinical and clinical trials for certain of our product candidates, primarily with respect to pegunigalsidase alfa.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $11.5 million for the year ended December 31, 2017, an increase of $2.2 million, or 23%, from $9.4 million for the year ended December 31, 2016. The increase resulted primarily from an increase in sales and marketing activities in connection with the sale of alfataliglicerase in Brazil.

Financial Expenses and Income

Financial expense was $48.9 million for the year ended December 31, 2017, compared to financial income of $4.0 million for the year ended December 31, 2016. Financial expenses included a charge of $38.1 million as a result of the re-measurement of the fair value of the 7.5% convertible notes embedded derivative. In addition, financial expenses is comprised primarily from interest expense on convertible notes.

Year Ended December 31, 2016 Compared to the Year Ended December 31, 2015

Revenues

We recorded revenues of $9.2 million for the year ended December 31, 2016, an increase of approximately $4.8 million, or 111%, compared to revenues of $4.4 million for the year ended December 31, 2015. Revenues represent products sold in Brazil and drug substance sold to Pfizer. The increase is mainly due to an increase of $4.8 million of drug substance sold to Pfizer.

Cost of Revenues

Cost of revenues was $8.4 million for the year ended December 31, 2016 compared to the cost of revenues of $730,000 for the year ended December 31, 2015. The increase is mainly due to cost of revenues that were attributed to an increase in the amount of drug substance sold to Pfizer at cost during the period and that a substantial portion of activities performed during 2015 were attributed to the development and production of PRX-102 for the entire period during which the phase III clinical trial is to be performed.

Research and Development Expenses

Research and development expenses were $30.4 million for the year ended December 31, 2016, an increase of $5.5 million, or 22% from $24.9 million for the year ended December 31, 2015. The increase resulted primarily from an increase of $3.7 million in clinical trial related costs.

We expect research and development expenses to continue to be our primary expense as we enter into a more advanced stage of preclinical and clinical trials for certain of our product candidates.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $9.4 million for the year ended December 31, 2016, an increase of $2.1 million, or 29%, from $7.3 million for the year ended December 31, 2015. The increase resulted primarily from an increase in sales and marketing activities in connection with the sale of alfataliglicerase in Brazil.

Financial Expenses and Income

Financial income was $4.0 million for the year ended December 31, 2016, compared to financial expense of $3.6 million for the year ended December 31, 2015. Financial income for the year ended December 31, 2016 resulted primarily from the exchange of $54.1 million of our 4.5% notes into $40.2 million aggregate principal amount of 7.5% senior secured notes and 23.8 million shares of our common stock. The exchange was accounted for as extinguishment of notes, and the difference between the net carrying value of the 4.5% notes exchanged and the fair value of the new notes and shares issued were accounted for as a gain on extinguishment of $14.1 million. The financial income was partially offset by $3.2 million of expenses resulting primarily from interest expense related to our outstanding convertible notes and by $6.5 million of change in fair value of convertible notes embedded derivative.

Liquidity and Capital Resources

Sources of Liquidity

As a result of our significant research and development expenditures and the lack of significant revenue from sales of taliglucerase alfa, we have generated operating losses from our continuing operations since our inception. To date, we have funded our operations primarily with proceeds equal to $31.3 million from the sale of shares of convertible preferred and ordinary shares of Protalix Ltd., and an additional $14.1 million in connection with the exercise of warrants issued in connection with the sale of such shares, through December 31, 2008. In addition, on October 25, 2007, we generated gross proceeds of $50 million in connection with an underwritten public offering of our common stock and on each of March 23, 2011 and February 22, 2012, we generated gross proceeds of $22.0 million and $27.2 million, respectively, in connection with underwritten public offerings of our common stock. We believe that the funds currently available to us as are sufficient to satisfy our capital needs for at least 12 months.

The following table summarizes our public funding sources since 2007:

Security	Year	Number of Shares	Amount
Common Stock	2007	10,000,000	$ 50,000,000
Common Stock	2011	4,000,000	$ 22,000,000
Common Stock	2012	5,175,000	$ 27,168,750

In addition to the foregoing, on September 18, 2013, we completed a private placement of $69.0 million in aggregate principal amount of 4.50% convertible notes due 2018, including $9.0 million aggregate principal amount of Notes related to the offering's initial purchaser's over-allotment option, which was exercised in full. In December 2016, we completed a private placement of $22.5 million in aggregate principal amount of 7.5% convertible notes due 2021. Finally, on July 25, 2017, we completed a private placement of an additional $10.0 million in aggregate principal amount of 7.5% convertible notes due 2021.

Pfizer paid Protalix Ltd. $60.0 million as an upfront payment in connection with the execution of the Pfizer Agreement and subsequently paid to Protalix Ltd. an additional $5.0 million upon Protalix Ltd.'s meeting a certain milestone. Protalix Ltd. also received a milestone payment of $25.0 million in connection with the FDA's approval of taliglucerase alfa in May 2012. Pfizer has also paid Protalix Ltd. $8.3 million in connection with the successful achievement of certain milestones under a clinical development agreement between Pfizer and Protalix Ltd. In connection with the execution of the Amended Pfizer Agreement, we received a $36.0 million payment from Pfizer, and Pfizer purchased 5,649,079 shares of our common stock for $10.0 million.

In the fourth quarter of 2017, Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the Chiesi Agreement.

Cash Flows

Net cash used in operations was $10.0 million for the year ended December 31, 2017. The net loss from continuing operations for the year ended December 31, 2017 of $85.3 million was partially offset by a change of $38.1 million in the fair value of convertible notes embedded derivative and an increase of $26 million in deferred revenues. Net cash used in investing activities for the year ended December 31, 2017 was $1.1 million and consisted primarily of purchase of property and equipment. Net cash used in financing activities was $1.4 million which consisted of cash settlement of $11.0 million for certain conversions of our convertible notes which was partially offset by $9.5 million of net proceeds from the issuance of our 7.5% convertible notes.

Net cash used in operations was $32.1 million for the year ended December 31, 2016. The net loss from continuing operations for the year ended December 31, 2016 of $29.2 million was further increased by $7.6 million non cash financial income, but was partially offset by $2.0 million in depreciation and a $2.1 million increase in accounts payable. Net cash used in investing activities for the year ended December 31, 2016 was $967,000 and consisted primarily of equipment purchases. Net cash provided by financing activities was $19.7 million and consisted primarily of proceeds from the private offering of our 7.5% convertible notes.

Future Funding Requirements

We expect to continue to incur significant expenditures in the near future, including significant research and development expenses related primarily to the clinical trials of PRX-102. We believe that our existing cash and cash equivalents will be sufficient for at least 12 months. We have based this estimate on assumptions that are subject to change and may prove to be wrong, and we may be required to use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials.

Our future capital requirements will depend on many other factors, including our progress in commercializing alfataliglicerase in Brazil, the progress and results of our clinical trials, the duration and cost of discovery and preclinical development and laboratory testing and clinical trials for our product candidates, conversions of our convertible notes from time to time, the timing and outcome of regulatory review of our product candidates, the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights, the number and development requirements of other product candidates that we pursue and the costs of commercialization activities, including product marketing, sales and distribution.

We may need to finance our future cash needs through corporate collaboration, licensing or similar arrangements, public or private equity offerings or debt financings. We currently do not have any commitments for future external funding, except with respect to the development-related payments and milestone payments that may become payable under the Chiesi Agreement. We may need to raise additional funds more quickly if one or more of our assumptions prove to be incorrect or if we choose to expand our product development efforts more rapidly than we presently anticipate. We may also decide to raise additional funds even before we need them if the conditions for raising capital are favorable. Any sale of additional equity or debt securities will likely result in dilution to our shareholders. The incurrence of indebtedness would result in increased fixed obligations and could also result in covenants that would restrict our operations. Additional equity or debt financing, grants or corporate collaboration and licensing arrangements may not be available on acceptable terms, if at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our planned commercialization efforts or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently.

Effects of Inflation and Currency Fluctuations

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the years ended December 31, 2015, 2016 or 2017.

Currency fluctuations could affect us by increased or decreased costs mainly for goods and services acquired outside of Israel. We do not believe currency fluctuations have had a material effect on our results of operations during the years ended December 31, 2015, 2016 or 2017.

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements as of December 31, 2016 and 2017.

Recently Issued Accounting Pronouncements

Certain recently issued accounting pronouncements are discussed in Note 1(q) of the financial statements included in Item 8 of this Annual Report on Form 10-K.

Contractual Obligations

The following table summarizes our significant contractual obligations at December 31, 2017:

(U.S. dollars in thousands)	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Convertible notes	$ 83,004	$ 10,646	$ 8,860	$ 63,498	-
Operating lease obligations	$ 3,935	$ 1,349	$ 2,006	$ 580	-
Purchase obligations (1)	$ 3,668	$ 3,668	-	-	-
Certain clinical contract	$ 19,170	$ 8,614	$ 10,427	$ 129	-
Liability for employee rights upon retirement	$ 2,586	-	-	-	$ 2,586
Total	$ 112,363	$ 24,277	$ 21,293	$ 64,207	$ 2,586

(1) Represents open purchase orders issued to certain suppliers and other vendors mainly in connection with our research and development activities that were outstanding as of December 31, 2017.

The foregoing table does not include (i) annual license fees, which are immaterial, (ii) payments we may be required to make to certain of our licensors in the time periods set forth above upon the achievement of agreed-upon milestones and (iii) royalty payments payable by us to certain of our licensors in connection with the commercial sale of our product candidates, if any. If all of the contingencies with respect to milestone payments under our research and license agreements are met, the aggregate milestone payments payable would be approximately $14.3 million and would be payable, if at all, as our projects progress over the course of a number of years. The royalty payments payable in connection with sales of each of our product candidates, if any, shall not exceed low, single-digit percentages of net sales of the product.

Selected Quarterly Financial Data (unaudited)

	Three Months Ended							
	2016				2017			
	(U.S. dollars in thousands)							
	March 31	June 30	Sept. 30	Dec. 31	March 31	June 30	Sept. 30	Dec. 31
Revenues	$ 679	$ 1,769	$ 4,670	2,081	$ 2,889	$ 6,358	$ 7,526	2,469
Gross profit	156	94	422	129	801	835	1,460	915
(Loss) income from continuing operations	(8,526)	(10,736)	(7,290)	(2,624)	(59,148)	450	(11,437)	(15,141)
Income (loss) from discontinued operations	(72)	(117)	0	0	-	-	-	
Net (loss) profit for the period	$ (8,598)	$ (10,853)	$ (7,290)	$ (2,624)	$ (59,148)	$ 450	$ (11,437)	$ (15,141)
Earnings (loss) per share of common stock, basic and diluted:								
Loss from continuing operations	$ (0.09)	$ (0.11)	$ (0.07)	$ (0.02)	$ (0.48)	$ 0.00	$ (0.09)	$ (0.11)
Income (loss) from discontinued operations	(0.00)	(0.00)	(0.00)	(0.00)				
Net basic income (loss) per share of common stock	$ (0.09)	$ (0.11)	$ (0.07)	$ (0.02)	$ (0.48)	$ 0.00	$ (0.09)	$ (0.11)
Net diluted loss per share of common stock	$ (0.09)	$ (0.11)	$ (0.07)	$ (0.02)	$ (0.48)	$ (0.06)	$ (0.09)	$ (0.11)

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Currency Exchange Risk

The currency of the primary economic environment in which our operations are conducted is the dollar. Most of our revenues and approximately 50% of our expenses and capital expenditures are incurred in dollars, and a significant source of our financing has been provided in U.S. dollars. Since the dollar is the functional currency, monetary items maintained in currencies other than the dollar are remeasured using the rate of exchange in effect at the balance sheet dates and non-monetary items are remeasured at historical exchange rates. Revenue and expense items are remeasured at the average rate of exchange in effect during the period in which they occur. Foreign currency translation gains or losses are recognized in the statement of operations.

Approximately 35% of our costs, including salaries, expenses and office expenses, are incurred in NIS. Inflation in Israel may have the effect of increasing the U.S. dollar cost of our operations in Israel. If the U.S. dollar declines in value in relation to the NIS, it will become more expensive for us to fund our operations in Israel. A revaluation of 1% of the NIS will affect our loss before tax by less than 1%. The exchange rate of the U.S. dollar to the NIS, based on exchange rates published by the Bank of Israel, was as follows:

	Year Ended December 31,		
	2015	**2016**	**2017**
Average rate for period	3.887	3.841	3.600
Rate at year-end	3.902	3.845	3.467

To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rate of the U.S. dollar against the NIS. These measures, however, may not adequately protect us from material adverse effects due to the impact of inflation in Israel.

Interest Rate Risk

Our exposure to market risk is confined to our cash and cash equivalents. We consider all short term, highly liquid investments, which include short-term deposits with original maturities of three months or less from the date of purchase, that are not restricted as to withdrawal or use and are readily convertible to known amounts of cash, to be cash equivalents. The primary objective of our investment activities is to preserve principal while maximizing the interest income we receive from our investments, without increasing risk. We invest any cash balances primarily in bank deposits and investment grade interest-bearing instruments. We are exposed to market risks resulting from changes in interest rates. We do not use derivative financial instruments to limit exposure to interest rate risk. Our interest gains may decline in the future as a result of changes in the financial markets.

Item 8. Financial Statements and Supplementary Data

See the Index to Consolidated Financial Statements on Page F-1 attached hereto.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We conducted an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this Form 10-K. The controls evaluation was conducted under the supervision and with the participation of management, including our Chief Executive Officer and Chief Financial Officer. Disclosure controls and procedures are controls and procedures designed to reasonably assure that information required to be disclosed in our reports filed under the Exchange Act, such as this Form 10-K, is recorded, processed, summarized and reported within the time periods specified in the Commission’s rules and forms. Disclosure controls and procedures are also designed to reasonably assure that such information is accumulated and communicated to our management, including the Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

The evaluation of our disclosure controls and procedures included a review of the controls' objectives and design, our implementation of the controls and their effect on the information generated for use in this Form 10-K. In the course of the controls evaluation, we reviewed identified data errors, control problems or acts of fraud, and sought to confirm that appropriate corrective actions, including process improvements, were being undertaken. This type of evaluation will be performed on a quarterly basis so that the conclusions of management, including the Chief Executive Officer and Chief Financial Officer, concerning the effectiveness of the disclosure controls and procedures can be reported in our periodic reports on Form 10-Q and Form 10-K. The overall goals of these various evaluation activities are to monitor our disclosure controls and procedures, and to modify them as necessary. Our intent is to maintain the disclosure controls and procedures as dynamic systems that change as conditions warrant.

Based on the controls evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the end of the period covered by this Form 10-K, our disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified by the Commission, and that material information related to our company and our consolidated subsidiaries are made known to management, including the Chief Executive Officer and Chief Financial Officer, particularly during the period when our periodic reports are being prepared.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles. Internal control over financial reporting includes those policies and procedures that: (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. generally accepted accounting principles, and that receipts and expenditures of our company are being made only in accordance with authorizations of management and our directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Management assessed our internal control over financial reporting as of December 31, 2017, the end of our fiscal year. Management based its assessment on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Management's assessment included evaluation of elements such as the design and operating effectiveness of key financial reporting controls, process documentation, accounting policies and our overall control environment.

Based on our assessment, management has concluded that our internal control over financial reporting was effective as of the end of the fiscal year to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles. We reviewed the results of management's assessment with the Audit Committee of our Board of Directors.

The effectiveness of our internal control over financial reporting as of December 31, 2017 has been audited by Kesselman & Kesselman, an independent registered public accounting firm, as stated in their report included herein.

Inherent Limitations on Effectiveness of Controls

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent or detect all error and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. The design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Further, because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, within a company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Controls can also be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Projections of any evaluation of controls effectiveness to future periods are subject to risks. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures.

Changes in internal controls

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15f and 15d-15f under the Exchange Act) that occurred during the year ended December 31, 2017 that have materially affected, or that are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information in our 2018 Proxy Statement regarding directors and executive officers appearing under the headings “Security Ownership of Certain Beneficial Owners and Management— Section 16(a) Beneficial Ownership Reporting Compliance” and “Proposal 1: Election of Directors” is incorporated by reference in this section.

Item 11. Executive Compensation

The information appearing in our 2018 Proxy Statement under the headings “Director Compensation,” “Compensation Discussion and Analysis,” “Report of the Compensation Committee,” and “Executive Compensation” is incorporated by reference in this section.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information appearing in our 2018 Proxy Statement under the heading “Security Ownership of Certain Beneficial Owners and Management” is incorporated by reference in this section.

Equity Compensation Plan Information

The following table provides information as of December 31, 2017 with respect to the shares of our common stock that may be issued under our existing equity compensation plan.

	A	B	C
Plan Category	**Number of Securities to be Issued Upon Exercise of Outstanding Options**	**Weighted Average Exercise Price of Outstanding Options**	**Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column A)**
Equity Compensation Plans Approved by Stockholders	4,929,617	3.59	2,554,075
Equity Compensation Plans Not Approved by Stockholders	-	-	-
Total	4,929,617	3.59	2,554,075

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information appearing in our 2018 Proxy Statement under the headings “Proposal 1: Election of Directors—Corporate Governance” and “—Certain Relationships and Related Transactions” is incorporated by reference in this section.

Item 14. Principal Accountant Fees and Services

The information appearing in our 2018 Proxy Statement under the heading “Proposal 4: Ratification of Appointment of Independent Registered Public Accounting Firm” is incorporated by reference in this section.

PART IV

Item 15. Exhibits and Financial Statement Schedules

The following documents are filed as part of this Annual Report on Form 10-K:

1. *Financial Statements*. The following Consolidated Financial Statements of Protalix BioTherapeutics, Inc. are included in Item 8 of this Annual Report on Form 10-K:

2. *Financial Statement Schedule.* Financial statement schedules have been omitted since they are either not required, are not applicable or the required information is shown in the consolidated financial statements or related notes.

3. *Exhibits.*

		Incorporated by Reference				
Exhibit Number	Exhibit Description	Form	File Number	Exhibit	Date	Filed Herewith
3.1	Certificate of Incorporation of the Company	8-K	333-48677	3.1	April 1, 2016	
3.2	Amendment to Certificate of Incorporation of the Company	Def 14A	001-33357	Appen. A	July 1, 2016	
3.3	Bylaws of the Company	8-K	001-33357	3.2	April 1, 2016	
4.1	Form of Restricted Stock Agreement/Notice	8-K	001-33357	4.1	July 18, 2012	
4.2	Indenture, dated as of September 18, 2013, between Protalix BioTherapeutics, Inc. and The Bank of New York Mellon Trust Company, N.A., as Trustee	8-K	001-33357	4.1	September 18, 2013	
4.3	Form of 4.50% Convertible Note due 2018	8-K	001-33357	4.2	September 18, 2013	
4.4	Indenture, dated as of December 7, 2016, between Protalix BioTherapeutics, Inc. the guarantors party thereto, The Bank of New York Mellon Trust Company, N.A., as trustee and Wilmington Savings Fund Society, FSB, as collateral agent	8-K	001-33357	4.1	December 7, 2016	

4.5	Form of 7.50% Convertible Note due 2018 (Issued in Financing)	8-K	001-33357	4.2	December 7, 2016
4.6	Form of 7.50% Convertible Note due 2018 (Issued in Exchange)	8-K	001-33357	4.3	December 7, 2016
4.7	First Supplemental to Indenture, dated as of July 24, 2017, by and among Protalix BioTherapeutics, Inc., the guarantors party thereto, The Bank of New York Mellon Trust Company, N.A., as trustee, and Wilmington Savings Fund Society, FSB, as collateral agent	8-K	001-33357	4.2	July 25, 2017
4.8	Second Supplemental Indenture, dated as of November 27, 2017, by and among Protalix BioTherapeutics, Inc., the guarantors party hereto and The Bank of New York Mellon Trust Company, N.A., as trustee, registrar, paying agent and conversion agent	8-K	001-33357	4.1	December 1, 2017
10.1	2006 Stock Incentive Plan, as amended	Def 14A	001-33357	Annex A	October 9, 2014
10.2	Employment Agreement between Protalix Ltd. and Yoseph Shaaltiel, dated as of September 1, 2004	8-K	001-33357	10.3	January 8, 2007
10.3	Employment Agreement between Protalix Ltd. and Einat Almon, dated as of December 19, 2004	8-K	001-33357	10.3	January 8, 2007
10.4	Employment Agreement between Protalix Ltd. and Yossi Maimon, dated as of October 15, 2006	8-K	001-33357	10.5	January 8, 2007
10.5	Lease Agreement between Protalix Ltd. and Angel Science Park (99) Ltd., dated as of October 28, 2003 as amended on April 18, 2005	8-K	001-33357	10.9	January 8, 2007
10.6	Unprotected Lease Agreement	10-K	001-33357	10.21	March 17, 2008
10.7	Employment Agreement by and between Protalix Ltd., and Tzvi Palash dated as of August 29, 2010	8-K	001-33357	10.1	September 7, 2010
10.8†	Amended and Restated Agreement between Protalix Ltd. and Comercio e Serviços Ltda. dated June 17, 2013	10-Q	001-33357	10.1	May 8, 2014
10.9†	Technology Transfer and Supply Agreement made as of June 18, 2013 by and between Protalix Ltd. and Fundação Oswaldo Cruz	10-Q	001-33357	10.3	May 8, 2014

10.10	Employment Agreement with Moshe Manor dated September 28, 2014	8-K	001-33357	10.1	September 29, 2014	
10.11†	Amended and Restated Exclusive License and Supply Agreement by and between Pfizer Inc. and Protalix Ltd., dated October 12, 2015	10-Q/A	001-33357	10.1	December 11, 2015	
10.12	Form of Note Purchase Agreement, dated of December 1, 2016 among Protalix BioTherapeutics, Inc. and the Purchasers	8-K	001-33357	10.1	December 7, 2016	
10.13	Form of Exchange Agreement, dated of December 1, 2016 among Protalix BioTherapeutics, Inc. and the Existing Holders	8-K	001-33357	10.2	December 7, 2016	
10.14	Form of U.S. Security Agreement, dated of December 7, 2016 among Protalix BioTherapeutics, Inc., the guarantors party thereto and Wilmington Savings Fund Society, FSB, as collateral agent	8-K	001-33357	10.3	December 7, 2016	
10.15	Form of Security Agreement/Debenture, dated of December 7, 2016 between Protalix BioTherapeutics, Inc. and Altshuler Shaham Trusts Ltd., as security trustee	8-K	001-33357	10.4	December 7, 2016	
10.16†	Exclusive License and Supply Agreement dated as of October 17, 2017, made by and between Protalix Ltd. and Chiesi Farmaceutici S.p.A.					X
21.1	Subsidiaries	10-K	001-33357	21.1	February 26, 2010	
23.1	Consent of Kesselman & Kesselman, Certified Public Accountants (Isr.), A member of PricewaterhouseCoopers International Limited, independent registered public accounting firm for the Registrant					X
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X

32.1	18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Certification of Chief Executive Officer	X
32.2	18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Certification of Chief Financial Officer	X
101.INS	XBRL INSTANCE FILE	X
101.SCH	XBRL SHEMA FILE	X
101.CAL	XBRL CALCULATION FILE	X
101.DEF	XBRL DEFINITION FILE	X
101.LAB	XBRL LABEL FILE	X
101.PRE	XBRL PRESENTATION FILE	X

† Portions of this exhibit were omitted and have been filed separately with the Secretary of the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment under Rule 24b-2 of the Exchange Act.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, as of March 6, 2018.

PROTALIX BIOTHERAPEUTICS, INC.

By: /s/ Moshe Manor
Moshe Manor

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Moshe Manor and Yossi Maimon, and each of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution and re-substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that said attorneys-in-fact and agents, or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Moshe Manor Moshe Manor	President, Chief Executive Officer (Principal Executive Officer) and Director	March 6, 2018
/s/ Yossi Maimon Yossi Maimon	Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer)	March 6, 2018
/s/ Shlomo Yanai Shlomo Yanai	Chairman of the Board	March 6, 2018
/s/ Amos Bar Shalev Amos Bar Shalev	Director	March 6, 2018
/s/ Zeev Bronfeld Zeev Bronfeld	Director	March 6, 2018
/s/ Yodfat Harel Buchris Yodfat Harel Buchris	Director	March 6, 2018
/s/ Aharon Schwartz Aharon Schwartz, Ph.D.	Director	March 6, 2018

PROTALIX BIOTHERAPEUTICS, INC.
CONSOLIDATED FINANCIAL STATEMENTS

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the board of directors and stockholders of

PROTALIX BIOTHERAPEUTICS, INC.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Protalix BioTherapeutics, Inc. and its subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations, changes in stockholders' equity (capital deficiency) and cash flows for each of the three years in the period ended December 31, 2017 including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2017 based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016 and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Kesselman & Kesselman
Certified Public Accountants (Isr.)
A member of PricewaterhouseCoopers International Limited

Tel Aviv, Israel

March 6, 2018

We have served as the Company's auditor since 2000.

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PROTALIX BIOTHERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(U.S. dollars in thousands, except share and per share amounts)

	December 31,	
	2016	**2017**
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 63,281	$ 51,163
Accounts receivable – Trade	693	1,721
Other assets	2,648	1,934
Inventories	5,245	7,833
Total current assets	71,867	62,651
FUNDS IN RESPECT OF EMPLOYEE RIGHTS UPON RETIREMENT	1,677	1,887
PROPERTY AND EQUIPMENT, NET	8,703	7,676
Total assets	$ 82,247	$ 72,214
LIABILITIES NET OF CAPITAL DEFICIENCY		
CURRENT LIABILITIES:		
Accounts payable and accruals:		
Trade	$ 4,007	$ 7,521
Other	7,496	9,310
Convertible notes	53,872	5,921
Deferred revenues	837	
Total current liabilities	66,212	22,752
LONG TERM LIABILITIES:		
Convertible notes	19,343	46,267
Deferred revenues		26,851
Liability for employee rights upon retirement	2,348	2,586
Other long term liabilities	4,301	5,051
Total long term liabilities	25,992	80,755
Total liabilities	92,204	103,507
COMMITMENTS (Note 6)		
CAPITAL DEFICIENCY:		
Common Stock, $0.001 par value: Authorized - as of December 31, 2016 and 2017, 250,000,000 shares; issued and outstanding, respectively - as of December 31, 2016 and 2017, 124,134,085 shares and 143,728,797 shares, respectively	124	144
Additional paid-in capital	202,575	266,495
Accumulated deficit	(212,656)	(297,932)
Total capital deficiency	(9,957)	(31,293)
Total liabilities net of capital deficiency	$ 82,247	$ 72,214

The accompanying notes are an integral part of the consolidated financial statements.

PROTALIX BIOTHERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(U.S. dollars in thousands, except share and per share amounts)

	Year ended December 31,		
	2015	**2016**	**2017**
REVENUES	$ 4,364	$ 9,199	$ 19,242
COST OF REVENUES	(730)	(8,398)	(15,231)
GROSS PROFIT	3,634	801	4,011
RESEARCH AND DEVELOPMENT EXPENSES	(24,889)	(30,412)	(32,170)
Less – grants	4,864	5,804	3,336
RESEARCH AND DEVELOPMENT EXPENSES, NET	(20,025)	(24,608)	(28,834)
SELLING, GENERAL AND ADMINISTRATIVE EXPENSES	(7,279)	(9,356)	(11,530)
OPERATING LOSS	(23,670)	(33,163)	(36,353)
FINANCIAL EXPENSES	(3,735)	(4,192)	(9,725)
FINANCIAL INCOME	123	589	188
LOSS FROM CHANGE IN FAIR VALUE OF CONVERTIBLE NOTES EMBEDDED DERIVATIVE		(6,473)	(38,061)
(LOSS) GAIN ON EXTINGUISHMENT OF CONVERTIBLE NOTES		14,063	(1,325)
FINANCIAL (EXPENSES) INCOME – NET	(3,612)	3,987	(48,923)
LOSS FROM CONTINUING OPERATIONS	(27,282)	(29,176)	(85,276)
(LOSS) INCOME FROM DISCONTINUED OPERATIONS	85,319	(189)	
NET (LOSS) INCOME FOR THE YEAR	$ 58,037	$ (29,365)	$ (85,276)
NET (LOSS) INCOME PER SHARE OF COMMON STOCK – BASIC AND DILUTED			
Loss from continuing operations	$ (0.29)	$ (0.29)	$ (0.65)
Income from discontinued operations	0.90	(0.00)	
Net (loss) income per share of common stock	$ 0.61	$ (0.29)	$ (0.65)
WEIGHTED AVERAGE NUMBER OF SHARES OF COMMON STOCK USED IN COMPUTING LOSS PER SHARE OF COMMON STOCK, BASIC AND DILUTED	94,922,390	101,387,704	131,085,958

The accompanying notes are an integral part of the consolidated financial statements.

PROTALIX BIOTHERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY
(CAPITAL DEFICIENCY)
(U.S. dollars in thousands, except share data)

	Common Stock	Common Stock	Additional paid–in Capital	Accumulated deficit	Total
	Number of shares	Amount			
Balance at January 1, 2015	**93,603,819**	**94**	**185,633**	**(241,328)**	**(55,601)**
Changes during 2015:					
Issuance of common stock	5,649,079	6	6,095		6,101
Share-based compensation related to stock options			1,273		1,273
Share-based compensation related to restricted stock award, net of forfeitures of 2,501 shares	(2,501)		529		529
Exercise of options granted to employee	550,000	*	534		534
Net loss from continuing operations				(27,282)	(27,282)
Net income from discontinued operations				85,319	85,319
Balance at December 31, 2015	**99,800,397**	**100**	**194,064**	**(183,291)**	**10,873**
Changes during 2016:					
Issuance of common stock, net of issuance cost	23,846,735	24	6,824		6,848
Equity component of convertible notes			685		685
Share-based compensation related to stock options			920		920
Share-based compensation related to restricted stock award	7,843	*	68		68
Exercise of options granted to employee (including net exercise)	479,110	*	14		14
Net loss from continuing operations				(29,176)	(29,176)
Net loss from discontinued operations				(189)	(189)
Balance at December 31, 2016	**124,134,085**	**124**	**202,575**	**(212,656)**	**(9,957)**
Changes during 2017:					
Share-based compensation related to stock options			337		337
Reclassification of embedded derivative			43,634		43,634
Convertible note conversions	19,594,712	20	18,634		18,654
Equity component of convertible notes			1,315		1,315
Net loss				(85,276)	(85,276)
Balance at December 31, 2017	**143,728,797**	**144**	**266,495**	**(297,932)**	**(31,293)**

* Represents an amount of less than $1 thousand.

The accompanying notes are an integral part of the consolidated financial statements.

PROTALIX BIOTHERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(U.S. dollars in thousands)

	Year ended December 31,		
	2015	**2016**	**2017**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net (loss) income	$ 58,037	$ (29,365)	$ (85,276)
(Loss) income from discontinued operations	85,319	(189)	
Loss from continuing operations	(27,282)	(29,176)	(85,276)
Adjustments required to reconcile net (loss) income to net cash used in operating activities:			
Share based compensation	1,802	988	337
Depreciation	2,370	1,983	1,920
Financial (income) expenses, net (mainly exchange differences)	124	13	(40)
Changes in accrued liability for employee rights upon retirement	59	10	(18)
(Gain) loss on amounts funded in respect of employee rights upon retirement	18	7	(21)
Loss (gain) on sale of fixed assets	(2)	(7)	6
Loss (gain) on extinguishment of convertible notes		(14,063)	1,325
Net income in connection with conversions of convertible notes			(116)
Change in fair value of convertible notes embedded derivative		6,473	38,061
Amortization of debt issuance costs and debt discount	445	568	2,334
Issuance of shares for interest payment in connection with conversions of convertible notes			2,391
Changes in operating assets and liabilities:			
Increase (decrease) in deferred revenues (including non-current potion)	362	(411)	26,014
(Increase) decrease in accounts receivable and other assets	523	(1,133)	25
Decrease (increase) in inventories	(2,316)	522	(2,588)
Increase (decrease) in accounts payable and accruals	(1,873)	2,139	4,902
Increase in other long term liabilities			750
Net cash used in continuing operations	(25,770)	(32,087)	(9,994)
Net cash provided by (used in) discontinued operations	1,486	(11)	
Net cash used in operating activities	$ (24,284)	$ (32,098)	$ (9,994)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property and equipment	$ (464)	$ (849)	$ (971)
Proceeds from sale of property and equipment	3	20	3
(Increase) decrease in restricted deposit	45	(106)	(146)
Amounts funded in respect of employee rights upon retirement, net	(96)	(32)	(5)
Net cash used in continuing operations	$ (512)	$ (967)	$ (1,119)
Net cash provided by discontinued operations	39,899		
Net cash (used in) provided by investing activities	$ 39,387	$ (967)	$ (1,119)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Net payment for conversion of convertible notes			(10,961)
Net proceeds from issuance of convertible notes		19,681	9,542
Issuance of shares, net of issuance cost	6,101		
Exercise of options	534	14	
Net cash (used in) provided by financing activities	$ 6,635	$ 19,695	$ (1,419)
EFFECT OF EXCHANGE RATE CHANGES ON CASH AND CASH EQUIVALENTS	(131)	277	414
NET (DECREASE) INCREASE IN CASH AND CASH EQUIVALENTS	21,607	(13,093)	(12,118)
BALANCE OF CASH AND CASH EQUIVALENTS AT BEGINNING OF YEAR	54,767	76,374	63,281
BALANCE OF CASH AND CASH EQUIVALENTS AT END OF YEAR	$ 76,374	$ 63,281	$ 51,163

The accompanying notes are an integral part of the consolidated financial statements.

PROTALIX BIOTHERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(U.S. dollars in thousands)

(CONTINUED)

	Year ended December 31,		
	2015	**2016**	**2017**
SUPPLEMENTARY INFORMATION ON INVESTING AND FINANCING ACTIVITIES NOT INVOLVING CASH FLOWS:			
Purchase of property and equipment	$ 489	$ 595	$ 526
Issuance of promissory note	$ 4,301		
Issuance of common stock, net of issuance cost		$ 6,848	
Convertible note conversions			$ 16,263
As to extinguishment of convertible notes see note 8.			
SUPPLEMENTARY DISCLOSURE ON CASH FLOWS			
Interest paid	$ 3,105	$ 3,659	$ 4,854

The accompanying notes are an integral part of the consolidated financial statements.

NOTE 1 - SIGNIFICANT ACCOUNTING POLICIES

a. General

Protalix BioTherapeutics, Inc. (collectively with its subsidiaries, the "Company"), and its wholly-owned subsidiaries, Protalix Ltd. and Protalix B.V. (the "Subsidiaries"), are biopharmaceutical companies focused on the development and commercialization of recombinant therapeutic proteins based on the Company's proprietary ProCellEx® protein expression system ("ProCellEx"). To date, the Company has successfully developed taliglucerase alfa (marketed under the name alfataliglicerase in Brazil and certain other Latin American countries and Elelyso® in the rest of the territories) for the treatment of Gaucher disease that has been approved for marketing in the United States, Brazil, Israel and other markets. The Company has a number of product candidates in varying stages of the clinical development process. The Company's current strategy is to develop proprietary recombinant proteins that are therapeutically superior to existing recombinant proteins currently marketed for the same indications.

The Company's product pipeline currently includes, among other candidates:

(1) pegunigalsidase alfa, or PRX-102, a therapeutic protein candidate for the treatment of Fabry disease, a rare, genetic lysosomal disorder;

(2) alidornase alfa, or PRX-110, a proprietary plant cell recombinant human Deoxyribonuclease 1, or DNase, under development for the treatment of Cystic Fibrosis, to be administered by inhalation; and

(3) OPRX-106, the Company's oral antiTNF product candidate which is being developed as an orally-delivered anti-inflammatory treatment using plant cells as a natural capsule for the expressed protein.

Obtaining marketing approval with respect to any product candidate in any country is directly dependent on the Company's ability to implement the necessary regulatory steps required to obtain such approvals. The Company cannot reasonably predict the outcome of these activities.

Since its approval by the FDA, taliglucerase alfa has been marketed by Pfizer Inc. ("Pfizer"), as provided in the exclusive license and supply agreement by and between Protalix Ltd. and Pfizer, which is referred to herein as the Pfizer Agreement. In October 2015, the Company entered into an Amended and Restated Exclusive License and Supply Agreement (the "Amended Pfizer Agreement") which amends and restates the Pfizer Agreement in its entirety. Pursuant to the Amended Pfizer Agreement, the Company sold to Pfizer its share in the collaboration created under the Pfizer Agreement for the commercialization of Elelyso in exchange for a cash payment equal to $36.0 million. As part of the sale, the Company agreed to transfer its rights to Elelyso in Israel to Pfizer while gaining full rights to it in Brazil. Under the Amended Pfizer Agreement, Pfizer is entitled to all of the revenues, and is responsible for 100% of expenses globally for Elelyso, excluding Brazil where the Company is responsible for all expenses and retains all revenues. For further details see note 2.

On June 18, 2013, the Company entered into a Supply and Technology Transfer Agreement (the "Brazil Agreement") with Fundação Oswaldo Cruz ("Fiocruz"), an arm of the Brazilian Ministry of Health for taliglucerase alfa. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, the Company has the right to terminate the Brazil Agreement. Notwithstanding, the Company is, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. Approximately 10% of adult Gaucher patients in Brazil are currently treated with alfataliglicerase. The Company is discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, the Company will determine what it believes to be the course of action that is in the best interest of the Company.

In 2017, the Company received a purchase order from the Brazilian Ministry of Health (the "Brazilian Ministry") for the purchase of alfataliglicerase for the treatment of Gaucher patients in Brazil for consideration of approximately $24.3 million. The purchase order consists of a number of shipments in increasing volumes. Shipments started in June 2017. The Company has recorded revenues of $7.1 million for sales of alfataliglicerase to Fiocruz in 2017.

NOTE 1 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

On October 19, 2017, Protalix Ltd. and Chiesi Farmaceutici S.p.A. ("Chiesi") entered into an Ex-US license (the "Chiesi Agreement") pursuant to which Chiesi was granted an exclusive, license for all markets outside of the United States to commercialize pegunigalsidase alfa. Under the terms and conditions of the Chiesi Agreement, Protalix Ltd. retained the right to commercialize pegunigalsidase in the United States.

Under the Chiesi Agreement, Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to $25 million in development costs, capped at $10 million per year. Protalix Ltd. is also eligible to receive additional payments of up to $320 million, in the aggregate, in regulatory and commercial milestone payments.

Under the terms of the agreement, Protalix Ltd. will manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi will make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa.

Based on its current cash resources and commitments, the Company believes it will be able to maintain its current planned development activities and the corresponding level of expenditures for at least 12 months from the date of approval of the financial statements as of December 31, 2017, although no assurance can be given that it will not need additional funds prior to such time. If there are unexpected increases in general and administrative expenses or research and development expenses, the Company may need to seek additional financing.

b. Basis of presentation

The Company's financial statements have been prepared in accordance with generally accepted accounting principles in the United States ("U.S. GAAP").

c. Use of estimates in the preparation of financial statements

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results may differ from those estimates.

d. Functional currency

The dollar is the currency of the primary economic environment in which the operations of the Company and its Subsidiaries are conducted. Most of the Company's revenues are derived in dollars. Most of the Company's expenses and capital expenditures are incurred in dollars, and the major source of the Company's financing has been provided in dollars.

Transactions and balances originally denominated in dollars are presented at their original amounts. Balances in non-dollar currencies are translated into dollars using historical and current exchange rates for non-monetary and monetary balances, respectively. For non-dollar transactions and other items (stated below) reflected in the statements of operations, the following exchange rates are used: (i) for transactions – exchange rates at the transaction dates or average rates; and (ii) for other items (derived from non-monetary balance sheet items such as depreciation and amortization, etc.) – historical exchange rates. Currency transaction gains and losses are recorded as financial income or expenses, as appropriate.

e. Cash equivalents

The Company considers all short-term, highly liquid investments, which include short-term bank deposits with original maturities of three months or less from the date of purchase, that are not restricted as to withdrawal or use and are readily convertible to known amounts of cash, to be cash equivalents.

NOTE 1 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

f. Inventories

Inventories are valued at the lower of cost or net realizable value. Cost of raw and packaging materials and purchased products is determined using the "moving average" basis.

Cost of finished products is determined as follows: the value of the raw and packaging materials component is determined primarily using the "moving average" basis; the value of the labor and overhead component is determined on an average basis over the production period.

Inventory is written down for estimated obsolescence based upon management assumptions about future demand and market conditions.

g. Property and equipment

1. Property and equipment are stated at cost, net of accumulated depreciation and amortization.

2. The Company's assets are depreciated by the straight-line method on the basis of their estimated useful lives as follows:

	Years
Laboratory equipment	5
Furniture	10-15
Computer equipment	3

Leasehold improvements are amortized by the straight-line method over the expected lease term, which is shorter than the estimated useful life of the improvements.

h. Impairment in value of long-lived assets

The Company tests long-lived assets for impairment if an indication of impairment exists. If the sum of expected future cash flows of definite life assets (undiscounted and without interest charges) is less than the carrying amount of such assets, the Company recognizes an impairment loss, and writes down the assets to their estimated fair values.

i. Income taxes

1. Deferred income taxes

Deferred taxes are determined utilizing the assets and liabilities method based on the estimated future tax effects of the differences between the financial accounting and tax bases of assets and liabilities under the applicable tax laws. Deferred tax balances are computed using the tax rates expected to be in effect when those differences reverse. A valuation allowance in respect of deferred tax assets is provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has provided a full valuation allowance with respect to its deferred tax assets. The Company used tax rates of 39%, 24% and 23%. See note 10.

2. Uncertainty in income taxes

Tax benefits recognized in the financial statements are those that the Company's management deems at least more likely than not to be sustained, based on technical merits. The amount of benefits recorded for these tax benefits is measured as the largest benefit the Company's management deems more likely than not to be sustained.

NOTE 1 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

j. Revenue Recognition

1. Revenues from supply agreements and from selling products

The Company recognizes revenues from supply agreements and from selling products upon delivery, when the sales price is fixed or determinable and collectability is reasonably assured.

2. Revenues from Chiesi Agreement

As Chiesi is obligated to acquire pegunigalsidase alfa from the Company and the development services are not considered to have a stand-alone value, development and manufacturing of a product to be commercialized by Chiesi is viewed as one unit of account. Since there is only one unit of account, all payments received by Chiesi prior to the satisfaction of Protalix's obligation will be deferred. Therefore, the $25 million upfront payment and future research and development reimbursement payments (up to $25 million) and any potential additional development milestone payments will be deferred until the commencement of commercial manufacturing.

k. Research and development costs

Research and development costs are expensed as incurred and consist primarily of personnel, subcontractors and consultants (mainly in connection with clinical trials), facilities, equipment and supplies for research and development activities. Grants received by the Israeli Subsidiary from the National Authority for Technological Innovation ("NATI"), which has replaced many of the functions of the Office of the Chief Scientist of Israel's Ministry of Industry, Trade and Labor (the "OCS"), are recognized when the grant becomes receivable, provided there is reasonable assurance that the Company or the Subsidiaries will comply with the conditions attached to the grant and there is reasonable assurance the grant will be received. The grant is deducted from the research and development expenses as the applicable costs are incurred. In connection with purchases of assets, amounts assigned to intangible assets to be used in a particular research and development project that have no alternative future use are charged to research and development costs at the purchase date.

Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and amortized over the period that the goods are consumed or the related services are performed.

l. Concentration of credit risks and trade receivable

Financial instruments that potentially subject the Company to concentration of credit risk consist principally of bank deposits. The Company deposits these instruments with highly rated financial institutions, mainly in Israeli banks, and, as a matter of policy, limits the amounts of credit exposure to any one financial institution. The Company has not experienced any credit losses in these accounts and does not believe it is exposed to any significant credit risk on these instruments. The Company's trade receivables represent amounts to be received from Pfizer, Brazil and Chiesi. The Company does not require Pfizer, Brazil or Chiesi to post collateral with respect to receivables.

m. Share-based compensation

The Company accounts for employee's share-based payment awards classified as equity awards using the grant-date fair value method. The fair value of share-based payment transactions is recognized as an expense over the requisite service period.

The Company elected to recognize compensation cost for an award with only service conditions that has a graded vesting schedule using the accelerated method based on the multiple-option award approach.

NOTE 1 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

When stock options are granted as consideration for services provided by consultants and other non-employees, the grant is accounted for based on the fair value of the stock options issued. Options granted are measured on a final basis at the end of the related service period and is recognized over the related service period using the straight-line method.

n. Net (loss) earnings per share

Basic and diluted loss per share ("LPS") are computed by dividing net loss by the weighted average number of shares of the Company's Common Stock, par value $0.001 per share (the "Common Stock") outstanding for each period.

Diluted LPS is calculated in continuing operations. The calculation of diluted LPS does not include 19,778,424, 23,532,492 and 76,848,199 shares of Common Stock underlying outstanding options, restricted shares of Common Stock and shares issuable upon conversion of the convertible notes for the fiscal years ended December 31, 2015, 2016 and 2017, respectively, because the effect would be anti-dilutive.

o. Convertible notes

All outstanding convertible notes are accounted for using the guidance set forth in the Financial Accounting Standards Board ("FASB") Accounting Standards Codification (ASC) 815 requiring that the Company determine whether the embedded conversion option must be separated and accounted for separately. ASC 470-20 regarding debt with conversion and other options requires the issuer of a convertible debt instrument that may be settled in cash upon conversion to separately account for the liability (debt) and equity (conversion option) components of the instrument in a manner that reflects the issuer's nonconvertible debt borrowing rate. The Company accounts for the 2013 Notes (as defined in note 8a) as a liability, on an aggregated basis, in their entirety. The 2016 Notes (as defined in note 8b) were accounted for partially as liability and equity components of the instrument and partially as a debt host contract with an embedded derivative resulting from the conversion feature. During the year ended December 31, 2017, the embedded derivative was reclassified to additional paid in capital, see note 8.

Issuance costs regarding the issuance of the 2016 Notes and the 2017 Notes (as defined in note 8c) were allocated to the liability, equity component, derivative and shares based on their relative fair values. Issuance costs that were allocated to the liability are amortized using the effective interest rate, other than issuance costs that were allocated to the derivative which were expensed immediately.

The debt discount and debt issuance costs regarding the issuance of the 2013 Notes are deferred and amortized over the 2013 Notes period (5 years).

p. Recently adopted standards

In March 2016, the FASB issued ASU 2016-09, "Compensation - Stock Compensation (Topic 718)" ("ASU 2016-09") which simplifies certain aspects of the accounting for share-based payments, including accounting for income taxes, classification of awards as either equity or liabilities, classification on the statement of cash flows as well as allowing an entity-wide accounting policy election to either estimate the number of awards that are expected to vest or account for forfeitures as they occur. ASU 2016-09 is effective for fiscal years beginning after December 15, 2016, including interim periods within those fiscal years. Early adoption is permitted in any annual or interim period for which financial statements have not yet been issued, and all amendments in the ASU that apply must be adopted in the same period. The Company adopted this standard in the fourth quarter of 2016. The Company elected to account for forfeitures as they occur. The implementation of this ASU did not have a material impact on the consolidated financial statements.

NOTE 1 - SIGNIFICANT ACCOUNTING POLICIES (continued)**:**

q. Recently issued accounting pronouncements

In May 2014, the FASB issued guidance on revenues from contracts with customers that will supersede most current revenue recognition guidance, including industry-specific guidance. The underlying principle is to recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which an entity expects to be entitled to in exchange for those goods or services. The guidance provides a five-step analysis of transactions to determine when and how revenue is recognized. Other major provisions require capitalization of certain contracts costs, consideration of the time value of money in the transaction price, and allowing estimates of variable consideration to be recognized before contingencies are resolved in certain circumstances. The guidance also requires enhanced disclosures regarding the nature, amount timing and uncertainty of revenues and cash flows arising from an entity's contracts with customers. The guidance is effective for the interim and annual periods beginning on or after December 15, 2017. The implementation of this ASU did not have a material impact on the consolidated financial statements.

In January 2016, the FASB issued ASU, No. 2016-01, Financial Instruments-Overall: Recognition and Measurement of Financial Assets and Financial Liabilities. The guidance affects the accounting for equity investments, financial liabilities under the fair value option and the presentation and disclosure requirements of financial instruments. The guidance is effective in annual reporting periods beginning after December 15, 2017. The implementation of this ASU is expected to have no material impact on the consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), which supersedes the existing guidance for lease accounting, Leases (Topic 840). ASU 2016-02 requires lessees to recognize leases on their balance sheets, and leaves lessor accounting largely unchanged. The amendments in this ASU are effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early application is permitted for all entities. ASU 2016-02 requires a modified retrospective approach for all leases existing at, or entered into after, the date of initial application, with an option to elect to use certain transition relief. The Company is currently evaluating the impact of this new standard on its consolidated financial statements.

NOTE 2 - COMMERCIALIZATION AGREEMENTS

1. On November 30, 2009, Protalix Ltd. and Pfizer entered into the Pfizer Agreement (as amended in June 2013) pursuant to which Pfizer was granted an exclusive, worldwide license to develop and commercialize taliglucerase alfa, except for Israel and Brazil. Under the Pfizer Agreement Protalix was entitled to 40% of the results (profits or losses) earned on Pfizer's sales of taliglucerase alfa.

   In October 2015, the Company entered into the following agreements with Pfizer:

   Amended Pfizer Agreement - Pursuant to the amendment, the Company granted Pfizer an exclusive license in the entire world, including Israel but excluding Brazil. Pfizer acquired all the information, knowledge and permission to manufacture and sell Elelyso.

   Protalix also agreed to provide Pfizer with:

   a. Manufacturing and supply of the drug substance for its incorporation into the licensed product in consideration of an agreed price per unit.

   b. Assistance in arranging for the manufacture of the drug substance by Pfizer or by alternative supplier chosen by Pfizer in consideration of an agreed hourly rate plus reimbursement of expenses.

   Stock Purchase Agreement - the Company issued 5,649,079 shares of Common Stock to Pfizer.

NOTE 2 - COMMERCIALIZATION AGREEMENTS (continued)**:**

Promissory note – as of the date of the amendment, the Company owed Pfizer $4.3 million as a result of the accumulated losses incurred by the Collaboration Operation. Following the new agreements, the Company committed to pay Pfizer the principal sum of the debt at the earlier of (a) November 12, 2020 and (b) the date upon which it becomes due pursuant to any event of default, as defined. The promissory note is presented in "other long term liabilities".

The Amended Pfizer Agreement resulted in a discontinued operation as defined under ASU 2014-08 because it represented a strategic shift for the Company that has a major effect on the entity's operations and financial results.

Revenues from the Pfizer Agreements as well as revenues from sales of Elelyso in Israel were presented as discontinued operations. See note 12.

2. In October 2017, Protalix Ltd. entered into the Chiesi Agreement with respect to the commercialization of pegunigalsidase alfa (hereafter – the drug) for treatment of the Fabry disease. Under the terms of the Chiesi Agreement, Protalix Ltd. granted to Chiesi exclusive licensing rights for the commercialization of the drug for all markets outside of the United States. Protalix Ltd. maintains the exclusive commercialization rights to the drug in the United States.

   Protalix Ltd. will be mainly responsible for (i) continuing the development of the drug until a regulatory approval is granted and (ii) manufacture and supply the drug to Chiesi, based on Chiesi's requests.

   The consideration consists of the following:

   a. Upfront, non-refundable payment of $25 million.

   b. Additional payments of up to $25 million in development costs, capped at $10 million per year.

   c. Milestone payments of up to $320 million with respect to certain regulatory and commercial events as defined in the Chiesi Agreement.

   d. Additional payments as consideration for the supply of the drug. The payment will vary from 15% to 35% of Chiesi's average selling price of the drug, depending on the amount of annual sales.

   e. Protalix will be the sole manufacturer of the drug.

   Chiesi does not have sublicensing rights (except for certain territories).

   The Company analyzed the agreement terms and concluded that the Chiesi Agreement qualifies as a contract with customer under ASC 605. Chiesi is a customer of the Company as it contracted with the entity to obtain goods or services that are an output of the entity's ordinary activities in exchange for consideration.

   As Chiesi is obligated to acquire pegunigalsidase alfa from the Company and the development services are not considered to have a stand-alone value, development and manufacturing of a product to be commercialized by Chiesi is viewed as one unit of account. Therefore, all payments received prior to the fulfillment of the one unit of account will be deferred until the commencement of commercial manufacturing. The Company will recognize revenues after the commencement of the drug supply over the period of the product's sales according to the Company's best estimate.

3. On June 18, 2013, the Company entered into the Brazil Agreement with Fiocruz for taliglucerase alfa. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, the Company has the right to terminate the Brazil Agreement. Notwithstanding, the Company is, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. Approximately 10% of adult Gaucher patients in Brazil are currently treated with alfataliglicerase. The Company is discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, the Company will determine what it believes to be the course of action that is in the best interest of the Company.

NOTE 3 - PROPERTY AND EQUIPMENT

a. Composition of property and equipment grouped by major classifications is as follows:

	December 31,	
(*U.S. dollars in thousands*)	**2016**	**2017**
Laboratory equipment	$ 16,265	$ 16,561
Furniture and computer equipment	2,342	2,438
Leasehold improvements	15,678	16,123
Equipment under construction	19	19
	$ 34,304	$ 35,141
Less – accumulated depreciation and amortization	(25,601)	(27,465)
	$ 8,703	$ 7,676

b. Depreciation in respect of property and equipment totaled approximately $2.4 million, $2.0 million and $1.9 million for the years ended December 31, 2015, 2016 and 2017, respectively.

NOTE 4 - INVENTORIES

Inventories at December 31, 2016 and 2017 consisted of the following:

	December 31,	
(*U.S. dollars in thousands*)	**2016**	**2017**
Raw materials	$ 2,591	$ 3,838
Work in progress	395	485
Finished goods	2,259	3,510
Total inventory	$ 5,245	$ 7,833

NOTE 5 - LIABILITY FOR EMPLOYEE RIGHTS UPON RETIREMENT

The Israeli Subsidiary is required to make a severance payment upon dismissal of an employee or upon termination of employment in certain circumstances. The severance pay liability to the employees (based upon length of service and the latest monthly salary - one month's salary for each year employed) is recorded on the Company's balance sheets under "Liability for employee rights upon retirement." The liability is recorded as if it were payable at each balance sheet date on an undiscounted basis.

The liability is funded in part from the purchase of insurance policies or by the establishment of pension funds with dedicated deposits in the funds. The amounts used to fund these liabilities are included in the Company's balance sheets under "Funds in respect of employee rights upon retirement." These policies are the Company's assets. However, under labor agreements and subject to certain limitations, any policy may be transferred to the ownership of the individual employee for whose benefit the funds were deposited. In the years ended December 31, 2015, 2016 and 2017, the Company deposited approximately $168,000, $164,000 and $166,000, respectively, with insurance companies in connection with its severance payment obligations.

In accordance with the current employment agreements with certain employees, the Company makes regular deposits with certain insurance companies for accounts controlled by each applicable employee in order to secure the employee's rights upon retirement. The Company is fully relieved from any severance pay liability with respect to each such employee after it makes the payments on behalf of the employee. The liability accrued in respect of these employees and the amounts funded, as of the respective agreement dates, are not reflected in the Company's balance sheets, as the amounts funded are not under the control and management of the Company and the pension or severance pay risks have been irrevocably transferred to the applicable insurance companies (the "Contribution Plans").

NOTE 5 - LIABILITY FOR EMPLOYEE RIGHTS UPON RETIREMENT (continued)**:**

The amounts of severance pay expenses were approximately $800,000, $842,000 and $906,000 for each of the years ended December 31, 2015, 2016 and 2017, respectively, of which approximately $675,000, $675,000 and $746,000 in the years ended December 31, 2015, 2016 and 2017, respectively, were in respect of the Contribution Plans. Gain (loss) on amounts funded in respect of employee rights upon retirement totaled approximately ($18,000), ($7,000) and $21,000 for the years ended December 31, 2015, 2016 and 2017, respectively.

The Company expects to contribute approximately $830,000 in the year ending December 31, 2018 to insurance companies in connection with its severance liabilities for its operations for that year, approximately $664,000 of which will be contributed to one or more Contribution Plans.

During the five-year period following December 31, 2017, the Company expects to pay future benefits to three employees upon each such employee's normal retirement age. The Company anticipates that the benefits payable will be approximately $250,000.

NOTE 6 - COMMITMENTS

a. Royalty Commitments

1. The Company is obligated to pay royalties to the National Authority for Technological Innovation ("NATI") on proceeds from the sale of products developed from research and development activities that were funded, partially, by grants from NATI or its predecessor, the Office of the Chief Scientist of the Israeli Department of Labor ("OCS"). At the time the grants were received, successful development of the related projects was not assured.

   In the case of failure of a project that was partly financed as described above, the Company is not obligated to pay any such royalties or repay funding received from NATI or the OCS.

   Under the terms of the applicable funding arrangements, royalties of 3% to 6% are payable on the sale of products developed from projects funded by NATI or the OCS, which payments shall not exceed, in the aggregate, 100% of the amount of the grant received (dollar linked), plus, commencing upon January 1, 2001, interest at an annual rate based on LIBOR. In addition, if the Company receives approval to manufacture products developed with government grants outside the State of Israel, it will be required to pay an increased total amount of royalties (possibly up to 300% of the grant amounts plus interest), depending on the manufacturing volume that is performed outside the State of Israel, and, possibly, an increased royalty rate.

   Royalty expenses to NATI or the OCS are included in the statement of operations as a component of the cost of revenues both in continuing and discontinued operations and were approximately $2.2 million, $288,000 and $1,384,000 during the years ended December 31, 2015, 2016 and 2017, respectively.

   At December 31, 2016 and 2017, the maximum total royalty amount payable by the Company under these funding arrangements is approximately $38.5 million and $42.2 million, respectively (without interest, assuming 100% of the funds are payable).

2. The Company is a party to certain research and license agreements. Under the agreements, the Company is obligated to pay royalties at varying rates from its future revenues. The aggregate royalties payable under all of the agreements is equal to a varying range of percentages of net sales of licensed products. Royalty expenses under the agreements are included in the statement of operations as a component of the cost of revenues both in continuing and discontinued operations and were approximately $51,000, $286,000 and $0 during the years ended December 31, 2015, 2016 and 2017, respectively.

   Under each agreement, the Company is also obligated to pay milestone, licensing and other payments to the counterparties of the agreement. The payments under the agreements are for varying amounts and are subject to varying conditions. If all of the contingencies with respect to milestone payments under the research and license agreements are met, the aggregate milestone payments total payable would be approximately $14.3 million and would be payable, if at all, as the Company's projects progress over the course of a number of years. Milestone payments of $0, $300,000 and $0 were made during the years ended December 31, 2015, 2016 and 2017, respectively.

NOTE 6 - COMMITMENTS (continued)**:**

None of the agreements has a fixed termination date. Subject to earlier termination for other reasons, each agreement terminates after a certain number of years following the first commercial sale of any licensed product under the agreement or after a certain number of years without the initiation of commercial sales of any product under the agreement.

b. Subcontracting Agreements

The Company has entered into sub-contracting agreements with several clinical providers and consultants in Israel, the United States and certain other countries in connection with its primary product development process. As of December 31, 2017, total commitments under said agreements were approximately $19.2 million.

c. Lease Agreements

The Company is a party to a number of lease agreements for its facilities, the latest of which has been extended until 2021. The Company has the option to extend certain of such agreements on two additional occasions for additional five-year periods each, for a total of 10 additional years. Under the leases, the aggregate monthly rental payments are approximately $65,000. As of December 31, 2017, the Company provided bank guarantees of approximately $306,000 in the aggregate, to secure the fulfillment of its obligations under the lease agreements. The future minimum lease payments required under the operating leases for such premises are approximately $783,000, $717,000, $717,000, $580,000, for fiscal years 2018 through 2021, respectively. Lease expenses totaled approximately $1.0 million for each of the years ended December 31, 2015, 2016 and approximately $775,000 for the year ended December 31,2017, respectively.

d. Vehicle Lease and Maintenance Agreements

The Company entered into several three-year lease and maintenance agreements for vehicles which are regularly amended as new vehicles are leased. The current monthly lease fees aggregate approximately $52,000. The expected lease payments for the years ending December 31, 2018, 2019 and 2020 are approximately $565,000, $385,000 and $186,000, respectively.

NOTE 7 - SHARE CAPITAL

a. Rights of the Company's Common Stock

The Company's Common Stock is listed on the NYSE American and on the Tel Aviv Stock Exchange. Each share of Common Stock is entitled to one vote. The holders of shares of Common Stock are also entitled to receive dividends whenever funds are legally available, when and if declared by the Board of Directors. Since its inception, the Company has not declared any dividends.

b. Stock based compensation

On December 14, 2006, the Board of Directors adopted the Protalix BioTherapeutics, Inc. 2006 Stock Incentive Plan, as amended (the "Plan"). The Plan has since been amended to, among other things, increase the number of shares of common stock available under the Plan to 13,841,655 shares. The grant of options to Israeli employees under the Plan is subject to the terms stipulated by Sections 102 and 102A of the Israeli Income Tax Ordinance. Each option grant is subject to the track chosen by the Company, either Section 102 or Section 102A of the Israeli Income Tax Ordinance, and pursuant to the terms thereof, the Company is not allowed to claim, as an expense for tax purposes, the amounts credited to employees as a benefit, including amounts recorded as salary benefits in the Company's accounts, in respect of options granted to employees under the Plan, with the exception of the work-income benefit component, if any, determined on the grant date. For Israeli non-employees, the share option plan is subject to Section 3(i) of the Israeli Income Tax Ordinance.

NOTE 7 - SHARE CAPITAL (continued)**:**

As of December 31, 2017, 2,554,075 shares of Common Stock remain available for grant under the Plan.

For purposes of determining the fair value of the options and restricted stock granted to employees and non-employees, the Company's management uses the fair value of the Common Stock.

From January 1, 2015 through December 31, 2017, the Company granted options and shares of restricted stock to certain employees and non-employees as follows:

1. **Options and restricted stock granted to employees:**

   a) Below is a table summarizing all of the options grants to employees during the year ended December 31, 2015:

Year of grant	No. of options granted	Exercise price	Vesting period	Fair value at grant (U.S. dollars in thousands)	Expiration period
2015	1,909,000	$ 1.72	4 years	$ 1,900	10 years

   Set forth below are grants made by the Company to employees (including related parties) during the three-year period ended December 31, 2017 (such grants appear in the table above):

   On March 23, 2015, the Company's compensation committee approved the grant of a 10-year option to purchase 1,909,000 shares of Common Stock to its officers and other employees with an exercise price equal to $1.72 per share under the Plan. The options vest over a four-year period; the first 25% shares vest on the first anniversary of the grant date and the remaining shares vest in 12 equal quarterly increments over the subsequent three-year period. Vesting of the options granted to certain executive officers is subject to acceleration in full upon a Corporate Transaction or a Change in Control, as those terms are defined in the Plan. The Company estimated the fair value of the options on the date of grant using the Black-Scholes option-pricing model to be approximately $1.9 million based on the following weighted average assumptions: dividend yield of 0% for all years; expected volatility of 61.7%; risk-free interest rates of 1.6%; and expected life of six years.

   b) The total unrecognized compensation cost of employee stock options at December 31, 2017 is approximately $130,000. The unrecognized compensation cost of employee stock options is expected to be recognized over a weighted average period of 0.54 years.

   The total cash received from employees as a result of employee stock option exercises for the years ended December 31, 2015, 2016 and 2017 was approximately $534,000, $14,000 and $0, respectively. The Company did not realize any tax benefit in connection with these exercises.

2. **Options granted to consultants, directors, and other service providers:**

   During the three years ended December 31, 2017 there were no option grants by the Company to its consultants, directors, and other service providers. In addition, during the three years ended December 31, 2017, there were no option exercises by any of the Company's consultants, directors, and other service providers and, consequently, no shares of Common Stock were issued in connection with exercises of options by, nor was any cash received from, the Company's consultants, directors, and other service providers during such period.

NOTE 7 - SHARE CAPITAL (continued)**:**

3. A summary of share option plans, and related information, under all of the Company's equity incentive plans for the years ended December 31, 2015, 2016 and 2017 is as follows:

a. Options granted to employees:

	Year ended December 31,					
	2015		2016		2017	
	Number of options	Weighted average exercise price	Number of options	Weighted Average Exercise Price	Number of options	Weighted average exercise price
Outstanding at beginning of year	5,870,309	$ 3.770	6,952,293	$ 3.363	4,884,211	$ 3.617
Changes during the year:						
Granted	1,909,000	1.72				
Forfeited and Expired	277,016	5.395	1,514,957	3.748	154,594	4.004
Exercised (*)	550,000	0.972	553,125	0.067		
Outstanding at end of year	6,952,293	$ 3.363	4,884,211	$ 3.617	4,729,617	$ 3.604
Exercisable at end of year	4,477,043	$ 4.182	3,498,492	$ 4.296	4,457,461	$ 3.696

(*) The total intrinsic value of options exercised during the years ended December 31, 2015, 2016 and 2017, was approximately $675,000, $213,000 and $0, respectively.

b. Restricted stock granted to employees:

	Year ended December 31,	
	2015	2016
	Number of restricted stock	
Outstanding at beginning of year	386,124	127,874
Changes during the year:		
Vested	255,749	127,874
Forfeited	2,501	-
Outstanding at end of year	127,874	-

c. Options and restricted stocks granted to consultants, directors, and other service providers:

	Year ended December 31,					
	2015		2016		2017	
	Number of options/ restricted stock	Weighted average exercise price	Number of options/ restricted stock	Weighted average exercise price	Number of options/ restricted stock	Weighted average exercise price
Outstanding at beginning of Year	1,208,592	$ 6.136	637,209	$ 11.638	208,000	$ 3.156
Changes during the year:						
Expired	466,883	0.001	429,209	15.748	8,000	0.001
Vested restricted stock	104,500					
Outstanding at end of year	637,209	11.638	208,000	3.156	200,000	3.282
Exercisable at end of year	549,709	$ 12.954	170,500	$ 3.109	200,000	$ 3.282

NOTE 7 - SHARE CAPITAL (continued)**:**

d. The following tables summarize information concerning outstanding and exercisable options and restricted stock as of December 31, 2017:

December 31, 2017					
Options outstanding			Options exercisable		
Exercise prices	Number of options outstanding at end of year	Weighted average remaining contractual life	Number of options exercisable	Weighted average remaining contractual life	
n/a (Restricted Stock)			n/a	n/a	
$ 1.720	1,720,685	7.22	1,617,279	7.22	
$ 2.350	40,000	0.81	40,000	0.81	
$ 2.370	900,000	6.74	731,250	6.74	
$ 2.650	211,682	1.15	211,682	1.15	
$ 3.020	50,000	0.10	50,000	0.10	
$ 3.370	150,000	6.56	150,000	6.56	
$ 5.000	949,250	0.10	949,250	0.10	
$ 6.900	680,000	2.15	680,000	2.15	
$ 7.550	160,000	2.65	160,000	2.65	
$ 9.660	68,000	2.83	68,000	2.83	
	4,929,617		4,657,461		

e. The following table illustrates the effect of share-based compensation on the statement of operations:

	Year ended December 31,		
(U.S. dollars in thousands)	**2015**	**2016**	**2017**
Research and development expenses	$ 904	$ 571	$ 182
Selling, general and administrative expenses	898	417	155
	$ 1,802	$ 988	$ 337

c. Private and 144A Offerings

1. On October 12, 2015, the Company completed a private offering of 5,649,079 shares of the Company's common stock to Pfizer. See also note 2.

2. On December 7, 2016, the Company exchanged with certain existing note holders $54.052 million aggregate principal amount of the Company's outstanding 4.50% Convertible Senior Notes due 2018 for, among other consideration, $40.186 million aggregate principal amount of convertible notes due 2021 (as described in note 8b) and for 23,846,735 shares of common stock. See also note 8b.

3. On July 24, 2017, the Company entered into a Note Purchase Agreement with certain institutional investors relating to the private issuance and sale by the Company of $10 million in aggregate principal amount of its 7.5% secured convertible promissory notes due 2021. The 7.5% convertible notes were issued pursuant to the base indenture dated December 7, 2016 (the existing 2016 Notes). Concurrently, the Company exchanged with certain existing note holders $9.0 million aggregate principal amount of the Company's outstanding 4.50% Convertible Senior Notes due 2018 for $8.55 million aggregate principal amount of newly issued 4.50% Senior Convertible Notes due 2022. See also note 8c.

NOTE 8 - CONVERTIBLE NOTES

a. 4.5% Convertible Notes ("2013 Notes")

On September 18, 2013, the Company completed a private placement of $69.0 million in aggregate principal amount of Senior Convertible Notes (the "2013 Notes"), including $9.0 million aggregate principal amount of 2013 Notes related to the initial purchaser's over-allotment option, which was exercised in full. In connection with the completion of the offering, the Company entered into an indenture with The Bank of New York Mellon Trust Company, N.A., as trustee, governing the 2013 Notes. The 2013 Notes accrue interest at a rate of 4.50% per year, payable semiannually in arrears on March 15 and September 15 of each year, beginning on March 15, 2014. In December 2016, $54.1 million aggregate principal amount of 2013 Notes were exchanged for 2016 Notes and shares of common stock (see also note 8b) and in July 2017, $9.0 million aggregate principal amount of 2013 Notes were exchanged for 2017 Notes as defined in note 8c (see also note 8c). Accordingly, $5.9 million aggregate principal amount of 2013 Notes remain outstanding as of December 31, 2017. The 2013 Notes mature on September 15, 2018.

Holders may convert their 2013 Notes at any time prior to the close of business on the business day immediately preceding September 15, 2018. The initial conversion rate for the 2013 Notes is 173.6593 shares of the Common Stock for each $1,000 principal amount of 2013 Notes (equivalent to an initial conversion price of approximately $5.76 per share of the Common Stock). Upon conversion, the Company will deliver a number of shares of Common Stock, per $1,000 principal amount of 2013 Notes, equal to the conversion rate. The conversion rate is subject to adjustment for certain events but will not be adjusted for any accrued and unpaid interest.

The following table sets forth total interest expense recognized for the years ended December 31, 2015, 2016 and 2017 related to the 2013 Notes:

	Year ended December 31,		
(U.S. Dollars in thousands)	**2015**	**2016**	**2017**
Contractual interest expense	$ 3,105	$ 2,943	$ 501
Amortization of debt issuance costs and debt discount	444	421	71
Total	**$ 3,549**	$ 3,364	$ 572

b. 7.5% Convertible Notes ("2016 Notes")

On December 1, 2016, the Company entered into a note purchase agreement with institutional investors, which held part of the 2013 Notes (the "2016 Purchasers"), relating to the sale by the Company of $22.5 million aggregate principal amount of 7.50% Senior Secured Convertible Notes due 2021 in a private placement pursuant to Section 4(a)(2) under the Securities Act of 1933, as amended (the "Securities Act"). Concurrently with the consummation of the private placement of the 2016 Notes, the Company entered into a privately negotiated exchange agreement (the "2016 Exchange Agreement") with certain existing note holders identified therein to exchange $54.1 million aggregate principal amount of the Company's outstanding 2013 Notes for (i) $40.186 million aggregate principal amount of 2016 Notes, (ii) 23,846,735 shares of Common Stock and (iii) cash, equal to the accrued and unpaid interest on the 2013 Notes and any fractional shares. The closing date of the purchase agreement and the 2016 Exchange Agreement was December 7, 2016. The issuance of the 2016 Notes and shares in the exchange and the private placement were made in reliance on the exemption from the registration requirements of the Securities Act pursuant to Section 4(a)(2) thereof. The net proceeds from the private placement were $19.7 million, after deducting the placement agent's fees and the Company's estimated offering expenses.

In connection with the completion of the exchange and the private placement, the Company entered into an indenture (the "2016 Indenture") with The Bank of New York Mellon Trust Company, N.A., as trustee, governing the 2016 Notes. The 2016 Notes accrue interest at a rate of 7.50% per year, payable semiannually in arrears on May 15 and November 15 of each year, beginning on May 15, 2017. A portion of the interest payable may be made in shares of Common Stock at the Company's election. The Notes will mature on November 15, 2021; provided that all of the then-outstanding 2013 Notes, or any Permitted Refinancing Indebtedness (as defined in the 2016 Indenture) have been redeemed, repurchased, otherwise retired, discharged in accordance with their terms or converted into common stock of the Company, or have been effectively discharged, in each case on or prior to June 16, 2018 or the scheduled maturity date of the 2013 Notes (or any Permitted Refinancing Indebtedness incurred in respect thereof) is extended to a date that is after February 15, 2022, otherwise the 2016 Notes will mature on June 15, 2018.

NOTE 8 - CONVERTIBLE NOTES (continued)**:**

On July 24, 2017, the Company entered into another note purchase agreement with certain institutional investors relating to the private issuance and sale by the Company of $10.0 million in aggregate principal amount of its 2016 Notes. The 2016 Notes were issued pursuant to the 2016 Indenture dated (December 7, 2016). The net proceeds from this purchase agreement were $9.5 million, after deducting the Company's offering expenses.

Holders may convert their 2016 Notes at any time. The initial conversion rate for the 2016 Notes is 1,176.4706 shares of the Common Stock for each $1,000 principal amount of 2016 Notes (equivalent to an initial conversion price of approximately $0.85 per share of the Common Stock). Upon conversion, the Company may settle the 2016 Notes by paying or delivering, as the case may be, cash, shares of Common Stock or a combination thereof, at the Company's election.

During 2017, approximately $13.6 million aggregate principal amount of the Company's 2016 Notes were converted. Settlement of the conversions resulted in the issuance of 8,827,624 shares of Common Stock and cash payments of approximately $11 million, in the aggregate. A total of $59.1 million aggregate principal amount of the 2016 Notes remains outstanding as of December 31, 2017.

Prior to the maturity date, the Company may redeem in cash:

a) any or all of the 2016 Notes if the last reported sale price of the common stock for at least 20 trading days (whether or not consecutive) during the period of 30 consecutive trading days exceeds 150% of the conversion price on each applicable trading day, or

b) all of the 2016 Notes then outstanding if the aggregate principal amount of the 2016 Notes then outstanding is less than 15% of the aggregate principal amount of the notes issued.

No redemption was made during the years 2016 and 2017.

The 2016 Notes are guaranteed by the Restricted Subsidiaries (as defined in the 2016 Indenture) and are secured by a first-priority security interest in all of the present and after-acquired assets of the Company and each of the Restricted Subsidiaries (the "Collateral"), including, but not limited to, (i) 100% of the capital stock of the Guarantors (as defined in the 2016 Indenture) and each Restricted Subsidiary of the Company that is held by the Company or any Restricted Subsidiary, (ii) intellectual property, including all copyrights, copyright licenses, patents, patent licenses, software, trademarks, trademark licenses and trade secrets and other proprietary information, including, but not limited to, domain names, (iii) all cash, deposit accounts, securities accounts, commodities accounts and contract rights, (iv) all real property and leased property, subject to applicable minimum thresholds, as set forth in the 2016 Indenture, and (v) all other tangible and intangibles of the Company and the Guarantors. In connection with the grant of such liens, the Company entered into certain agreements with both Wilmington Savings Fund Society, FSB, as collateral agent in the United States, and with Altshuler Shaham Trusts Ltd., as security trustee in Israel. The 2016 Indenture restricts the ability of the Company, the Subsidiaries and any future subsidiaries to make certain investments, including transfers of the Company's assets that constitute collateral securing the 2016 Notes, in its existing and future foreign subsidiaries, subject to certain exceptions.

NOTE 8 - CONVERTIBLE NOTES (continued)**:**

Upon (i) the occurrence of a fundamental change (as defined in the 2016 Indenture) or (ii) if the Company calls the 2016 Notes for redemption as described below (either event, a "make-whole fundamental change") and a holder elects to convert its 2016 Notes in connection with such make-whole fundamental change, the Company will, in certain circumstances, increase the conversion rate by a number of additional shares (the "Additional Shares"). In no event will the conversion rate exceed the maximum conversion rate, which is 1,787.3100 shares per $1,000 principal amount of 2016 Notes, which amount is inclusive of repayment of the principal of the 2016 Notes.

If a fundamental change occurs at any time, holders will have the right, at their option, to require the Company to purchase for cash any or all of the 2016 Notes, or any portion of the principal amount thereof, that is equal to $1,000 or an integral multiple of $1,000 in excess thereof, on a date of the Company's choosing that is not less than 20 calendar days nor more than 35 calendar days after the date of the applicable fundamental change company notice. The price the Company is required to pay for a 2016 Note is equal to 100% of the principal amount of such 2016 Note plus accrued and unpaid interest, if any, to, but excluding, the fundamental change purchase date.

For accounting purposes, since the terms of the 2013 Notes and the 2016 Notes are substantially different, the 2016 Exchange Agreement was considered as an extinguishment, which in essence means recording a gain due to the 2013 Notes that were exchanged for the 2016 Notes recorded at fair value as of the closing date. The gain on extinguishment of $14.1 million was recognized.

As the settlement upon conversion was subject to compliance with the listing standards of the NYSE American, until the Company's stockholders' approval was obtained, the Company was prohibited by these rules from issuing shares in excess of 20% of its outstanding shares (calculated as of December 1, 2016). The accounting guidance assumed that the conversion will be settled in cash and, as such, is precluded from equity classification for any part of the 2016 Notes that may have cash settlement. As such, that part of the conversion feature was accounted for as a derivative which is bifurcated from the debt host contract and was measured at fair value through the statement of operations until the Company's stockholders approved, in April 2017, the issuance of shares in excess of 20% of its outstanding shares. On April 12, 2017, the Company's stockholders approved the issuance of shares of the Company's Common Stock in excess of 20% of the Company's outstanding shares of Common Stock to settle conversion requests and pay interest on the Company's issued 7.5% convertible notes. As a result, the Company reclassified the embedded derivative to additional paid in capital. During 2017, the measurement of the derivative resulted in a non-cash charge to the Company's statement of operations of $38,061 thousand. The conversion feature of the 7.5% convertible notes issued in July 2017 is accounted for as equity, which is bifurcated from the debt host contract. With respect to the remainder of the 2016 Notes, for which the conversion feature qualifies for equity classification (since upon conversion the Company at its election may settle the 2016 Notes by paying cash, shares of Common Stock or a combination of cash and shares of Common Stock) separate liability (debt) and equity (conversion option) components of such 2016 Notes were recorded. The Company measures the liability according to amortized cost using the effective interest method.

The Company prepared a valuation of the fair value of the 2016 Notes (a Level 3 valuation) for the issuance dates. The value of the 2016 Notes was estimated by implementing the binomial model. The liability component was valued based on the Income Approach. The following parameters were used:

	December 7, 2016	July 24, 2017
Stock price (USD)	0.3	0.77
Expected term	4.94	4.32
Risk free rate	1.86%	1.74%
Volatility	54.12%	63.79%
Yield	13.98%	11.56%

NOTE 8 - CONVERTIBLE NOTES (continued)**:**

The following table sets forth total interest expense recognized related to the 2016 Notes:

	Year Ended December 31,	
	2016	**2017**
(U.S. Dollars in thousands)		
Contractual interest expense	$ 313	$ 4,434
Debt discount amortization	147	2,309
Gain on extinguishment	(14,063)	
Change in fair value of convertible note embedded derivative	6,473	38,061
Interest payment in connection with conversions		3,918
Income in connection with conversions		(1,643)
Total	$ (7,130)	$ 47,079

c. 4.5% Convertible Notes Due 2022 ("2017 Notes")

On July 24, 2017, the Company entered into a privately negotiated exchange agreement (the "2017 Exchange Agreement") with certain existing note holders identified therein to exchange $9.0 million aggregate principal amount of the Company's outstanding 2013 Notes for (i) $8.55 million aggregate principal amount of the Company's 4.5% convertible promissory notes due 2022, (ii) $275,000 in cash consideration and (iii) cash, equal to the accrued and unpaid interest on the exchanged 2013 Notes.

As the terms of the 2013 Notes and the 2017 Notes are substantially different, the 2017 Exchange Agreement was considered an extinguishment of debt, which in essence means recording a loss due to the 2013 Notes that were exchanged for the 2017 Notes recorded at fair value as of the closing date. The Company recognized a loss of $1.3 million due to the extinguishment.

The Company prepared a valuation of the fair value of the 2017 Notes (a Level 3 valuation) for the issuance date. The value of the 2017 Notes was estimated by implementing the binomial model. The liability component was valued based on the Income Approach. The following parameters were used:

	July 24, 2017
Stock price (USD)	0.77
Expected term	4.57
Risk free rate	1.78%
Volatility	62.68%
Yield	15.21%

The Company accounts for the convertible notes as a liability, on an aggregated basis, in their entirely. The debt discount and debt issuance costs are deferred and amortized over the applicable convertible period.

All of the 2017 Notes were converted during the year ended December 31, 2017 into 11,239,641 shares of Common Stock.

The following table sets forth total interest expense recognized related to the 2017 Notes:

	Year Ended December 31, 2017
(U.S. Dollars in thousands)	
Contractual interest expense	$ 55
Debt premium amortization	(46)
Loss on extinguishment	1,325
Total	$ 1,334

NOTE 9 - FAIR VALUE MEASUREMENT

The Company discloses fair value measurements for financial assets and liabilities. Fair value is based on the price that would be received from the sale of an asset, or paid to transfer a liability, in an orderly transaction between market participants at the measurement date.

The accounting standard establishes a fair value hierarchy that prioritizes observable and unobservable inputs used to measure fair value into three broad levels, which are described below:

Level 1: Quoted prices (unadjusted) in active markets that are accessible at the measurement date for assets or liabilities. The fair value hierarchy gives the highest priority to Level 1 inputs.

Level 2: Observable prices that are based on inputs not quoted on active markets, but corroborated by market data.

Level 3: Unobservable inputs are used when little or no market data is available. The fair value hierarchy gives the lowest priority to Level 3 inputs.

In determining fair value, the Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible and considers counterparty credit risk in its assessment of fair value.

The fair value of the financial instruments included in the working capital of the Company is usually identical or close to their carrying value.

The fair value of the convertible notes derivative is based on level 3 measurement.

The fair value of the remaining $5.9 million 2013 Notes and the $59.1 million 2016 Notes as of December 31, 2017 is approximately $5.7 million and $76.6 million, respectively, based on a level 3 measurement.

The Company prepared a valuation of the fair value of the 2013 Notes and the 2016 Notes (a Level 3 valuation) as of December 31, 2017. The value of these notes were estimated by implementing the binomial model. The liability component was valued based on the Income Approach. The following parameters were used:

	2013 Notes	2016 Notes
Stock price (USD)	0.6612	0.6612
Expected term	0.71	3.88
Risk free rate	1.66%	2.08%
Volatility	79.57%	68.89%
Yield	11.86%	11.89%

NOTE 10 - TAXES ON INCOME

a. The Company

Protalix BioTherapeutics, Inc. is taxed according to U.S. tax laws. The Company’s income is taxed in the United States at the rate of up to 39%.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act, which among other changes reduces the federal corporate tax rate to 21%.

NOTE 10 - TAXES ON INCOME (continued)**:**

b. Protalix Ltd.

The Israeli Subsidiary is taxed according to Israeli tax laws:

1. **Tax rates**

The income of the Israeli Subsidiary, other than income from "Approved Enterprises," is taxed in Israel at the regular corporate tax rates which were 26.5% for fiscal year 2015.

In January 2016, the Law for the Amendment of the Income Tax Ordinance (No. 216) was published, enacting a reduction of corporate tax rate beginning in 2016 and thereafter, from 26.5% to 25%.

In December 2016, the Economic Efficiency Law (Legislative Amendments for Implementing the Economic Policy for the 2017 and 2018 Budget Year), 2016 was published, introducing a gradual reduction in corporate tax rate from 25% to 23%. However, the law also included a temporary provision setting the corporate tax rate in 2017 at 24%. As a result, the corporate tax rate was 24% in 2017 and will be 23% in 2018 and thereafter.

Capital gain is subject to capital gain tax according to the corporate tax rate for the year during which the assets are sold.

2. **The Law for the Encouragement of Capital Investments, 1959 (the "Encouragement of Capital Investments Law")**

Under the Encouragement of Capital Investments Law, including Amendment No. 60 to the Encouragement of Capital Investments Law as published in April 2005, by virtue of the "Approved Enterprise" or "Benefited Enterprise" status the Israeli Subsidiary is entitled to various tax benefits as follows:

a. **Reduced tax rates**

Income derived from the Approved Enterprise during a 10-year period commencing upon the year in which the enterprise first realizes taxable income is tax exempt, provided that the maximum period to which it is restricted by the Encouragement of Capital Investments Law has not elapsed.

The Israeli Subsidiary has an "Approved Enterprise" plan since 2004 and "Benefited Enterprise" plan since 2009. The period of benefits in respect of the main enterprise of the Company has not yet commenced. The period during which the Company is entitled to benefits in connection with the Benefited Enterprise expires in 2021.

If the Israeli Subsidiary subsequently pays a dividend out of income derived from the "Approved Enterprise" or "Benefited Enterprise" during the tax exemption period, it will be subject to tax on the gross amount distributed (including the company tax on these amounts), at the rate which would have been applicable had such income not been exempted.

b. **Accelerated depreciation**

The Israeli Subsidiary is entitled to claim accelerated depreciation, as provided by Israeli law, in the first five years of operation of each asset, in respect of buildings, machinery and equipment used by the Approved Enterprise and the Benefited Enterprise.

NOTE 10 - TAXES ON INCOME (continued)**:**

c. **Conditions for entitlement to the benefits**

The Israeli Subsidiary's entitlement to the benefits described above is subject to its fulfilling the conditions stipulated by the law, rules and regulations published thereunder, and the instruments of approval for the specific investment in an approved enterprise. Failure by the Israeli Subsidiary to comply with these conditions may result in the cancellation of the benefits, in whole or in part, and the Subsidiary may be required to refund the amount of the benefits with interest. The Israeli Subsidiary received a final implementation approval with respect to its "Approved Enterprise" from the Investment Center.

d. **Amendment of the Law for the Encouragement of Capital Investments, 1959**

In recent years, several amendments have been made to the Encouragement of Capital Investments Law which have enabled new alternative benefit tracks, subject to certain conditions.

The Encouragement of Capital Investments Law was amended as part of the Economic Policy Law for the years 2011-2012, which was passed by the Israeli Knesset on December 29, 2010. The amendment sets alternative benefit tracks to those currently in effect under the provisions of the Encouragement of Capital Investments Law. On December 29, 2016, Amendment 73 to the Encouragement of Capital Investments Law was published. This amendment sets new benefit tracks, inter alia, "Preferred Technological Enterprise" and "Special Preferred Technological Enterprise" (the "Capital Investments Law Amendment").

The Company elected not to have the Capital Investments Law Amendment apply to the Company.

c. Tax losses carried forward to future years

As of December 31, 2017, the Company had aggregate net operating loss ("NOL") carry-forwards equal to approximately $207 million that are available to reduce future taxable income as follows:

1. **The Company**

The Company's carry-forward NOLs, equal to approximately $23 million (as of December 31, 2016, approximately $20 million), may be restricted under Section 382 of the Internal Revenue Code ("IRC"). IRC Section 382 applies whenever a corporation with NOL experiences an ownership change. As a result of IRC Section 382, the taxable income for any post change year that may be offset by a pre-change NOL may not exceed the general IRC Section 382 limitation, which is the fair market value of the pre-change entity multiplied by the IRC long-term tax exempt rate.

2. **Protalix Ltd.**

At December 31, 2017, the Israeli Subsidiary had approximately $184 million (as of December 31, 2016, approximately $133 million) of carry-forward NOLs that are available to reduce future taxable income with no limited period of use.

d. Deferred income taxes:

The components of the Company's net deferred tax assets at December 31, 2016 and 2017 were as follows:

	December 31,	
	2016	**2017**
(U.S. dollars in thousands)		
In respect of:		
Timing Differences	$ 3,520	$ 11,335
Net operating loss carry forwards	38,515	47,033
Valuation allowance	(42,035)	(58,368)
	-	-

Deferred taxes are computed using the tax rates expected to be in effect when those differences reverse.

NOTE 10 - TAXES ON INCOME (continued)**:**

e. Reconciliation of the theoretical tax expense to actual tax expense

The main reconciling item between the statutory tax rate of the Company and the effective rate is the provision for a full valuation allowance in respect of tax benefits from carry forward tax losses due to the uncertainty of the realization of such tax benefits (see above).

f. Tax assessments

In accordance with the Income Tax Ordinance, as of December 31, 2017, all of Protalix Ltd.'s tax assessments through tax year 2012 are considered final.

A summary of open tax years by major jurisdiction is presented below:

Jurisdiction:	Years:
Israel	2013-2017
United States (*)	2013-2017

(*) Includes federal, state and local (or similar provincial jurisdictions) tax positions.

NOTE 11 - SUPPLEMENTARY FINANCIAL STATEMENT INFORMATION

Balance sheets:

	December 31,	
	2016	2017
(U.S. dollars in thousands)		
a. Other assets:		
Institutions	$ 333	$ 394
State of Israel (see note 6a)	1,046	195
Restricted deposit	477	623
Prepaid expenses	416	433
Assets of discontinued operation	327	215
Sundry	49	74
	$ 2,648	$ 1,934

	December 31,	
	2016	2017
(U.S. dollars in thousands)		
b. Accounts payable and accruals – other:		
Payroll and related expenses	$ 1,190	$ 1,386
Interest payable	511	645
Provision for vacation	1,399	1,650
Accrued expenses	3,575	4,802
Royalties payable	226	301
Property and equipment suppliers	595	526
	$ 7,496	$ 9,310

Statements of operations:

	December 31,		
	2015	2016	2017
(U.S. dollars in thousands)			
Revenues:			
Pfizer		$ 5,226	$ 12,181
Brazil	$ 4,364	$ 3,973	$ 7,061
	$ 4,364	$ 9,199	$ 19,242

NOTE 12 - DISCONTINUED OPERATIONS

As mentioned in note 2, the Company accounted for the termination of the Pfizer Agreement and the sale of the license as a discontinued operation, in accordance with ASU No. 2014-08.

The following summarizes financial information related to the Company's discontinued operations, in the Company's consolidated statements of operations:

(U.S. dollars in thousands)	2015	2016
REVENUES	$ 48,674	$ 209
COMPANY'S SHARE IN COLLABORATION AGREEMENT	5,048	
COST OF REVENUES	(7,697)	(373)
GROSS PROFIT (LOSS)	46,025	(164)
RESEARCH AND DEVELOPMENT EXPENSES	(586)	
Less –reimbursements	545	
RESEARCH AND DEVELOPMENT EXPENSES, NET	(41)	
SELLING, GENERAL AND ADMINISTRATIVE EXPENSES	(564)	(25)
NET (LOSS) INCOME FOR THE YEAR FROM DISCONTINUED OPERATIONS	$ 45,420	$ (189)
GAIN ON THE DISPOSAL	39,899	
NET (LOSS) INCOME	$ 85,319	$ (189)

NOTE 13 - RELATED PARTY TRANSACTIONS

	Year ended December 31,		
	2015	2016	2017
(U.S. dollars in thousands)			
Compensation (including share based compensation) to the non-executive directors (includes the interim Chairman of the Board through 2015 and the Chairman of the Board for part of 2015)	$ 631	$ 560	$ 499

Exhibit 10.16

EXECUTION VERSION

Portions of this exhibit have been omitted pursuant to a request for confidential treatment pursuant to 17 C.F.R. Sections 200.80(b)(4) and 240.24b-2(b). The omitted portions, marked by [***], have been separately filed with the Securities and Exchange Commission.

EXCLUSIVE LICENSE AND SUPPLY AGREEMENT

by and between

CHIESI FARMACEUTICI S.p.A.

and

PROTALIX LTD.

October 17, 2017

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[***] Redacted pursuant to confidential treatment request.

[***] Redacted pursuant to confidential treatment request.

[***] Redacted pursuant to confidential treatment request.

EXCLUSIVE LICENSE AND SUPPLY AGREEMENT

This Exclusive License and Supply Agreement (this "Agreement") dated as of the 17th day of October, 2017 is made by and between Protalix Ltd., a limited liability company incorporated under the laws of Israel with offices located at 2 Snunit Street, Science Park, P.O. Box 455, Carmiel 20100, Israel ("Protalix"), and Chiesi Farmaceutici S.p.A., a company incorporated under the laws of Italy with offices located at Largo F. Belloli, 11/A - 43122 Parma, Italy ("Chiesi") (each, a "Party" and collectively, the "Parties").

WHEREAS, Protalix owns or otherwise controls certain patents, patent applications, technology, know-how and scientific and technical information relating to an enzyme replacement therapy for the treatment of Fabry Disease;

WHEREAS, Chiesi has extensive experience and expertise in the development and commercialization of drug products, and desires to acquire an exclusive license in the Territory (as defined below) to such patents, patent applications, technology, know-how and scientific and technical information, upon the terms and subject to the conditions set forth herein; and

WHEREAS, Protalix desires to grant such license to Chiesi.

NOW, THEREFORE, in consideration of the mutual covenants and agreements provided herein, Protalix and Chiesi hereby agree as follows:

Section 1. DEFINITIONS

For purposes of this Agreement, the following definitions shall be applicable:

1.1 "Acquisition" means, with respect to Protalix Parent (i) a completed Business Combination Transaction, unless, immediately following such completed Business Combination Transaction all or substantially all of the individuals and entities who were the beneficial owners of the outstanding voting securities of Protalix Parent immediately prior to such completed Business Combination Transaction beneficially own, directly or indirectly (including through one more holding companies or subsidiaries) at least fifty percent (50%) of the then-outstanding voting securities entitled to vote generally in the election of directors of the corporation or other entity resulting from such completed Business Combination Transaction (including a corporation or other entity that as a result of such transaction owns Protalix Parent or all or substantially all of a Protalix Parent's assets either directly or through one or more subsidiaries); (ii) the acquisition, directly or indirectly, by any Person (other than Chiesi or its Affiliates) of beneficial ownership of at least fifty percent (50%) or more of the outstanding voting securities of Protalix Parent, or (iii) the acquisition by a Third Party of all or substantially all of the assets of Protalix or Protalix Parent. As used in this Agreement, "voting securities" means any securities of Protalix Parent entitled to vote on the election of directors.

1.2 "Additional Studies" means [***].

[***] Redacted pursuant to confidential treatment request.

1.3 "Affiliate" means any entity directly or indirectly controlled by, controlling, or under common control with, a Party to this Agreement, but only for so long as such control shall continue. For purposes of this definition, "control" (including, with correlative meanings, "controlled by", "controlling" and "under common control with") means (a) possession, direct or indirect, of the power to direct or cause direction of the management or policies of an entity (whether through ownership of securities or other ownership interests, by contract or otherwise), or (b) beneficial ownership of at least fifty-percent (50%) of the voting securities or other ownership interest (whether directly or pursuant to any option, warrant or other similar arrangement) or other comparable equity interests of an entity, it being understood and agreed that for purposes of clause (a), neither ownership of voting securities or other ownership interests of an entity nor membership or representation on (if less than half of the members of) an entity's board of directors shall, by themselves, be presumed to constitute the power to direct or cause direction of the management or policies of such entity. With respect to the definition of Protalix Patent Rights and the definition of Protalix Technology, and with respect to the grant of license rights by Protalix to Chiesi under Section 2 in respect of such Protalix Patent Rights and Protalix Technology, "Affiliates" of Protalix shall exclude any Third Party that becomes an Affiliate due to such Third Party's acquisition of Protalix.

1.4 "Alliance Manager" shall have the meaning assigned to it in Section 3.3(a).

1.5 "Annual Cap" shall have the meaning assigned to it in Section 5.3(c).

1.6 "Annual Net Sales" means Net Sales for any Commercial Year.

1.7 "Applicable Rate" shall have the meaning assigned to it in Section 4.6(f).

1.8 "Audit" shall have the meaning assigned to it in Section 6.6.

1.9 "Average Sales Price" shall have the meaning assigned to it in Section 4.6(e).

1.10 "Business Combination Transaction" means any tender or exchange offer to Protalix Parent's stockholders, or any other offer or proposal to Protalix Parent or its stockholders for any merger, consolidation, restructuring, recapitalization or similar transaction with or involving Protalix Parent.

1.11 "Business Day" means a day other than a Saturday, Sunday, or bank or other public holiday in New York, New York, Parma, Italy or Carmiel, Israel.

1.12 "Buy-Back Payment" shall have the meaning assigned to it in Section 12.1(d).

1.13 "Calendar Quarter" means each of the four (4) three (3) month periods commencing on January 1 of any Calendar Year and ending on (respectively) March 31, June 30, September 30, and December 31 of such Calendar Year.

1.14 "Calendar Year" means the twelve (12) month period commencing on January 1 and ending on December 31 of any calendar year; provided that the first Calendar Year of the Term, shall commence on the Effective Date and end on December 31 of such calendar year and the last Calendar Year of the Term shall end on the date of expiration or termination of this Agreement.

1.15 "Change of Control" means the occurrence of any of the following: (a) any consolidation or merger of a Party with or into any Third Party, or any other corporate reorganization involving a Third Party, in which those persons or entities that are stockholders of such Party immediately prior to such consolidation, merger or reorganization own less than fifty percent (50%) of the surviving entity's voting power immediately after such consolidation, merger or reorganization; (b) a change in the legal or beneficial ownership of fifty percent (50%) or more of the voting securities of any Party (whether in a single transaction or series of related transactions) where, immediately after giving effect to such change, the legal or beneficial owner of more than fifty percent (50%) of the voting securities of such Party is a Third Party; or (c) the sale, transfer, lease, license or other disposition of all or substantially all of a Party's assets related to this Agreement in one or a series of related transactions to a Third Party.

1.16 "Chiesi Chair" means one of the Chiesi representatives on the Steering Committee designated by Chiesi as Chiesi's chair for Steering Committee Meetings.

1.17 "Chiesi Confidential Information" means all information or data of a proprietary or confidential nature relating to the Commercialization of the Licensed Product in the Field in the Territory, as well as any other information regarding the business, operations, Technology and Commercialization activities of Chiesi, whether in oral, written, graphic, machine-readable form, or any other form, (provided that data and information disclosed orally or visually are confirmed in writing by Chiesi within thirty (30) days after the date of such disclosure), disclosed and/or made available by or on behalf of Chiesi to Protalix, Protalix's Affiliates, and its and their respective directors, officers, employees, consultants, contractors and agents or otherwise acquired by any such Persons as a result of or in connection with this Agreement and/or the Parties' discussions (whether prior to the execution hereof or thereafter). Notwithstanding the foregoing, unmarked information and un-confirmed information will be considered Chiesi Confidential Information under this Agreement if a reasonable person familiar with the Licensed Product and given the nature of information and the circumstances of disclosure would consider such information to be confidential. Such information shall not be considered to be Chiesi Confidential Information to the extent that such information is: (a) as of the date of disclosure known to Protalix or its Affiliates, as demonstrable in any tangible medium in existence at the time of disclosure; or (b) wholly disclosed in published literature, or otherwise is or becomes generally known to the public through no breach by Protalix of this Agreement; or (c) obtained by Protalix or its Affiliates from a Third Party free from any obligation of confidentiality to Chiesi; or (d) independently developed by Protalix or its Affiliates without use of or reference to the Chiesi Confidential Information.

1.18 "Commercial Medical Affairs and Pharmacovigilance" has the meaning assigned to it in Section 3.6(d)(iv).

1.19 "Commercial Quarter" means each of the four (4) consecutive three (3) month periods of each Commercial Year, with the first Commercial Quarter commencing on first day of such Commercial Year (other than the first Commercial Quarter of the first Commercial Year, which shall commence on the first day of such Commercial Year, but end on the last day of the subsequent Calendar Quarter, i.e., including the period from Launch through the end of the subsequent full Calendar Quarter) and the last Commercial Quarter ending on the last day of such Commercial Year.

1.20 "Commercial Year" means (a) for the sole purpose of calculating whether an Event Milestone under Section 5.2 has been achieved, the twelve (12) month period commencing on either (i) the Launch date, or (ii) January 1 of the subsequent Calendar Year, if during such first twelve (12) month period starting from the Launch date, Event Milestone 2 has not been achieved; or (b) for all other purposes, the period commencing on the Launch Date and ending twelve (12) months after the first day of the subsequent Calendar Quarter, and (in each case (a) and (b)) any subsequent twelve (12) month period.

1.21 "Commercialization" means any and all activities directed to and including marketing, promoting, advertising, distributing, disposing, offering for sale, selling, Labelling and Packaging, final product release testing, exporting and importing of a Licensed Product for commercial sale (to the extent applicable). When used as a verb, "Commercialize" means to engage in Commercialization.

1.22 "Commercialization Plan" shall have the meaning set forth in Section 3.7(a).

1.23 "Commercially Reasonable Efforts" means, with respect to the efforts to be expended by a Party with respect to the objective that is the subject of such efforts, reasonable, good faith efforts and resources to accomplish such objective that such Party would normally use to accomplish a similar objective under similar circumstances, it being understood and agreed that with respect to the Commercialization of the Licensed Product in the Field in the Territory by Chiesi, such efforts shall be similar to those efforts and resources consistent with the usual practice of Chiesi in pursuing the Commercialization of drug products owned by it or to which it otherwise has rights that are of similar market potential as a Licensed Product in the Territory, taking into account all relevant factors, including the orphan drug status (if any) of the Licensed Product and other regulatory matters, safety and efficacy matters, product labeling or anticipated labeling, pricing, present and future market potential, past performance of the Licensed Product, past performance of Chiesi's own drug products that are of similar market potential (taking into account that the Licensed Product is intended for the treatment of a rare disease), financial return [***], medical and clinical considerations, present and future regulatory environment and competitive market conditions, all as measured by the facts and circumstances at the time such efforts are due. It is anticipated that the level of effort constituting Commercially Reasonable Efforts may change over time. With respect to the Commercialization of the Licensed Product in the Field in the Territory by Chiesi, such efforts shall include [***].

1.24 "Competing Product" means [***].

1.25 "Compliance Records" shall have the meaning assigned to it in Section 6.6.

1.26 "Compound" means (a) a plant cell-expressed recombinant form of human alpha-Galactosidase-A, including pegunigalsidase alfa (PRX-102) and (b) any analogs, derivatives and variants thereof.

[***] Redacted pursuant to confidential treatment request.

1.27 "Confidential Information" means the Protalix Confidential Information or the Chiesi Confidential Information, as applicable.

1.28 "Control" or "Controlled" means, with respect to any compound, material, information, or intellectual property right, that a Party owns or has a license to use, commercialize, manufacture, market, distribute or sell, and has the ability to grant to the other Party access and/or a license or a sublicense (as applicable under this Agreement) to, such compound, material, information, or intellectual property right as provided for herein without violating (a) the terms of any agreement or other arrangements with any Third Party existing before or after the Effective Date or (b) any Law applicable to such license or sublicense.

1.29 "Country" means any generally recognized sovereign entity.

1.30 "CMC" means, in respect of a regulatory filing, "Chemistry, Manufacturing, and Controls".

1.31 "Deferred Milestone" shall have the meaning assigned to it in Section 5.2(d).

1.32 "Development" or "Develop" means conducting non-clinical (including pre-clinical studies and CMC activities) and clinical trials (including the Ongoing Clinical Studies and the Required Studies), collecting, validating and analyzing pre-clinical and clinical trial data, preparing and submitting any regulatory filings prior to obtaining Regulatory Approvals, preparing the clinical and Manufacturing portions of any regulatory filing seeking Regulatory Approval (including portions relating to CMC), and regulatory affairs related to the foregoing. When used as a verb, "Develop" means to engage in Development. For clarity, Development does not include any regulatory affairs or commitments in respect of the Licensed Product in a Country following Regulatory Approval for such Licensed Product in such Country, or any of the foregoing in connection therewith. When used as a verb, "Developing" means to engage in Development.

1.33 "Development Costs" means Protalix's fully-loaded costs related to the Development of (and obtaining Regulatory Approval from the EMA for) the Licensed Product, excluding Patent Costs, and including any (a) direct, out-of-pocket costs and expenses, including clinical or medical grants, clinical laboratory fees, positive controls and the cost of pre-clinical and clinical studies conducted and services provided by contract research organizations, and (b) the conduct of clinical studies, including costs and expenses associated with data management, statistical designs and studies, document preparation and any and all other costs and expenses associated with preparing and submitting regulatory filings, obtaining (including, solely with respect to approvals granted upon specific conditions requiring the conduct of specified additional required studies to maintain such granted Regulatory Approval, maintaining) Regulatory Approval for the Licensed Product, and the conduct of the clinical Development program for the Licensed Product, including as set out in the Development Plan [***].

[***] Redacted pursuant to confidential treatment request.

1.34 "Development Costs Cap" shall have the meaning assigned to it in Section 5.3(b).

1.35 "Development Plan" shall have the meaning assigned to it in Section 3.1.

1.36 "Direct Sublicensee Revenue A" means all amounts paid or due from Sublicensees to Chiesi or its Affiliates [***].

1.37 "Direct Sublicensee Revenue B" means all amounts paid or due from Sublicensees to Chiesi or its [***].

1.38 "Drug Substance" means the Compound component of a pharmaceutical drug product.

1.39 "Drug Product" means unlabeled vials of Licensed Product [***], but not Labeling and Packaging.

1.40 "Early Access Program" means any program to provide patients with the Licensed Product prior to Regulatory Approval and prior to Launch in any Country in the Territory. Early Access Programs include, for example, any named patient programs in the EU and compassionate use or other expanded access programs in other Countries in the Territory.

1.41 "Effective Date" means the date of this Agreement.

1.42 "EMA" means the European Medicine Agency or any successor agency thereto.

1.43 "European Economic Area" means the member states of the EU together with Iceland, Norway and Liechtenstein.

1.44 "European Union" or "EU" means the Countries that are members of the European Union as of the Effective Date or that become members of the European Union thereafter, and includes, for the avoidance of doubt, any Countries that as of the Effective Date, or at any point during the Term thereafter, cease being members of the European Union, but that remain subject to any applicable Law of the EU.

1.45 "Event Milestone" shall have the meaning set forth in Section 5.2(a).

1.46 "Event Milestone 1a", "Event Milestone 1b", "Event Milestone 2", "Event Milestone 3", "Event Milestone 4", "Event Milestone 5", "Event Milestone 6", "Event Milestone 7", "Event Milestone 8", "Event Milestone 9", and "Event Milestone 10" shall each have the meanings assigned to those terms in Section 5.2(a).

[***] Redacted pursuant to confidential treatment request.

1.47 "Event Milestone 1a Studies" means [***].

1.48 "Event Milestone Payments" means the amounts set forth in Section 5.2(a) opposite the respective Event Milestones, subject to Sections 5.2(b), 5.2(c) and 5.2(d).

1.49 "Facility" means, as applicable, Protalix's Manufacturing facility and such other facilities used by Protalix (or its Affiliates, licensees, sublicensees or designees [***]) in the Manufacture or storage of (a) Drug Substance, (b) Drug Product or (c) materials utilized in the Manufacture of Drug Substance or Drug Product.

1.50 "Failure to Supply" shall have the meaning assigned to it in Section 4.14(a).

1.51 "Field" means enzyme replacement therapy for the treatment of Fabry Disease.

1.52 [***].

1.53 [***].

1.54 "Financial Records" shall have the meaning assigned to it in Section 6.6.

1.55 "Force Majeure Event" shall have the meaning assigned to it in Section 15.1.

1.56 "Forecast" shall have the meaning assigned to it in Section 4.5(a).

1.57 "FTE" shall mean one or more persons allocated on a full-time basis to the Commercialization of the Licensed Product in the Territory (both at a headquarter and country level, and including, for clarity, any product specialists, key asset managers, sales representatives, medical science liaisons, or medical, regulatory, market access and marketing personnel).

1.58 "GAAP" means United States generally accepted accounting principles consistently applied.

1.59 "Good Manufacturing Practices" or "GMP" means all applicable Good Manufacturing Practices including, (i) the applicable part of quality assurance to ensure that products are consistently produced and controlled in accordance with the quality standards appropriate for their intended use, as defined in European Commission Directive 2003/94/EC laying down the principals and guidelines of good manufacturing practice, (ii) the principles detailed in the U.S. Current Good Manufacturing Practices, 21 C.F.R. Sections 210 and 211, (iii) the Rules Governing Medicinal Products in the European Community, Volume IV Good Manufacturing Practice for Medicinal Products, (iv) the principles detailed in the ICH Q7A guidelines, and (v) the equivalent Laws in any relevant Country, each as may be amended and applicable from time to time.

[***] Redacted pursuant to confidential treatment request.

1.60 "Governmental Authority" means any court, agency, department, authority or other instrumentality of any national, supra national, state, county, city or other political subdivision.

1.61 "ICC Rules" shall have the meaning assigned to it in Section 14.2(b).

1.62 "Included Sublicensee Revenue" means, with respect to a Licensed [***].

1.63 "IND" means (i) an investigational new drug application as defined in 21 CFR 312.3 and all amendments and supplements thereto filed with the FDA or (ii) an equivalent application filed with any equivalent foreign agency or Governmental Authority including all documents, data and other information concerning use of an investigational pharmaceutical product which are necessary for gaining authorization from such equivalent foreign agency or Governmental Authority to ship and use such product in clinical investigations.

1.64 "Indemnified Party" shall have the meaning assigned to it in Section 13.4(a).

1.65 "Indemnifying Party" shall have the meaning assigned to it in Section 13.4(a).

1.66 "Initial Forecast" shall have the meaning assigned to it in Section 4.5(a).

1.67 "Initiation" means, with respect to the Phase 1 Clinical Trial for a New Use, the first study-specific screening activities.

1.68 "Joint Legal Counsel" shall have the meaning assigned to it in Section 14.3(a).

1.69 "Joint Legal Opinion" shall have the meaning assigned to it in Section 14.3(a).

1.70 "Label" means, with respect to a Licensed Product, all labels and other written, printed, or graphic matter (a) on the Licensed Product containers or wrappers, or (b) accompanying the Licensed Product.

1.71 "Labeling and Packaging" means the final product labeling and packaging of the Drug Product, including materials to be inserted such as patient inserts, patient medication guides, professional inserts and any other written, printed or graphic materials accompanying the Drug Product.

1.72 "Launch" with respect to any Country or jurisdiction in the Territory, means the first shipment of a Licensed Product in commercial quantities for commercial sale by Chiesi, its Affiliates or its Sublicensees to a Third Party in such Country or jurisdiction in the Territory after receipt of the first Regulatory Approval (and Price Approval and Governmental Authority or Third Party reimbursement approval where applicable and required) for such Licensed Product in such Country. "Launched", when used in respect of the Licensed Product in a Country, means that the Launch of such Licensed Product has already occurred in such Country.

[***] Redacted pursuant to confidential treatment request.

1.73 "Laws" means all laws, statutes, rules, regulations, codes, administrative or judicial orders, judgments, decrees, injunctions and/or ordinances of any Governmental Authority, and common law or other legal requirements of any kind, whether currently in existence or hereafter promulgated, enacted, adopted or amended.

1.74 "Licensed Product" means any finished dosage form of a drug product that contains the Drug Substance and either: (a) the manufacture, sale, offer for sale, importation, or use of which (i) would, absent the license granted by Protalix to Chiesi herein, infringe at least one Valid Claim of a Protalix Patent Right or (ii) embodies, incorporates or uses Protalix Technology, or (b) is supplied by Protalix to Chiesi under this Agreement as Drug Product or, after the [***] (subject to Chiesi performing Labeling and Packaging in respect of such Drug Product and, after [***].

1.75 "Long Range Forecast" shall have the meaning assigned to it in Section 4.5(b).

1.76 "Manufacture" or "Manufacturing" means all activities related to the manufacturing of the Drug Substance, Drug Product or Licensed Product (as applicable), and/or any ingredient thereof, including manufacturing for clinical use or commercial sale, in-process and finished product testing, the final product labeling and packaging of the product, release of product, quality assurance activities related to manufacturing and release of product and ongoing stability tests and regulatory activities related to any of the foregoing.

1.77 "Manufacturing Certificate of Analysis" shall have the meaning assigned to it in Section 4.8(a)(i).

1.78 "Material Change" shall have the meaning assigned to it in Section 7.2(a).

1.79 "Maximum Order Quantity" shall have the meaning assigned to it in Section 4.6(i).

1.80 "Minimum Batch Size" means the minimum batch size for Drug Product (as may be updated by Protalix from time to time, in its sole discretion for any variance of [***] or less, and only with Chiesi's prior consent for any variance of more than [****], such consent not to be unreasonably withheld, conditioned or delayed), which currently is [***] of Licensed Product.

1.81 "Minimum Payment" shall have the meaning assigned to it in Section 4.6(h).

1.82 "NDA" means a New Drug Application or Biologics License Application (as applicable) filed with the United States Food and Drug Administration (or any successor agency thereto) with respect to a drug product or an analogous application or filing with any Regulatory Authority outside of the United States (including any supra-national entity such as the European Union) for the purpose of obtaining approval to market and sell a drug product in such jurisdiction.

[***] Redacted pursuant to confidential treatment request.

1.83 "Negotiation Period" means the ninety (90)-day period beginning on the date as set forth in Section 2.5(b).

1.84 "Net Sales" means, with respect to a Licensed Product, the gross amounts invoiced by Chiesi or its Affiliates for sale of Licensed Product, less the following customary deductions, determined in accordance with GAAP and standard internal policies and procedures and accounting standards and methods consistently applied throughout Chiesi's organization, to the extent specifically and solely allocated to such Licensed Product and actually taken, paid, accrued, allowed, included or allocated: [***].

1.85 "New Indication" means a distinct type of disease or medical condition in humans to which a Licensed Product is directed that is not the Field.

1.86 [***].

1.87 "New Use" shall have the meaning assigned to it in Section 2.5(a).

1.88 "Notice of Non-Conformance" shall have the meaning assigned to it in Section 4.8(a)(i).

1.89 "Ongoing Clinical Study" means [***].

1.90 "Other Patent Challenge" shall have the meaning assigned to it in Section 2.6(c).

1.91 "Other Sublicensee Revenue" means [***].

1.92 "Other Sublicensee Revenue Payment" [***].

1.93 "Outside of the Scope Product" shall have the meaning assigned to it in Section 7.2(a).

1.94 "Patent Application" means any application for a Patent.

1.95 "Patent Costs" means any and all costs and expenses incurred by Protalix in respect of the exercise of any of its rights and obligations under Section 7 of this Agreement.

1.96 "Patent Rights" means Patents and Patent Applications.

1.97 "Patents" means issued patents, whether domestic or foreign, including all continuations, continuations-in-part, divisions, provisionals and renewals, and letters of patent granted with respect to any of the foregoing, patents of addition, supplementary protection certificates, registration or confirmation patents and all reissues, re-examination and extensions thereof.

1.98 "Patent Ownership Challenge" shall have the meaning assigned to it in Section 2.6(a).

[***] Redacted pursuant to confidential treatment request.

1.99 "PCT" means the Patent Cooperation Treaty, opened for signature June 19, 1970, 28 U.S.T. 7645.

1.100 "Person" means an individual, corporation, partnership, company, joint venture, unincorporated organization, limited liability company or partnership, sole proprietorship, association, bank, trust company or trust, whether or not legal entities, or any Governmental Authority.

1.101 "Pharmacovigilance Agreement" shall have the meaning assigned to it in Section 3.6(f).

1.102 "Phase 1 Clinical Trial" means a human clinical trial of the initial Licensed Product that would satisfy the requirements of 21 C.F.R. § 312.21(a) or any other equivalent foreign requirements.

1.103 "Post-Approval Studies" means any pre-clinical or clinical studies for a Licensed Product (or for the Drug Substance therein) commenced after receipt of Regulatory Approval for such Licensed Product, that are not Required Studies.

1.104 "Price" means the price to be charged by Protalix and paid by Chiesi for Drug Product [***] sold by Protalix to Chiesi under this Agreement as specifically determined in accordance with Section 4.6.

1.105 "Price Approval" means, in any Country where a Governmental Authority authorizes reimbursement for, or approves or determines pricing for, drug products, receipt (or, if required to make such authorization, approval or determination effective, publication) of such reimbursement authorization or pricing approval or determination (as the case may be).

1.106 "Product Specifications" means those Manufacturing, performance, quality - control release, and other specifications for Drug Substance, Drug Product or Licensed Product in the Territory, which are initially as set forth in the applicable Regulatory Approval for a Licensed Product, as such specifications may be amended from time to time pursuant to the terms of this Agreement.

1.107 "Protalix Chair" means one of the Protalix representatives on the Steering Committee designated by Protalix as Protalix's chair for Steering Committee Meetings.

[***] Redacted pursuant to confidential treatment request.

1.108 "Protalix Confidential Information" means all information or data of a proprietary or confidential nature relating to the Protalix Technology, Compound or Licensed Product as well as any other information, including proprietary information and materials, regarding the business, operations, research, Technology and the supply, Manufacture, Development and Commercialization activities of Protalix, whether in oral, written, graphic, machine-readable form, or any other form, (provided that data and information disclosed orally or visually are confirmed in writing by Protalix within thirty (30) days after the date of such disclosure), disclosed and/or made available by or on behalf of Protalix to Chiesi, Chiesi's Affiliates, and its and their respective directors, officers, employees, consultants, contractors and agents or otherwise acquired by any such Persons as a result of or in connection with this Agreement and/or the Parties' discussions (whether prior to the execution hereof or thereafter). Notwithstanding the foregoing, unmarked information and un-confirmed information will be considered Protalix Confidential Information under this Agreement if a reasonable person familiar with the Licensed Product and given the nature of information and the circumstances of disclosure would consider such information to be confidential. Such information shall not be considered to be Protalix Confidential Information to the extent that such information is: (a) as of the date of disclosure known to Chiesi or its Affiliates, as demonstrable in any tangible medium in existence at the time of disclosure; or (b) wholly disclosed in published literature, or otherwise is or becomes generally known to the public through no breach by Chiesi of this Agreement; or (c) obtained by Chiesi or its Affiliates from a Third Party free from any obligation of confidentiality to Protalix; or (d) independently developed by Chiesi or its Affiliates without use of or reference to the Protalix Confidential Information.

1.109 "Protalix Parent" means Protalix Biotherapeutics, Inc.

1.110 "Protalix Patent Rights" means all Patent Rights owned or otherwise Controlled by Protalix or any of its Affiliates as of the Effective Date or at any time during the Term that claim the composition of matter, manufacture or use of the Compound, Drug Substance or a drug product that contains Drug Substance, including the Patent Rights listed in Exhibit A.

1.111 "Protalix System Patent Rights" means Protalix Patent Rights that relate primarily to the System.

1.112 "Protalix Trademarks" shall have the meaning assigned to it in Section 3.10.

1.113 "Protalix Technology" means any Technology owned or otherwise Controlled by Protalix or any of its Affiliates as of the Effective Date or at any time during the Term that is necessary or useful for the Development, Manufacture, use or Commercialization of Compound, Drug Substance or a drug product that contains Drug Substance, including the System.

1.114 "Purchase Order" shall have the meaning assigned to it in Section 4.5(a).

1.115 "Quality Agreement" means the Quality Agreement(s) to be entered into between Protalix and Chiesi (which the Parties shall use Commercially Reasonable Efforts to finalize within one hundred and eighty (180) days from the Effective Date) with respect to the Drug Product (and, after the [***].

1.116 [***]

1.117 [***]

[***] Redacted pursuant to confidential treatment request.

1.118 "Reconciliation Adjustment" shall have the meaning assigned to it in Section 4.6(h).

1.119 "Referent Person" shall have the meaning assigned to it in Section 8.5.

1.120 "Registry" shall mean an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes and meets the requirements of the applicable Regulatory Authority.

1.121 "Reimbursed Party" shall have the meaning assigned to it in Section 5.3(h).

1.122 "Reimbursing Party" shall have the meaning assigned to it in Section 5.3(h).

1.123 "Regulatory Approval" means any and all approvals, with respect to any Country, or authorizations (other than Price Approvals) of a Regulatory Authority, that are necessary for the commercial Manufacture, distribution, use, marketing or sale of a drug product in such Country, including but not limited to any NDAs.

1.124 "Regulatory Authority" means, in respect of a particular Country or jurisdiction, the Governmental Authority having responsibility for granting Regulatory Approvals in such Country or jurisdiction.

1.125 "Regulatory Exclusivity" means any rights or protections which are recognized, afforded or granted by a Regulatory Authority in any Country or region of the Territory, in association with the Regulatory Approval of a Licensed Product, providing such Licensed Product: (a) a period of marketing exclusivity, during which the Regulatory Authority recognizing, affording or granting such marketing exclusivity will refrain from either reviewing or approving a marketing authorization application or similar regulatory submission, submitted by a Person other than Chiesi, its Affiliates or its Sublicensees seeking to market a drug product in which the Drug Substance is the primary ingredient, or during which such an application or submission may be reviewed or approved by a Regulatory Authority, but the product may not be placed on the market or (b) a period of data exclusivity, during which a Person, other than Chiesi, its Affiliates or its Sublicensees, seeking to market a drug product in which the Drug Substance is the primary ingredient, is precluded from either referencing or relying upon a Licensed Product's clinical dossier or relying on previous findings of safety or effectiveness with respect to a Licensed Product to support the submission, review or approval of a marketing authorization application or similar regulatory submission before the applicable Regulatory Authority. Regulatory Exclusivity shall include rights conferred in the European Union/European Economic Area pursuant to Section 10.1 of Directive 2001/EC/83 or section 14.11 of Regulation (EC) No. 726/2004.

1.126 [***].

[***] Redacted pursuant to confidential treatment request.

1.127 "Required Registry" shall have the meaning assigned to it in Section 3.2(c).

1.128 [***].

1.129 [***].

1.130 [***].

1.131 [****].

1.132 "Safety Stock" shall have the meaning assigned to it in Section 4.12(a).

1.133 "Safety Stock Amount" shall have the meaning assigned to it in Section 4.12(a).

1.134 "Shortage" shall have the meaning assigned to it in Section 4.11.

1.135 [***].

1.136 "Standby License" shall have the meaning assigned to in Section 2.2(d).

1.137 "Steering Committee" shall have the meaning assigned to it in Section 3.3(a).

1.138 "Steering Committee Meeting" shall have the meaning assigned to it in Section 3.3(b).

1.139 "Sublicense" means the grant by Chiesi of a sublicense under, or an agreement of Chiesi not to assert, any of the rights licensed by Protalix to Chiesi pursuant to Section 2.1.

1.140 "Sublicensee" means a Third Party to whom Chiesi has granted a Sublicense in accordance with the terms and conditions set forth herein.

1.141 "Sublicensee Net Sales" means, with respect to a Licensed Product, the gross amounts invoiced by Sublicensees for sale of Licensed Product, less the following customary deductions, determined in accordance with GAAP and standard internal policies and procedures and accounting standards and methods consistently applied throughout such Sublicensee's organization, to the extent specifically and solely allocated to such Licensed Product and actually taken, paid, accrued, allowed, included or allocated: [***].

[***] Redacted pursuant to confidential treatment request.

1.142 "Sublicense Threshold" means an amount, where [***].

1.144 "System" means Protalix's proprietary protein expression system, ProCellEx™.

1.145 "Technology" means proprietary materials, technology, data, results and non-public technical, scientific and clinical information, in any tangible or intangible form, including know-how, expertise, trade secrets, practices, techniques, methods, processes, developments, specifications, formulations, formulae, including any intellectual property rights embodying any of the foregoing, but excluding Patent Rights.

1.146 "Term" shall have the meaning assigned to it in Section 11.

1.147 "Territory" means the entire world, excluding the United States (and its territories and possessions).

1.148 "Third Party" means any Person other than Chiesi, Protalix, or any of their respective Affiliates.

1.149 "Third Party Claim" shall have the meaning assigned to it in Section 13.4(a).

1.150 "Third Party License" means each license agreement between Protalix and a Third Party pursuant to which or from which Protalix licenses Protalix Patent Rights or Protalix Technology, including those listed on Exhibit B.

1.151 "Top 5 EU" means each of the following Countries: [***].

1.152 "United States" or "U.S." means the United States of America, its territories and possessions.

1.153 [***].

1.154 "Valid Claim" means (a) a claim of an issued and unexpired Patent (including the term of any patent term extension, supplemental protection certificate, renewal or other extension) which has not been held unpatentable, invalid or unenforceable in a final decision of a court or other Governmental Authority of competent jurisdiction from which no appeal may be or has been taken, and which has not been admitted to be invalid or unenforceable through reissue, re-examination or disclaimer; or (b) a claim of a Patent Application, which claim has been pending less than seven (7) years from the original priority date of such claim in a given jurisdiction, unless or until such claim thereafter issues as a claim of an issued Patent (from and after which time the same shall be deemed a Valid Claim subject to paragraph (a) above).

1.155 "Yearly Reconciliation" shall have the meaning assigned to it in Section 4.6(h).

[***] Redacted pursuant to confidential treatment request.

1.156 Construction. Except where expressly stated otherwise in this Agreement, the following rules of interpretation apply to this Agreement: (a) "include", "includes" and "including" are not limiting and mean include, includes and including, without limitation; (b) definitions contained in this Agreement are applicable to the singular as well as the plural forms of such terms; (c) references to an agreement, statute or instrument mean such agreement, statute or instrument as from time to time amended, modified or supplemented; (d) references to a Person are also to its permitted successors and assigns; (e) references to an "Article", "Section", "Exhibit" or "Schedule" refer to an Article or Section of, or any Exhibit or Schedule to, this Agreement unless otherwise indicated; (f) the word "will" shall be construed to have the same meaning and effect as the word "shall"; and (g) the word "any" shall mean "any and all" unless otherwise indicated by context.

Section 2. LICENSE

2.1 Exclusive License. Subject to the terms of this Agreement, including Section 2.2, Protalix hereby grants to Chiesi, and Chiesi hereby accepts, an exclusive (including as to Protalix and its Affiliates, except as set forth in Section 2.2), non-transferable, license during the Term, solely in the Territory and within the Field, including the right to Sublicense (solely as permitted under and in accordance with Section 2.4):

(a) under the Protalix Patent Rights to (i) Commercialize the Licensed Product in the Field in the Territory, (ii) on a non-exclusive basis, following the completion of [***] (if any), carry out [***] activities with respect to the Licensed Product in the Field in the Territory, and (iii) seek and obtain Regulatory Approval, Price Approval and Governmental Authority or Third Party reimbursement approval (where applicable and required) for the Licensed Product in the Field in the Territory (in each case, in accordance with Section 3); and

(b) to use Protalix Technology as necessary to (i) seek and obtain Regulatory Approval, Price Approval and Governmental Authority or Third Party reimbursement approval (where applicable and required) for the Licensed Product in the Field in the Territory, including following the transfer contemplated by Section 3.6(c), to prepare and submit any regulatory filings and communicate with Regulatory Authorities with respect to the Licensed Product in the Field in the Territory (in each case, in accordance with Section 3), (ii) following completion of the transfers contemplated by Section 3.6(d)(iv), on a non-exclusive basis, carry out its Commercial Medical Affairs and Pharmacovigilance responsibilities, (iii) on a non-exclusive basis, following the completion of [***] (if any), carry out [***] activities with respect to the Licensed Product in the Field in the Territory, and (iv) Commercialize the Licensed Product in the Field in the Territory.

2.2 Other License Provisions.

(a) The licenses granted to Chiesi pursuant to Section 2.1 shall be co-exclusive with Protalix to the extent it is necessary or useful for Protalix to perform its obligations under this Agreement.

[***] Redacted pursuant to confidential treatment request.

(b) The Parties expressly acknowledge and agree that, the exclusivity grant in favor of Chiesi in Section 2.1 shall not be construed as limiting (i) Protalix's right to Develop or Manufacture the Licensed Product (or the Compound, Drug Substance or Drug Product for use in the Licensed Product), (ii) Protalix's right to Commercialize the Licensed Product outside of the Field or outside of the Territory, or (iii) any of Protalix's rights in respect of the Licensed Product (including its rights under the Protalix Patent Rights) outside of the Territory.

(c) For purposes of clarity, Chiesi acknowledges that in the event Protalix does not have exclusive rights to Protalix Patent Rights or Protalix Technology licensed or obtained by Protalix from Third Parties vis à vis the Third Party licensor, Chiesi's rights to such Protalix Patent Rights or Protalix Technology under the sublicenses granted under Section 2.1 would not be exclusive vis à vis the Third Party licensor or its licensees (but would have the same scope of rights licensed or obtained by Protalix thereunder to the extent such rights are granted to Chiesi by Protalix hereunder and permitted to be granted by Protalix to Chiesi under such Third Party License).

(d) Protalix shall use Commercially Reasonable Efforts to obtain an agreement between Chiesi and such Third Party licensor pursuant to which, in the event that the applicable Third Party License is terminated for any reason, such Third Party licensor would grant Chiesi a license to the Protalix Patent Rights or Protalix Technology (as applicable) that Protalix has licensed from that Third Party licensor to the extent included in, and solely for the purpose of, the license granted to Chiesi hereunder (each such agreement, a "Standby License").

2.3 Non-Assertion of Rights.

(a) During the Term, Chiesi shall not, and shall cause its Affiliates not to, assert any Patent Rights or Technology owned or Controlled by Chiesi and its Affiliates against Protalix, its Affiliates or permitted sublicensees for (i) exercising its rights and performing its obligations pursuant to this Agreement or (ii) using, making, having made, selling, offering for sale, supplying, causing to be supplied and importing the Drug Substance or Licensed Product outside the Territory.

(b) The covenant not to sue in Section 2.3(a) shall inure to the benefit of any permitted assignee of this Agreement pursuant to Section 15.6.

(c) During the Term, Protalix shall not, and shall cause its Affiliates not to, assert any Protalix System Patent Rights owned or Controlled by Protalix and its Affiliates against Chiesi, its Affiliates or permitted Sublicensees for exercising its rights and performing its obligations pursuant to and in accordance with this Agreement and the license granted herein. Such covenant not to sue shall inure to the benefit of any permitted assignee of this Agreement pursuant to Section 15.6.

2.4 Sublicensing and Subcontracting.

(a) Chiesi may only grant Sublicenses to (i) its Affiliates, which Sublicense shall automatically terminate when such Affiliate ceases to be an Affiliate of Chiesi, and (ii) reputable Third Parties [***].

(b) Each Sublicense granted by Chiesi pursuant to Section 2.4(a) shall be subject and subordinate to the terms and conditions of this Agreement and shall contain terms and conditions consistent with, and at least as protective of Protalix, the Protalix Patent Rights, the Protalix Technology and the Protalix Confidential Information as, those set forth in this Agreement, and shall not in any way diminish, reduce or eliminate any of Chiesi's obligations under this Agreement. Without limiting the foregoing, each Sublicense agreement with permitted Sublicensees shall contain the following provisions: (i) a requirement that such Sublicensee submit applicable sales or other reports consistent with the requirements set forth in Section 6.1, (ii) a requirement to keep books and records, and permit Protalix to audit (either directly or through an independent auditor) such books and records, consistent with the requirement set forth in Section 6.6, (iii) a requirement that such Sublicensee comply with the confidentiality and non-use provisions of Section 8 with respect to both Parties' Confidential Information, (iv) a requirement to comply with all other applicable terms of this Agreement, and (v) a provision prohibiting such Sublicensee from further sublicensing the rights granted to it under the Sublicense. Chiesi shall provide Protalix with a copy of each such Sublicense agreement within thirty (30) days after the execution thereof; provided that Chiesi may redact confidential information from such Sublicense agreement that is not reasonably necessary to demonstrate Chiesi's compliance with the obligations set forth in this Agreement, including this Section 2.4(b).

(i) Right to Subcontract. Each Party may, subject to Section 4.3 and Section 8, subcontract its rights and obligations under this Agreement to an Affiliate or Third Party as it would in the normal course of its business without the prior written consent of the other Party, except that Chiesi may not subcontract to any Third Party (including sub-distributors and contract sales organizations), without the prior written consent of Protalix, such consent not to be unreasonably delayed, withheld or conditioned, its rights or obligations to promote the Licensed Product (and the majority of the members of Chiesi's sales force shall be employees of Chiesi or its Affiliate).

(c) Liability for Affiliates, Sublicensees and Subcontractors. Each Party shall ensure that each of its Affiliates, permitted Sublicensees (in the case of Chiesi) and permitted subcontractors accepts and complies with all of the applicable terms and conditions of this Agreement as if such Affiliates or permitted Sublicensees or subcontractors were Parties to this Agreement and each Party shall remain fully responsible and fully liable for its Affiliates' and permitted Sublicensees' or subcontractors' performance under this Agreement.

[***] Redacted pursuant to confidential treatment request.

2.5 New Indications.

(a) Protalix shall notify the Steering Committee, at least every six (6) months during the Term, of any material updates with respect to any material Development activities, with respect to the Licensed Product for a New Indication (a "New Use").

(b) [***].

(c) [***].

2.6 Patent Challenges.

(a) During the Term of this Agreement, Chiesi and its Affiliates hereby covenant and agree not to, directly or indirectly, commence any legal proceeding, or to, directly or indirectly, provide support or assistance in respect of any legal proceeding commenced by a Third Party, that challenges the ownership of any Protalix Patent Right, including any Protalix System Patent Right, to the extent such Protalix Patent Right relates to the Compound or Licensed Product or the Development, Manufacture or Commercialization of the Compound or Licensed Product (a "Patent Ownership Challenge").

(b) If Chiesi, its Affiliate or Sublicensee directly or indirectly commences (or provides any support or assistance in respect of) any Patent Ownership Challenge or any Other Patent Challenge, Protalix shall have the right to immediately terminate this Agreement by written notice effective upon receipt by Chiesi. The foregoing right of Protalix to terminate this Agreement shall not apply to any such challenge that arises out of or is in connection with any legal action commenced by Protalix against Chiesi, in which Protalix asserts any Protalix Patent Rights or other Patent Rights against Chiesi, whether arising out of or in connection with this Agreement or otherwise.

(c) For the purpose of this Section 2.6, the term "Other Patent Challenges" means any legal proceeding that challenges the validity or enforceability of any Protalix Patent Right, including any Protalix System Patent Right, to the extent such Protalix Patent Right relates to the Compound or Licensed Product or the Development, Manufacture or Commercialization of the Compound or Licensed Product ("Other Patent Challenge").

(d) Without limiting the generality of the foregoing, Chiesi specifically agrees that filing a request for re-examination, knowingly copying patent claims so as to institute an interference, or filing an opposition with respect to any of the Protalix Patent Rights shall be deemed an Other Patent Challenge hereunder.

[***] Redacted pursuant to confidential treatment request.

2.7 No Implied License. Except for the licenses and other rights expressly granted to Chiesi herein, all right, title and interest in and to the Protalix Patent Rights, Protalix Technology, and Protalix Confidential Information (and all modifications, derivatives and improvements thereof), and any other rights of Protalix and its Affiliates not expressly granted to Chiesi hereunder (including, for clarity, all of the foregoing with respect to any Outside of the Scope Products), shall remain solely with Protalix, its Affiliates and its Third Party licensors, as applicable. To the extent any such rights vest in Chiesi (by operation of Chiesi's exercise of its step-in rights under Section 3.2(b) or otherwise), then Chiesi shall, and hereby does, irrevocably assign all such right, title and interest in and to the Protalix Patent Rights, Protalix Technology, and Protalix Confidential Information (and all modifications, derivatives and improvements thereof) to Protalix, and hereby acknowledges and agrees that any such rights are and shall remain owned solely by Protalix. Except as expressly provided in this Section 2 or elsewhere in this Agreement, neither Party will be deemed by this Agreement to have been granted any license or other rights to the other Party's intellectual property rights, either expressly or by implication, estoppel or otherwise. Notwithstanding anything to the contrary in this Agreement, the Parties acknowledge and agree that the Development and Commercialization of any Outside of the Scope Products (including any New Uses) shall not be within the scope of the licenses granted to Chiesi pursuant to Section 2 hereunder (except as expressly provided in Section 2.5).

Section 3. DEVELOPMENT, REGULATORY APPROVALS AND MARKETING

3.1 Development Plan. The Development of the Licensed Product in the Field shall be governed by a development plan to be prepared by Protalix that describes the proposed Development program of the Licensed Product in the Field, including the continuing conduct by Protalix of each Ongoing Clinical Study (the "Development Plan"). [***]

3.2 Development Responsibilities.

(a) Clinical Development by Protalix. Pursuant to the Development Plan, and subject to the oversight of the Steering Committee, Protalix will be responsible for the Development of the Licensed Product in the Field, including continuing to conduct the Ongoing Clinical Studies. Protalix will also be responsible for preparing and promptly submitting to Chiesi the clinical sections of any regulatory filings in respect of obtaining Regulatory Approval with the EMA for the Licensed Product and, subject to Chiesi's approval rights in respect of such regulatory filing as a whole, Protalix shall consider in good faith any proposed revision reasonably made by Chiesi thereto.

(b) Chiesi Step-in Right. Notwithstanding Section 3.2(a), but subject to Section 3.2(f), in the event of a delay, for reasons within Protalix's reasonable control (and, for clarity, not for reasons outside Protalix's reasonable control, i.e., a Force Majeure Event [***], of more than [***] (as compared to the timelines expressly identified as "step-in" timelines in the Development Plan) that occurs in the course of conducting the Ongoing Clinical Studies and/or a Required Study being conducted by Protalix, Chiesi shall have the right (subject to Section 5.3(g)) to assume responsibility for conducting, or having conducted on its behalf, and to be the sponsor of, such Ongoing Clinical Studies and/or [***] (as applicable), upon no less than sixty (60) days' prior written notice to Protalix. Promptly following Protalix's receipt of such notice, the Parties shall cooperate in good faith to develop a written plan for the orderly transfer of responsibility for conducting the Ongoing Clinical Studies and/or [***] to Chiesi, with due regard for patient safety and the rights of any subjects that are participants in the Ongoing Clinical Studies and/or the [***], and in compliance with all applicable Laws and agreements with Third Parties; provided, that Chiesi shall assume sole responsibility for the conduct of, and any liability arising out of, the conduct of the Ongoing Clinical Studies and/or [***] immediately upon the completion of such transfer, including responsibility for all Development Costs (subject to Section 5.3(g)).

[***] Redacted pursuant to confidential treatment request.

(c) Chiesi's Regulatory Approval Responsibilities. Except as described in Sections 3.2(a) and 3.2(b), Chiesi shall be responsible for conducting [***]. For the avoidance of doubt, Chiesi shall be solely responsible for conducting [***].

(d) Chiesi's Post-Regulatory Approval Responsibilities. Except as described in Sections 3.2(a) and 3.2(b), immediately following any obtained Regulatory Approval for which Chiesi submitted a regulatory filing in its own name in a given Country in the Territory, Chiesi will assume sole responsibility for (i) the Commercialization of the Licensed Product in the Field in such Country in the Territory, and (ii) all post-approval commitments in respect of the Licensed Product in the Field in such Country in the Territory, including interactions or communications with the applicable Regulatory Authority (subject to Section 3.6(g)), the conduct of any Post-Approval Studies (subject to Section 5.3(f)), pharmacovigilance reporting (subject to Section 3.6(f)), medical affairs (subject to Section 3.6(d)(iv)) and related requirements.

(e) Responsibility for Costs. Each Party's responsibility for paying the costs associated with such Development activities is set forth in Section 5.3.

(f) Rights Outside the Territory. Notwithstanding anything to the contrary herein, Chiesi acknowledges and agrees that, at all relevant times during the Term, Protalix shall remain the sole and unencumbered owner of any IND, NDA or any other regulatory filing relating to the Compound, Drug Substance or Licensed Product outside of the Territory. Prior to (and as a condition of) the exercise of any step-in right under Section 3.2(b), Chiesi must first take all necessary steps, to the extent required, to ensure that Protalix remains, and is able to remain, the sole and unencumbered owner of any IND, NDA or any other regulatory filing relating to the Compound, Drug Substance or Licensed Product outside of the Territory.

3.3 Steering Committee.

(a) Formation and Membership. The Parties shall, within sixty (60) days after the Effective Date, form a steering committee (the "Steering Committee"). The Steering Committee shall consist of three (3) representatives appointed by Protalix and three (3) representatives appointed by Chiesi; provided that at least one (1) person appointed by each Party is a senior officer of such Party, vested with the appropriate decision-making and resource-allocating authority, and the requisite experience, to participate in discussion of, and decide on, the matters set out in Section 3.3(c) below. Each Party shall nominate a representative as contact point to discuss the agenda (such representative, the "Alliance Manager"), who can be selected or not among the three members nominated by the Parties as Steering Committee representatives. The Steering Committee shall be chaired by the Protalix Chair. From time to time, each Party may substitute its representatives on the Steering Committee in its sole discretion (but subject to the terms of this section), effective upon written notice to the other Party of such change. Additional representatives or consultants may from time to time, in the Steering Committee's discretion, be invited to attend Steering Committee Meetings, subject to such representatives' and consultants' written agreement to comply with the requirements of Section 8.

[***] Redacted pursuant to confidential treatment request.

(b) Meetings. During the Term, the Steering Committee shall meet at least once each Calendar Quarter or as otherwise determined by the Parties (each such meeting, a "Steering Committee Meeting"). Upon the reasonable request of the Steering Committee, Protalix will provide written materials relating to its activities under the Development Plan in advance of a Steering Committee Meeting. All Steering Committee Meetings may be conducted in person, by videoconference or by teleconference at such times and such Chiesi or Protalix locations as shall be determined by the Steering Committee Alliance Managers. In-person meetings of the Steering Committee shall be held at least once every six (6) months (unless otherwise agreed by the Parties) and will alternate between appropriate offices of each Party. The Parties shall each bear all expenses of their respective representatives relating to their participation on the Steering Committee. The members of the Steering Committee also may convene or be polled or consulted from time to time by means of telecommunications, video conferences, electronic mail or correspondence, as deemed necessary or appropriate.

(c) Responsibilities. The Steering Committee shall have the following roles and responsibilities:

(i) review and approve any material amendments to the Development Plan (subject to Section 3.3(d)). Any proposed material amendment to the Development Plan, including arguments to support such amendment, shall be made available to the Steering Committee with reasonable advance notice and at least five (5) Business Days ahead of the scheduled meeting;

(ii) provide reasonably detailed updates, data and other information regarding Protalix's progress in Developing the Licensed Product in the Field;

(iii) provide updates in respect of any New Use in accordance with Section 2.5;

(iv) discuss the timing of transferring any regulatory filings in the Territory with respect to the Compound, Drug Substance, Drug Product or Licensed Product from Protalix to Chiesi in accordance with the terms of Section 3.6(c), and discuss and agree upon appropriate timelines for, and the responsibilities of each Party in respect of, preparing any regulatory filings for obtaining Regulatory Approval in any Country in the Territory. As part of such discussions, the Steering Committee shall discuss and agree on appropriate timelines and processes for the orderly transfer of all medical affairs functions from Protalix to Chiesi in accordance with Section 3.6(d)(iv);

(v) act as a forum pursuant to which the Parties will review and discuss plans and strategies relating to (x) the Development of the Licensed Product in the Field, (y) regulatory matters with respect to the Licensed Product in the Field in the Territory, and (z) Commercialization of the Licensed Product in the Field in the respective territories of the Parties, to ensure aligned communication at medical congresses and other scientific events as well as scientific publication plans;

(vi) modify the division of regulatory responsibilities as between the Parties in accordance with Section 3.6(d)(v);

(vii) subject to the terms of Section 8.5, review and/or approval of each Party's scientific publication plans;

(viii) oversee any Early Access Programs for the Licensed Product in the Field in the Territory;

(ix) review and agree upon the final version of the Initial Commercialization Plan, in accordance with Section 3.7(a), and review and provide comment upon any proposed revisions to, or any subsequent versions of, the Commercialization Plan (such comments to be considered in good faith by Chiesi);

(x) receiving from Chiesi reasonably detailed updates, data and other information regarding the status and details of any Price Approvals or Governmental Authority and Third Party reimbursement approvals in the Territory, in accordance with Section 3.7(c);

(xi) subject to Section 4.8(c), review and in good faith seek to resolve any disputes regarding any Notice of Non-Conformance issued in respect of a shipment of Drug Substance or Drug Product under the terms of this Agreement;

(xii) subject to Section 7.6(a), discuss any pertinent Third Party Patent Rights and decide upon whether a license to or acquisition of such Third Party Patent Rights or Technology is appropriate;

(xiii) discuss the possibility, from time to time, of sharing Licensed Product positioning and promotional materials for the Licensed Product in the Field, inside and outside the Territory;

(xiv) define the manner and timelines for Chiesi's access to sites and records of the Ongoing Clinical Studies and [***] conducted by Protalix;

(xv) appoint the Referent Persons in accordance with Section 8.5;

(xvi) establish, if deemed necessary, the creation of a Joint Project Team ("JPT") to oversee operations or activities. The composition of the JPT will be decided by the Steering Committee according to the type of activity and decision making in accordance with Section 3.3(d). The JPT shall be comprised of representatives from each Party with appropriate competence and level of decision-making authority. The JPT shall meet with a frequency to be agreed on by the Parties; and

[***] Redacted pursuant to confidential treatment request.

(xvii) such other roles and responsibilities provided for in this Agreement or as may be assigned to the Steering Committee in writing by mutual agreement of the Parties.

(d) Decision-Making by the Steering Committee. All decisions of the Steering Committee made pursuant to this Agreement shall be made by consensus with each Party having one vote; provided, however, that in the event of a disagreement between Chiesi and Protalix with respect to any such proposed decision for which another decision-making mechanism is not expressly provided for herein and subject to the relevant provisions hereunder:

(i) the Chiesi Chair shall have the final decision-making authority with respect to (A) Commercialization of the Licensed Product in the Field in the Territory, (B) regulatory plans and strategies relating to the Licensed Product in the Field in the Territory, (C) following Launch in a Country, Commercial Medical Affairs and Pharmacovigilance in such Country, and (D) following the transfer contemplated in Section 3.6(c), on a Country-by-Country basis, any and all regulatory matters concerning the Licensed Product, including in respect of any Regulatory Approvals, associated regulatory filings, or post-approval communications with or requirements of any Regulatory Authorities, subject to the obligation to consider the other Party's comments in good faith;

(ii) the Protalix Chair shall have the final decision-making authority with respect to (A) the Development of the Licensed Product (and the Ongoing Clinical Studies but not the [***], Registry, Required Registry or [***], which shall be addressed as otherwise expressly provided herein), including any regulatory matters concerning the Licensed Product prior to the transfers contemplated in Section 3.6(c), any medical affairs and pharmacovigilance functions prior to the transfers contemplated in Section 3.6(d) (and, for the avoidance of doubt, any issues relating to the Licensed Product outside the Field or outside the Territory), subject to the obligation to consider the other Party's comments in good faith, (B) the Protalix Patent Rights and Protalix Technology and Protalix's rights in or to the Protalix Patent Rights and Protalix Technology, and (C) [***] or other issues relating to the Licensed Product outside the Territory or outside the Field; and

(iii) in the event of a disagreement in respect of a matter unrelated to the subject-matter of Sections 3.3(d)(i) or 3.3(d)(ii), such matters shall be subject to the escalation and dispute resolution procedures set out in Section 14.2.

For the avoidance of doubt, to the extent that Protalix, in its sole discretion, deems it necessary due to a request or demand of a Regulatory Authority (but only where such request is mandatory or where failure to comply with such request could result in a penalty or actions against Protalix being imposed by such Regulatory Authority or a violation of applicable Law) or identified and immediate risk to patient safety, Protalix shall have the sole authority and the exclusive right to decide any matter in respect of the Development of the Licensed Product in the Field (other than with respect to (i) approving regulatory plans and strategies, and (ii) preparing and submitting regulatory filings and obtaining Regulatory Approvals after the transfer contemplated in Section 3.6(c)) without the approval of or any decision by the Steering Committee; provided, however, that Protalix shall use its reasonable efforts to provide notice to, and consult with, members of the Steering Committee, prior to exercising such discretion.

[***] Redacted pursuant to confidential treatment request.

(e) Minutes. The Alliance Managers will coordinate and alternate in preparing draft of the minutes collecting input from the attendees and distributing to all members of the Steering Committee the final minutes of each meeting reasonably promptly after a Steering Committee Meeting. Such minutes will report in reasonable detail actions taken by the Steering Committee during such meeting, issues requiring resolution and resolutions of previously reported issues. Such minutes will be reviewed and, if reasonably complete and accurate, signed by one Steering Committee member from each Party.

3.4 Records. During the Term, each Party will prepare and maintain accurate records and books relating to the progress and status of its activities under the Development Plan and otherwise in relation to the Development of the Drug Substance and Licensed Product.

3.5 Diligence. Subject to Chiesi's compliance with Section 5.3, Protalix will use Commercially Reasonable Efforts to carry out the Development Plan in order to Develop the Licensed Product in the Field in the Territory. Subject to Protalix's compliance with Section 3.6(c), Chiesi will use Commercially Reasonable Efforts to seek as soon as reasonably practicable Regulatory Approval, Price Approval and Governmental Authority or Third Party reimbursement approval (where applicable) for the Licensed Product in the Field in the Territory. Chiesi will use Commercially Reasonable Efforts to Launch and Commercialize the Licensed Product in each such Country in the Territory for which Regulatory Approval is obtained, promptly following such Regulatory Approval of the Licensed Product in the Field in such Country.

3.6 Regulatory Affairs.

(a) Copies of Regulatory Filings. Protalix shall provide to Chiesi, at Chiesi's expense, copies in electronic form of any regulatory filings in the Territory relating to the Licensed Product, including any clinical trial authorizations (including any regulatory filings in the Territory seeking approval to conduct a study or clinical trial of the Licensed Product), other filings with Regulatory Authorities, supplements or amendments thereto, written correspondence with Regulatory Authorities regarding such regulatory filings, and existing written minutes of meetings and memoranda of formal conversations between Protalix (including, to the extent practicable, Protalix's investigators) and Regulatory Authorities and any other document required to maintain the Regulatory Approvals (e.g. Trial Master Files) in Protalix's possession (but, for clarity, excluding any informal communications, i.e., e-mails) to the extent Protalix has the right to access and provide to Chiesi such materials.

(b) Regulatory Responsibilities. Subject to Section 3.3(d), and prior to the transfer contemplated in Section 3.6(c) below, Protalix shall, subject to Chiesi's direction and approval (by and through the Steering Committee or otherwise), be responsible for implementing all pre-Regulatory Approval regulatory plans and strategies for, and making any regulatory filings in respect of, the Licensed Product in the Field in the Territory (excluding, for the avoidance of doubt, any application to a Regulatory Authority seeking Regulatory Approval, which shall in each case, be in the name of, and submitted by, Chiesi). Without limiting the foregoing, following the transfer contemplated in Section 3.6(c):

(i) Chiesi (or one or more of its designated Affiliates) will own and be responsible for preparing, seeking, and submitting such regulatory filings as are necessary to obtain Regulatory Approval and then maintaining all Regulatory Approvals and any post-approval regulatory filings, for the Licensed Product in the Field in such Country in the Territory, including preparing all reports necessary as part of such Regulatory Approvals or post-approval regulatory filings. Protalix shall have the right and be responsible to prepare and promptly submit to Chiesi any non-clinical, clinical and Manufacturing portions (including CMC) of such regulatory filings and any related reports (subject to Chiesi's approval rights with respect to such regulatory filing as a whole), at Chiesi's sole cost and expense (unless such costs are Development Costs or other costs expressly addressed hereunder or by a separate agreement between the Parties, such as in relation to [***] or costs for Event Milestone 1a Studies). Protalix shall consider in good faith any proposed revision reasonably made by Chiesi thereto and Protalix shall otherwise provide such assistance as Chiesi reasonably requires, at Chiesi's sole cost and expense (unless such costs are Development Costs or other costs expressly addressed hereunder or by a separate agreement between the Parties, such as in relation to [***] or costs for Event Milestone 1a Studies), to obtain Regulatory Approvals for the Licensed Product in the Field in the Territory.

(ii) Following the transfer contemplated in Section 3.6(c), but in any event, no later than the grant of Regulatory Approval, on a Country-by-Country basis, Chiesi shall (A) subject to Section 5.3(d), assume sole responsibility for seeking authorization in respect of, conducting, and otherwise interacting with Regulatory Authorities in respect of, any Post-Approval Studies, and (B) have the right to apply for, and secure, exclusivity rights that may be available under the Laws of such Countries in the Territory, including any Regulatory Exclusivity. Protalix shall reasonably cooperate with Chiesi, and take such reasonable actions to assist Chiesi, at Chiesi's sole cost and expense, in obtaining such exclusivity rights in each Country, as Chiesi may reasonably request from time to time.

For the avoidance of doubt (A) at all relevant times during the Term, Chiesi shall have the final decision-making authority in respect of all regulatory plans and strategies for the Licensed Product in the Field in the Territory; provided that Chiesi shall reasonably consider any comments on such plans and strategies that Protalix may communicate (through the Steering Committee or otherwise); and (B) following a Regulatory Approval in a Country in the Territory, Chiesi shall be solely responsible for any such activities as are initiated after the date of such Regulatory Approval that would otherwise constitute Development activities had they been initiated prior to the grant of such Regulatory Approval.

[***] Redacted pursuant to confidential treatment request.

(c) Transfer of Regulatory Filings. To the extent permitted by applicable Law, at a time to be agreed by and through the Steering Committee and on a Country-by-Country basis, with such time to be prior to any application to a Regulatory Authority seeking Regulatory Approval for the Licensed Product in the Field in any Country in the Territory [***], and at Chiesi's sole cost and expense, Protalix shall assign and transfer to Chiesi Protalix's entire right, title and interest in and to all regulatory filings in such Country with respect to the Compound, Drug Substance, Drug Product or Licensed Product in the Field, and shall perform all other actions reasonably requested by Chiesi to effect and confirm such assignment and transfer, at Chiesi's sole cost and expense; provided, however, that, for the avoidance of doubt, all right, title and interest in and to any clinical trial authorizations or other clinical regulatory filings as are necessary to support the continued conduct of and completion of the Ongoing Clinical Studies and any [***] (including as necessary to obtain Regulatory Approval with the EMA or outside the Territory) shall remain vested in Protalix until completion of such studies.

(d) Transfer of Regulatory Responsibilities. Subject to the terms of the Development Plan:

(i) The Parties shall cooperate through the Steering Committee to ensure that any such assignments and transfers under Section 3.6(c), do not impede Protalix's ability to conduct and complete the Ongoing Clinical Studies and [***]. After each such assignment and transfer is effective, Chiesi shall (and does hereby) grant Protalix a right to use and make reference to such regulatory filings so assigned and transferred (and any subsequent regulatory filings made or Regulatory Approvals in such Countries as are obtained by Chiesi in respect of the Licensed Product in the Field) as necessary for Protalix (x) to conduct and complete the Ongoing Clinical Studies and any [***], and (y) to conduct and complete any other clinical studies as necessary for Protalix to complete in order to file, and to file, for Regulatory Approval for (A) the Licensed Product outside the Territory, or (B) any New Use (or other drug product containing the Drug Substance outside of the Field) anywhere in the world.

(ii) After such transfer of ownership of such regulatory filings relating to the Drug Substance (or Drug Product) as incorporated into the Licensed Product (and for the avoidance of doubt, excluding any regulatory filings and Regulatory Approvals with respect to the Drug Substance (or Drug Product) as part of any New Use), or Licensed Product in the Field in the Territory, during the Term, all regulatory filings seeking Regulatory Approval in such Countries in the Territory and all subsequent post-approval regulatory filings that are filed with the applicable Regulatory Authorities and which pertain to the Drug Substance (or Drug Product) as incorporated into the Licensed Product (and for the avoidance of doubt, excluding any such regulatory filings with respect to the Drug Substance (or Drug Product) as part of any New Use), or Licensed Product in the Field, in each case, in the Territory, shall be made in the name of Chiesi or its Affiliates in accordance with Section 3.6(e), and any Post-Approval Studies shall be conducted in the name of, and shall be the sole responsibility of, Chiesi and its Affiliates (subject to Section 5.3(f)).

[***] Redacted pursuant to confidential treatment request.

(iii) For the avoidance of doubt, Protalix shall remain responsible for the preparation of any non-clinical (including pre-clinical and CMC), clinical, and Manufacturing portions of regulatory filings submitted by Chiesi seeking Regulatory Approval with the EMA, and shall otherwise provide reasonable assistance to Chiesi in finalizing such regulatory filings for submission to the applicable Regulatory Authority (in each case subject to Chiesi's approval rights with respect to the regulatory filing as a whole).

(iv) As part of the process of fixing a time for the regulatory transfer contemplated under Section 3.6(c), and subject to the terms of the Pharmacovigilance Agreement, on a Country-by-Country basis, the Steering Committee shall also set out a timeline for the orderly transfer of any pharmacovigilance (for post-Launch Commercialization) and medical affairs functions from Protalix to Chiesi (as well as the role of primary contact for KOL management and patient advocacy) (such functions, following the completion of such transfer from Protalix to Chiesi, to be referred to as "Commercial Medical Affairs and Pharmacovigilance"), with such medical affairs functions to be fully transferred within twelve (12) months of the Effective Date, but prior to the grant of Regulatory Approval in such Country, and with such pharmacovigilance functions to be fully transferred upon Launch; provided, that until such time as each of the Ongoing Clinical Trials and any [***] are completed, and the clinical study reports for each such clinical study are finalized, Protalix shall retain responsibility for patient safety monitoring, and shall remain the primary contact with each applicable KOL, in respect of such clinical studies.

(v) Notwithstanding anything to the contrary herein, but subject to the terms of the Pharmacovigilance Agreement, the Steering Committee may by mutual agreement modify the division of regulatory responsibilities as between the Parties, including by having Protalix retain certain regulatory responsibilities following the transfer contemplated by Section 3.6(c), or by having Chiesi assume certain regulatory responsibilities prior to the transfer contemplated by Section 3.6(c) (including, for the avoidance of doubt, where such division of responsibilities differs from the terms of the Development Plan); provided, however, that (i) in no circumstances may Chiesi assume responsibility for or control over any clinical aspects of the Development Plan, including the conduct of the Ongoing Clinical Studies (except in the case of Chiesi exercising its step-in rights as provided for in Section 3.2 or the conduct by Chiesi of any [***], Additional Studies, Registry, Required Registry or [***] as provided hereunder); and (ii) in any event, all regulatory responsibilities in respect of the Licensed Product in the Field in the Territory (including, for clarity, each of the transfers of regulatory responsibility contemplated in this Section 3.6), on a Country-by-Country basis, must be completely assumed by Chiesi within [***]; provided, that until such time as each of the Ongoing Clinical Trials and any [***] are completed, and the clinical study reports for each such clinical study are finalized, Protalix shall retain responsibility for patient safety monitoring, and shall remain the primary contact with each applicable KOL, in respect of such clinical studies.

[***] Redacted pursuant to confidential treatment request.

(e) Rights of Reference and Access to Data. Chiesi shall (and does hereby) grant to Protalix a non-exclusive "Right of Reference," as that term is defined in 21 C.F.R. § 314.3(b), or an equivalent non-exclusive right of access/reference in the United States and in the EU and in each other Country in the Territory (A) solely for use by Protalix in connection with the Development and/or Commercialization of any Licensed Product outside of the Territory or any New Use (or other drug product containing the Drug Substance outside of the Field), to any data in any regulatory filing in the EU or any other Country in the Territory Controlled by Chiesi that relates to the Drug Substance or Licensed Product, and (B) solely for use by Protalix in connection with the Development of drug products made using the System, to any safety data (but not efficacy data) in any regulatory filing in the EU or any other Country in the Territory Controlled by Chiesi that relates to the Drug Substance or Licensed Product. Chiesi shall provide a signed statement to this effect, if requested by Protalix, in accordance with 21 C.F.R. § 314.50(g)(3) or the equivalent as required in the EU or any other Country in the Territory, or otherwise provide appropriate notification of such right of Protalix to the applicable Regulatory Authority. To the extent Chiesi shall need an equivalent "Right of Reference," as that term is defined in 21 C.F.R. § 314.3(b), to exploit the rights granted hereunder in the Territory, Protalix shall (and does hereby) grant to Chiesi a non-exclusive Right of Reference, or an equivalent non-exclusive right of access/reference in the United States and in the EU and in each other Country in the Territory, solely for use by Chiesi in connection with the Development and/or Commercialization of the Licensed Product in the Field in the Territory, and solely if and to the extent that Chiesi is authorized under this Agreement to conduct such Development and/or Commercialization, (A) to any data in any regulatory filing Controlled by Protalix that relates to the Drug Substance or Licensed Product, and (B) to any safety data (but not efficacy data) in any regulatory filing that relates to the Drug Substance or Licensed Product. Protalix shall provide a signed statement to this effect, if requested by Chiesi, in accordance with 21 C.F.R. § 314.50(g)(3) or the equivalent as required in the EU or any other Country in the Territory, or otherwise provide appropriate notification of such right of Chiesi to the applicable Regulatory Authority.

(f) Pharmacovigilance. After the Effective Date [***], the safety units of each of the Parties shall meet and agree upon a written pharmacovigilance agreement that defines Chiesi's pharmacovigilance responsibilities for the post-Launch Commercialization of Licensed Product in the Territory and Protalix's pharmacovigilance responsibilities for the Licensed Product outside the Territory and for pre-Launch Development activities in the Territory, and the process for exchanging adverse event reports and other safety information relating to a Licensed Product that will permit each Party to comply with applicable Laws and requirements of Regulatory Authorities (such agreement, the "Pharmacovigilance Agreement"); provided, that until such time as each of the Ongoing Clinical Trials and any [***] conducted by Protalix are completed, and the clinical study reports for each such clinical study are finalized, Protalix shall retain sole responsibility and be the primary contact for pharmacovigilance matters in respect of the Licensed Product.

[***] Redacted pursuant to confidential treatment request.

(g) Communications with Regulatory Authorities.

(i) For so long as [***], Protalix, and after the assignment and transfer to Chiesi of such regulatory filings pursuant to Section 3.6(c), Chiesi, shall provide the other Party with notice of all meetings, conferences, and discussions (including advisory committee meetings or any other meeting of experts convened by a Regulatory Authority concerning any topic relevant to the Licensed Product) scheduled with a Regulatory Authority concerning any regulatory matters relating to the Licensed Product in the Field promptly after the scheduling of such meeting, conference, or discussion. The Party that does not, at the time of such meeting, own the regulatory filings described in Section 3.6(c) for the Licensed Product shall be entitled to have one or more representatives present at all such meetings to the extent permissible under applicable Law and reasonably practicable under the circumstances. Protalix and Chiesi shall use all reasonable efforts to agree in advance on the scheduling of such meetings, conferences and discussions and on the objectives to be accomplished at such meetings, conferences and discussions and the agenda for the meetings, conferences and discussions with the applicable Regulatory Authority, if any [***].

(ii) For so long as [***], Protalix, and after [***], Chiesi, shall provide the other Party with copies, which copies may be in draft form, of all material submissions to any Regulatory Authority relating to the Licensed Product in the Field. Such copies shall be provided sufficiently in advance of such planned submission to the applicable Regulatory Authority in order to allow such other Party to provide comments regarding such submission. The Party making the submission shall consider the other Party's comments in good faith with respect to such submission [***].

(iii) Each Party shall provide to the other Party, as soon as reasonably practicable but in no event more than [***] after its receipt, copies of any material documents or other material correspondence received from a Regulatory Authority pertaining to the Licensed Product in the Field.

(h) Regulatory Information. Each Party agrees to provide the other with all reasonable assistance and take all actions reasonably requested by the other Party that are necessary or desirable to enable the other Party to comply with any Law applicable to the Licensed Product. For clarity, to the extent that either Party provides reasonably requested assistance to the other Party in compliance with this Section 3.6(h), the requesting Party shall reimburse such Party for any reasonable costs and expenses incurred in respect thereof.

(i) Recalls or Other Corrective Action. Each Party shall promptly notify the other Party of any material actions to be taken by such Party in the Territory or outside the Territory (as the case may be), with respect to any recall or market withdrawal or other corrective action related to the Licensed Product prior to such action, if reasonably practicable under the circumstances, to permit the other Party a reasonable opportunity to consult with such Party with respect thereto. [***].

[***] Redacted pursuant to confidential treatment request.

3.7 Commercialization and Pricing.

(a) An initial draft Commercialization plan for the Licensed Product in the Field in the Territory prepared by Chiesi is attached as Schedule 3.7 hereto, and the final version of such Commercialization plan shall be discussed and agreed upon between the Parties within [***] from the first Steering Committee Meeting (the "Initial Commercialization Plan"). Chiesi shall update such plan (any such updated plan, the "Commercialization Plan") at least once per Calendar Year. Each such subsequent Commercialization Plan shall be submitted to the Steering Committee for review and discussion no later than thirty (30) days prior to the beginning of the immediately succeeding Calendar Year. Protalix may, through its representatives on the Steering Committee, propose to Chiesi revisions to any such subsequent Commercialization Plan, and any proposed material updates or amendments to the Initial Commercialization Plan and any subsequent Commercialization Plan, that Protalix reasonably believes are appropriate, and Chiesi shall consider any such proposed revisions in good faith, but such Initial Commercialization Plan or Commercialization Plan, or any material amendments or updates thereto, shall not require approval of the Steering Committee.

(b) Chiesi shall have the sole authority and exclusive right to Commercialize, and shall be responsible for paying all costs and expenses associated with the Commercialization of, the Licensed Product in the Field in the Territory, including marketing, promoting, advertising, distributing, disposing, offering for sale, selling, Labeling and Packaging, final product release testing, exporting and importing, and [***] and obtaining any necessary Price Approvals at its sole discretion. Chiesi hereby agrees to refrain from selling the Licensed Product in the Territory to any Person if Chiesi has knowledge or reason to believe that such Licensed Product is intended for transshipment or delivery by such Person outside the Territory.

(c) At meetings of the Steering Committee, Chiesi will provide Protalix with periodic updates regarding the status and details of Price Approvals and Governmental Authority and Third Party reimbursement approvals in each applicable Country in the Territory.

3.8 Early Access Programs. The Parties shall discuss at the Steering Committee the appropriate mechanism for considering, approving, providing for supply of Licensed Product in respect of, and otherwise administering, any Early Access Programs [***].

3.9 Trademarks.

(a) License to Chiesi. Protalix hereby grants to Chiesi an exclusive (except as to Protalix) license, free of charge, to use the Protalix Trademarks in the Territory solely in connection with the Commercialization of the Licensed Product in the Field during the Term in the Territory, solely to the extent requested to be used by Protalix pursuant to, and solely for the purposes set forth in, Section 3.10. If Chiesi decides to use the Protalix Trademarks in the Territory, then Chiesi shall cooperate with Protalix in respect of [***] recording the trademark license instrument with the appropriate Governmental Authorities throughout the Territory.

[***] Redacted pursuant to confidential treatment request.

(b) Choice of Trademarks. Chiesi may choose, in its sole discretion, to use any trademarks to Commercialize the Licensed Product in the Field in the Territory, and Chiesi shall own all such trademarks, other than the Protalix Trademarks or any other trademark owned or Controlled by Protalix at such time (such trademarks of Chiesi, the "Product Marks").

(c) License to Protalix. Chiesi hereby grants to Protalix an exclusive (except as to Chiesi) license, free of charge, to use the Product Marks outside the Territory solely in connection with the packaging, sale, marketing, promotion, advertising, disposition and distribution of the Licensed Product in the Field during the Term outside the Territory. If Protalix decides to use the Product Marks outside the Territory, Protalix shall cooperate with Chiesi in respect of [***] recording the trademark license instrument with the appropriate Governmental Authorities outside the Territory.

(d) Quality Control.

(i) The quality of the Licensed Product sold by Protalix outside the Territory under or in connection with the Product Marks must be of a sufficiently high quality to be generally comparable to the quality of the Licensed Product sold by Chiesi in the Territory under or in connection with the Product Marks. The quality of the Licensed Product sold by Chiesi in the Territory under or in connection with the Protalix Trademarks must be of a sufficiently high quality to be generally comparable to the quality of the Licensed Product sold by Protalix outside of the Territory under or in connection with the Protalix Trademarks.

(ii) Protalix shall comply with all applicable Laws pertaining to the proper use and designation of the Product Marks. Chiesi shall comply with all applicable Laws pertaining to the proper use and designation of the Protalix Trademarks.

(iii) Protalix agrees to use the Product Marks only in the form and manner and with appropriate legends as prescribed from time to time during the Term by Chiesi. Chiesi agrees to use the Protalix Trademarks only in the form and manner and with appropriate legends as prescribed from time to time during the Term by Protalix.

(iv) Protalix shall display the proper form of trademark notice associated with the Product Marks. Chiesi shall display the proper form of trademark notice associated with the Protalix Trademarks.

(v) Protalix shall not use any Product Mark as a corporate name, business name, or trade name. Chiesi shall not use any Protalix Trademark as a corporate name, business name, or trade name.

(vi) Protalix shall not use any Product Mark in a manner that would reasonably be expected to materially impair the validity, reputation, or distinctiveness of any Product Mark. Chiesi shall not use any Protalix Trademark in a manner that would reasonably be expected to materially impair the validity, reputation, or distinctiveness of any Protalix Trademark.

[***] Redacted pursuant to confidential treatment request.

(vii) Protalix shall not use any Product Mark in a manner that would reasonably be expected to materially impair the reputation of Chiesi or any of its Affiliates. Chiesi shall not use any Protalix Trademark in a manner that would reasonably be expected to materially impair the reputation of Protalix or any of its Affiliates.

(e) Prosecution and Maintenance of Trademarks. Chiesi shall have the sole right, but not the obligation, through counsel of its choosing, to prosecute and maintain the Product Marks in the Territory. [***] Protalix shall have the sole right, but not the obligation, through counsel of its choosing, to prosecute and maintain the Protalix Trademarks and the first right, but not the obligation, through counsel of its choosing, to prosecute and maintain the Product Marks outside of the Territory on behalf of Chiesi. In the event Protalix elects not to prosecute or maintain any Product Marks outside of the Territory, Protalix shall provide reasonable prior written notice to Chiesi of its intention not to prosecute or maintain any such Product Marks outside of the Territory, and Chiesi shall have the right to do so directly. [***]

(f) Enforcement of Trademarks. Each Party will promptly notify the other in the event of any actual, potential or suspected infringement of a Protalix Trademark or Product Mark by any Third Party.

(i) Chiesi shall have the sole right, but not the obligation, to institute litigation or take other remedial measures in connection with Third Party infringement of Product Marks in the Territory. Any recoveries obtained by Chiesi resulting from such litigation or other appropriate action in the Territory in relation to the Product Marks, will be deemed Net Sales after having deducted any amount necessary to cover all costs and expenses incurred by Chiesi pursuant to the following sentence. All costs and expenses incurred by Chiesi in enforcing the Product Marks in the Territory shall be at Chiesi's sole cost and expense. Protalix shall have the sole right, but not the obligation, to institute litigation or take other remedial measures in connection with Third Party infringement of Protalix Trademarks in the Territory. Upon request of Protalix, Chiesi agrees to timely join as party-plaintiff in any litigation in the Territory in relation to the Protalix Trademarks, and in any event to cooperate with Protalix in connection with any infringement action in the Territory in relation to the Protalix Trademarks, at Protalix's cost and expense. All costs and expenses incurred by Protalix in enforcing the Protalix Trademarks in the Territory [***]. Protalix shall retain all recoveries received by Protalix as a result of its enforcement of the Protalix Trademarks in the Territory.

(ii) Protalix shall have the sole right, but not the obligation, to institute litigation or take other remedial measures in connection with Third Party infringement of Protalix Trademarks outside the Territory and the first right, but not the obligation, to institute litigation or take other remedial measures in connection with Third Party infringement of Product Marks outside the Territory. If Protalix declines to initiate litigation or take other remedial measures against a Third Party who is alleged to be infringing a Product Mark outside the Territory within ninety (90) days after becoming aware of the basis for such litigation or action, then Chiesi may, in its discretion, have the right to initiate litigation or take other appropriate action that it believes is reasonably required to protect its rights to the Product Marks outside the Territory. Upon request of Chiesi, Protalix agrees to timely join as party-plaintiff in any such litigation, and in any event to cooperate with Chiesi in connection with such infringement action at Chiesi's cost and expense. Any recoveries obtained by Protalix resulting from such litigation or other appropriate action outside of the Territory in relation to the Product Marks or Protalix Trademarks shall be retained by Protalix. All costs and expenses incurred by Protalix in enforcing the Product Marks and Protalix Trademarks outside the Territory shall be at Protalix's sole expense. All costs and expenses incurred by Chiesi in enforcing the Product Marks outside the Territory [***]. Chiesi shall retain all recoveries received by Chiesi as a result of its enforcement of the Product Marks outside the Territory.

[***] Redacted pursuant to confidential treatment request.

3.10 Use of Names. No right, expressed or implied, is granted by this Agreement to a Party to use in any manner the name or any other trade name of the other Party or its Affiliates in connection with this Agreement. Notwithstanding the foregoing, Chiesi agrees, during the Term, to display the Protalix corporate name and logo (the "Protalix Trademarks") on the trade packaging used for the Licensed Product in the Field in the Territory in a reasonable manner in each applicable Country in which the Licensed Product has been Launched (or as may be required under applicable Law in any such Country), unless to do so would be prohibited under applicable Laws, would not be reasonable from a commercial perspective in such Country, or is not in accordance with the request of a Regulatory Authority, subject to Protalix's trademark usage guidelines applicable to the Protalix Trademarks provided from time to time during the Term, including at least sixty (60) days prior to the date of Chiesi's first use of the Protalix Trademarks. Upon the written request of Protalix, Chiesi shall submit to Protalix a sample of each proposed use of the Protalix Trademarks.

3.11 [***]

Section 4. MANUFACTURE AND SUPPLY.

4.1 Commercial Supply of Licensed Product. In respect of each Country in the Territory, other than to the extent this provision would be a violation of any applicable Laws in such Country, Protalix shall Manufacture and supply, and Chiesi shall purchase from Protalix, all of Chiesi's and its Affiliates' and Sublicensees' requirements of the Drug Product (and, after [***] for incorporation into Licensed Product for commercial sale in the Field in the Territory pursuant to and in accordance with this Agreement. Such supply shall be subject to and in accordance with the terms of this Section 4 and the Quality Agreement.

4.2 [***].

(a) Prior to [***]. Prior to [***], (i) Protalix shall be responsible for delivery of Drug Substance to [***] with respect to commercial supply of Licensed Product for sale in the Territory and shall use Commercially Reasonable Efforts to cause [***] to conduct, pursuant and subject to and in accordance with the terms and conditions of the [***], [***] activities for supply of Drug Product to Chiesi, and (ii) Chiesi shall be responsible for Labeling and Packaging with respect to commercial supply of Licensed Product for sale in the Territory and shall ensure, in all material respects, that Labeling and Packaging activities for commercial supply of Licensed Product for sale in the Territory comply with applicable Law, GMP and the Regulatory Approvals for the Licensed Product in the Territory, including the Product Specifications.

[***] Redacted pursuant to confidential treatment request.

(b) [***]

4.3 Protalix Manufacturing Activities. Protalix shall have the sole authority and exclusive right for, and Protalix shall be responsible for, the Manufacture of Drug Product and, after [***].

4.4 Compliance of Third Parties. In the event that Protalix conducts any Manufacturing activities through an Affiliate or Third Party, Protalix shall be responsible for the performance of such Affiliate or Third Party in accordance with the terms of this Section 4. In the event that Chiesi conducts any Labeling and Packaging or, after [***] activities through an Affiliate or Third Party (such performance by an Affiliate or Third Party to comply with the terms of Section 2.4), Chiesi shall be responsible for the performance of such Affiliate or Third Party in accordance with the terms of this Section 4.

4.5 Forecasting and Ordering.

(a) Forecasts; Purchase Orders. [***], Chiesi shall deliver to Protalix Chiesi's quarterly projection of the quantities of Drug Product [***] that Chiesi anticipates ordering from Protalix pursuant to this Agreement for the four (4) Commercial Quarters commencing with the first Commercial Quarter that includes the first requested delivery date (the "Initial Forecast"), together with a firm purchase order (a "Purchase Order") for such Drug Product [***] for the first Commercial Quarter covered by such Initial Forecast and for at least [***] of the second Commercial Quarter covered by such Initial Forecast. The quantities of Drug Product [***] specified for the following [***] of such Initial Forecast shall be non-binding. Thereafter, [***] prior to the first Business Day of each subsequent Commercial Quarter during the Term, Chiesi shall deliver to Protalix a rolling [***] Commercial Quarter forecast updating the prior forecast (together with the Initial Forecast, each a "Forecast"), together with a Purchase Order for such Drug Product [***] for the first Commercial Quarter covered by such Forecast and for at least [***] of the second Commercial Quarter covered by such Forecast. The quantities of Drug Product [***] specified for the following two (2) Commercial Quarters of such Forecast shall be non-binding. Unless agreed separately between the Parties, each Purchase Order shall (i) specify no more than one (1) delivery date for the Drug Product [***] in each Commercial Quarter (unless each such delivery date in such Commercial Quarter is for a quantity of vials equal to the Minimum Batch Size or an exact multiple thereof), and (ii) be for a minimum quantity of the Minimum Batch Size. Purchase Orders shall be in writing and no verbal communications or e-mail shall be construed to mean a commitment to purchase or sell. Each Purchase Order delivered by Chiesi to Protalix pursuant to this Section 4.5(a) shall be binding on Protalix, unless Protalix notifies Chiesi in writing of its rejection thereof within [***] of receipt of such Purchase Order; provided that Protalix may only reject Purchase Orders that do not comply with the terms of this Agreement or are otherwise not valid Purchase Orders (e.g., do not contain the requisite details).

[***] Redacted pursuant to confidential treatment request.

(b) Long Range Capacity Planning. Concurrent with the Initial Forecast, for the purposes of discussion and planning of Manufacturing capacity, Chiesi shall provide a non-binding forecast of its projected Drug Product [***] needs for the [***] Commercial Quarters following that specified in the Initial Forecast as described in Section 4.5(a) (a "Long Range Forecast"). Each Long Range Forecast shall be deemed to be revised by any subsequent Forecast. In the event Protalix anticipates that it will be unable to supply the quantities of Drug Product [***] reflected in a Long Range Forecast, Protalix shall promptly notify Chiesi and the Parties shall work to remedy the shortfall in accordance with and subject to the terms of this Section 4 in an effort to assure that the necessary capacity exists. Unless otherwise agreed to by the Parties during the Term, the Long Range Forecast shall be updated by Chiesi annually by July 1 of each Commercial Year during the Term.

(c) Receipt and Acceptance. Chiesi shall purchase all Drug Product [***] ordered and specified in a Purchase Order. Purchase Orders may be delivered electronically or by other means to such location as Protalix shall designate. Nothing in any such Purchase Order or written acceptance shall supersede the terms and conditions of this Agreement or the Quality Agreement. All Purchase Orders, confirmations of receipt of Purchase Orders and other notices contemplated under this Section 4.5(c) shall be sent to the attention of such persons as each Party may identify to the other in writing from time to time in accordance with Section 15.8.

(d) First-Expired First-Out. Chiesi shall use its inventory of Licensed Product, and any shipments of Drug Product [***], and each Party shall use its Safety Stock Amounts (as and when necessary), in each case, on a first-expired first-out (FEFO) basis in order to ensure that the Licensed Product in Chiesi's inventory (and the supply of Drug Product or, after [***], [***], used in the production of such Licensed Product inventory) always has the maximum period of time remaining on the retest period.

4.6 Pricing, Invoicing and Supply Price Reconciliation.

(a) Supply Delivery Price; Invoices.

(i) Each delivery of Drug Product [***] under a Purchase Order hereunder shall be accompanied by an invoice. Protalix shall invoice such Drug Product [***] at the Price as at the date of such invoice. Chiesi shall issue payment against such invoices within [***] of the invoice date. Protalix shall include the following information, where applicable, on all invoices: the type, description, and quantity of the product delivered; the date of shipment; the prices; any applicable taxes, transportation charges or other charges provided for in the applicable Purchase Order; and the applicable Purchase Order number.

[***] Redacted pursuant to confidential treatment request.

(b) Taxes. All sales and use taxes which Protalix is required by applicable Law to collect from Chiesi with respect to the Manufacture and supply of Drug Product [***] to Chiesi shall be separately stated in Protalix's invoice and shall be paid by Chiesi to Protalix. For the avoidance of doubt, any and all applicable taxes shall be payable by Chiesi in addition to the Price payable on such Licensed Products. Protalix shall be solely responsible for the timely payment of all such taxes to the applicable taxing authority.

(c) Initial Price. Subject to the terms and conditions of this Agreement, before the start of the first Commercial Year in which Protalix is obligated to deliver Drug Product [***] pursuant to a Purchase Order issued by Chiesi, Protalix shall sell, and Chiesi shall purchase, the amount of Drug Product [***] ordered for delivery in the first Commercial Year at a Price determined by the Parties in good faith on a Country-by-Country basis at least one Commercial Quarter prior to the anticipated start of the first Commercial Year in such Country, reflecting [***] in all relevant Countries of the Territory.

(d) Ongoing Price. Subject to the terms and conditions of this Agreement, in any Commercial Year other than the first Commercial Year, Protalix shall sell, and Chiesi shall purchase, the amount of Drug Product [***] ordered for delivery in such Commercial Year at a Price determined on a Country-by-Country basis equal to [***].

(e) [***]

(f) For the purposes of this Agreement, the "Applicable Rate" shall mean [***]:

Aggregate Annual Net Sales of Licensed Products (together with Direct Sublicensee Revenue B)	**Applicable Rates**
Less than [***]	[***]
Equal to or greater than [***] and less than [***]	[***]
Equal to or greater than [***] and less than [***]	[***]
Equal to or greater than [***] and less than [***]	[***]
Equal to or greater than [***]	[***]

[***] Redacted pursuant to confidential treatment request.

(g) Quarterly Reconciliation. Notwithstanding the foregoing, in no event shall the Price paid by Chiesi for the Drug Product [***] ordered for delivery in any Commercial Quarter be less than [***]. If, at the end of a Commercial Quarter, the Price paid by Chiesi for the supply of Drug Product [***] during any Commercial Quarter is less than [***], Chiesi shall pay Protalix the difference between such amounts against receipt of a proper invoice within [***] of the invoice date. In addition to the foregoing and any other payments provided for herein, [***], Chiesi shall pay to Protalix an amount equal to the Applicable Rate for such Commercial Year, multiplied by the Other Sublicensee Revenue received during such Commercial Quarter (the "Other Sublicensee Revenue Payment"), subject to Section 5.3(e).

(h) Yearly Reconciliation. The amounts due from Chiesi for Drug Product [***] ordered for delivery in each Commercial Year, as listed on the first invoice delivered to Chiesi for such Commercial Year, shall be increased or decreased, as the case may be, by the amount of a Reconciliation Adjustment aggregated for all Countries in the Territory and meant to compensate in such Commercial Year for any inaccuracy in the Price paid in each such Country in the prior Commercial Year (the "Yearly Reconciliation"); provided that, notwithstanding anything to the contrary herein, in no event shall the amount due from Chiesi for the Drug Product [***] ordered for delivery in any Commercial Year be less than [***] for any Commercial Year (the "Minimum Payment"), subject to the potential pro rata reduction of the Minimum Payment for failure to supply provided for in Section 4.14(f). For purposes of this Agreement, the "Reconciliation Adjustment" shall mean the aggregate for all Countries in the Territory of the difference for each Country between:

(i) [***]; and,

(ii) [***].

Each Reconciliation Adjustment shall be settled against receipt of a proper credit note or debit note within [***] of the note date; provided that if any Reconciliation Amount is in the favor of Chiesi, such amounts shall be credited against the amount stated on the next issued invoice relating to the delivery of Drug Product [***] by Protalix to Chiesi under this Agreement.

(i) Maximum Order Quantity. [***], the Parties shall agree in good faith on a maximum order quantity for the [***] and subsequent Commercial Years in such Country (the "Maximum Order Quantity"), expressed as a percentage above the amount of vials sold in such Country in the prior Commercial Year [***] to mitigate the risk to Protalix of Chiesi ordering more Licensed Product than will be sold in such Commercial Year. If the Parties are unable to reach agreement on the Maximum Order Quantity for a given Country by [***], the issue shall be escalated to the Parties' respective Chief Executive Officers, who shall attempt to resolve the issue within thirty (30) days. Notwithstanding anything to the contrary in this Agreement, Protalix shall have no obligation to supply Drug Product [***] in excess of the Maximum Order Quantity for any Country.

[***] Redacted pursuant to confidential treatment request.

4.7 Shipping and Delivery.

(a) Delivery. Protalix shall deliver (or have delivered) to Chiesi in accordance with this Section 4.7 the quantities of the Drug Product [***] specified for a given delivery date in each Purchase Order, [***]. Protalix shall deliver (or have delivered) (i) after [***], [***] with a remaining shelf life of [***], or (ii) prior to [***], with a remaining shelf life of [***].

(b) Delivery Terms. The Drug Product [***] shall be supplied to Chiesi [***]. The Drug Product [***] shall be shipped at [***]. Chiesi shall be [***]. For the avoidance of doubt, Protalix shall be responsible for the importation of the Drug Substance in the EU with respect to the shipment of Drug Substance from Protalix to [***], and for compliance with all applicable Laws relating to such importation.

(c) Retention. Unless the Parties agree otherwise, Protalix shall maintain analytical samples of each batch of Drug Product (or, if necessary, Drug Substance) in storage for a time period based upon Protalix's sample retention policy.

4.8 Certificate of Analysis; Acceptance and Returns.

(a) Certificate of Analysis; Notice of Non-Conformance.

(i) Protalix shall supply to Chiesi the applicable batch number for the Drug Product [***] delivered, as well as such other information as the Parties may set forth in the Quality Agreement with respect to Manufacture (a "Manufacturing Certificate of Analysis") for all Drug Product [***] shipped to Chiesi hereunder. Chiesi shall (within the time period specified in Section 4.8(b)) inspect, or cause to have inspected, each shipment of the Drug Product [***] for any material damage, defect or shortage and give Protalix written notice of any such material damaged, defective or short shipment (a "Notice of Non-Conformance") within the time periods specified in Sections 4.8(a)(ii) and 4.8(b), as applicable.

(ii) Latent defects shall be communicated to Protalix, together with appropriate detail, within fifteen (15) Business Days of the date on which such latent defect was first discovered by Chiesi or was notified to Chiesi by the relevant Party discovering the defect.

(b) Rejection. Chiesi shall have [***] following its receipt of each shipment of the Drug Product [***] to inspect such shipment. If Chiesi determines that any shipment of the Drug Product [***] does not conform to the Product Specifications (or is otherwise a short shipment) in any material respect, it shall promptly notify Protalix within [***] following such determination in compliance with the procedures set forth in the Quality Agreement(s). Failure to provide such written notice with such time periods specified in Sections 4.8(a)(ii) and this 4.8(b), as applicable, shall be deemed acceptance of such shipment of Drug Product [***] by Chiesi.

[***] Redacted pursuant to confidential treatment request.

(c) Disputes. If Chiesi delivers a Notice of Non-Conformance in respect of all or any part of a shipment of the Drug Product [***], and Protalix does not agree with Chiesi's determination that such shipment fails to meet the Product Specifications (or is otherwise a short shipment) in any material respect, the Parties shall in good faith attempt to resolve such dispute at the Steering Committee; provided, however, that the Steering Committee must resolve any such dispute by consensus, and for the avoidance of doubt, neither the Protalix Chair nor Chiesi Chair shall have final decision-making authority in respect of such Steering Committee discussions; provided, however, that for the duration of such Steering Committee discussions, Protalix shall use Commercially Reasonable Efforts to promptly replace such alleged non-conforming Drug Product [***] (or short shipment) in order to avoid any possible out-of-stock situation. The dispute shall be resolved at the Steering Committee within thirty (30) days, unless otherwise agreed in writing by the Parties, from the date of Protalix's receipt of a Notice of Non-Conformance to resolve such dispute regarding whether all or any part of such shipment was not Manufactured in conformance with the Product Specifications (or was otherwise a short shipment) in any material respect. If the dispute regarding whether all or any part of a shipment rejected by Chiesi was not Manufactured in conformance with the Product Specifications (or was otherwise a short shipment) in any material respect is not resolved by the Steering Committee in such thirty (30) day period, [***].

(d) Remedies. In the event any shipment of Drug Product [***] is rejected pursuant to this Section 4.8 as a result of any act or omission of Protalix, then (i) Chiesi shall, at the direction of Protalix, either (x) destroy such rejected Drug Product [***] (in accordance with applicable Law) or (y) return such rejected Drug Product [***] to Protalix, at a location designated by Protalix [***]; and (ii) Protalix [***] shall (in its sole discretion) either (x) use its Commercially Reasonable Efforts to promptly replace such non-conforming Drug Product [***] (or short shipment) or (y) give Chiesi a credit in an amount equal to the amount paid or payable by Chiesi with respect to such rejected Drug Product [***] (or short shipment).

4.9 Product Specification and Manufacturing Changes. Prior to the Parties entering into the Quality Agreement, Protalix shall inform Chiesi of material Product Specification and Manufacturing changes, including those resulting from a request received by Protalix from a Governmental Authority. Protalix shall notify Chiesi within a reasonable time prior to implementing such change, to allow Chiesi to assess the potential impact of such change upon the Drug Product supplied or its use by Chiesi and the implementation of such change shall not occur prior Chiesi's written approval (which approval shall not be unreasonably withheld, conditioned or delayed). After the Parties enter into the Quality Agreement, Product Specification and Manufacturing changes, including those resulting from a request received by either Party from a Governmental Authority, shall be dealt with pursuant to the Quality Agreement; provided that all applicable Regulatory Approvals shall be prepared and filed by the Parties in accordance with the provisions of Section 3.

[***] Redacted pursuant to confidential treatment request.

4.10 Labeling. Chiesi shall be responsible for the design of the Label for the Licensed Product in each Country in the Territory and for ensuring that such Label is accurate and complies with all applicable Laws. Chiesi shall be responsible for obtaining approval from applicable Governmental Authorities for any new Label or packaging or change to Label or packaging and shall bear all costs arising therefrom, including in respect of any write-off of materials and work-in-progress unless otherwise included or required as part of the Development of the Licensed Product.

4.11 Shortages. In the event that the materials and/or Manufacturing capacity required to Manufacture and to deliver in a timely manner to Chiesi the Drug Product [***] required under outstanding Purchase Orders are in short supply ("Shortage"), Protalix shall notify Chiesi of such Shortage and the Steering Committee shall promptly meet to discuss the Shortage. Protalix shall provide to the Steering Committee a written plan of action stating in reasonable detail the proposed measures to address such Shortage and the date such Shortage is expected to end. Protalix shall use its Commercially Reasonable Efforts to minimize the duration of any Shortage. During any such Shortage, Protalix shall allocate the materials and resources used in the supply of the Drug Product [***], such that Chiesi receives [***] for the Territory and Protalix receives [***] for outside the Territory.

4.12 Safety Stock Obligations

(a) Build-Up. [***], Protalix shall operate its Facility in order to start building inventory of [***], Drug Substance and Drug Product (the "Safety Stock") with the quantity of [***], Drug Substance and Drug Substance remaining after Protalix supplies the quantities of Drug Product and, if applicable, Drug Substance necessary to conduct the Ongoing Clinical Studies and any [***] and, after the first Launch in the Territory, to meet commercial demand. Protalix shall operate its Facility in such manner until there is a quantity of Safety Stock consisting of (i) Drug Product capable of fulfilling the [***] commercial needs for Licensed Product in the Territory [***], based on the rolling Forecasts submitted by Chiesi pursuant to Section 4.5, (ii) Drug Substance capable of fulfilling the [***] commercial needs for Licensed Product in the Territory, based on the rolling Forecasts submitted by Chiesi pursuant to Section 4.5, and (iii) [***] capable of fulfilling the [***] commercial needs for Licensed Product in the Territory, based on the rolling Forecasts submitted by Chiesi pursuant to Section 4.5 (collectively, the "Safety Stock Amount"). Thereafter, subject to Section 4.12(b), Protalix shall operate its Facility as necessary to maintain the Safety Stock Amount. The Safety Stock may be used to fulfill Protalix's obligations to supply in the event there is a shortage as described in Section 4.11 or a Supply Failure (so long as such Safety Stock complies with the remaining shelf life required under Section 4.7(a), unless otherwise reasonably agreed by the Parties in a given circumstance); provided that [***] of such Safety Stock Amount shall be maintained for the exclusive use of Chiesi.

[***] Redacted pursuant to confidential treatment request.

(b) Sharing of Responsibility and Cost.

(i) For so long as subclause (x) of Section 4.6(h)(ii) applies in a given Country in the Territory, (A) Chiesi shall bear the [***] responsibility for maintaining the Drug Product included in the Safety Stock Amount for such Country through the inclusion of and payment for such Drug Product (as part of, and not in addition to) in applicable Purchase Orders placed in accordance with Section 4.5 and, for clarity, in the Yearly Reconciliation provided for under Section 4.6(h), and (B) Protalix shall bear the [***] responsibility for maintaining the Drug Substance included in the Safety Stock Amount for such Country. On and from the date that such subclause (x) of Section 4.6(h)(ii) no longer applies in a given Country in the Territory in accordance with such Section, the Parties shall share equally the responsibility [***] of building and maintaining the Safety Stock Amount for Drug Substance and Drug Product for such Country, in a manner to be mutually agreed upon by the Parties in good faith at the same time the Maximum Order Quantity is agreed upon in accordance with Section 4.6(i) (and, for clarity, such Safety Stock Amount shall not be included in the Drug Product [***] ordered for such Country for purposes of the Yearly Reconciliation). For clarity, following [***], Chiesi shall be solely responsible for the maintenance of any Safety Stock Amount of Drug Product [***]. Chiesi shall reimburse Protalix for its [***] share of the Safety Stock consisting of [***] within [***] of Protalix providing Chiesi an invoice therefor.

(ii) The Forecasts and Purchase Orders submitted by Chiesi pursuant to Section 4.5 shall make a distinction between the amounts of Drug Product and Drug Substance required by Chiesi for commercial needs in the Territory and the amounts of Drug Product and Drug Substance needed for Safety Stock. For the avoidance of doubt, Protalix shall hold and keep the Safety Stock Amount of Drug Substance and, at Chiesi's option, Chiesi or [***] shall hold and keep the Safety Stock Amount (or a portion thereof) of Drug Product. Protalix shall, upon reasonable request and during regular business hours with as minimal disruption to Protalix's operations as reasonably practicable, allow Chiesi to audit the quantity of Safety Stock in Protalix's possession.

4.13 [***]

(a) [***]

(b) [***]

(c) Business Continuity Plan. Within [***], Protalix shall provide Chiesi with a copy of a business continuity risk assessment and plan for Protalix in relation to the Manufacture and supply of the Drug Product by Protalix hereunder. Such plan (i) shall include an assessment regarding a potential alternative to the current quality control laboratory, and (ii) is intended to be reviewed by Protalix on a yearly basis. Upon Chiesi's request, Protalix shall provide Chiesi information regarding the results of any such review.

[***] Redacted pursuant to confidential treatment request.

4.14 Failure to Supply.

(a) "Failure to Supply" shall occur in the event that Protalix does not supply according to the terms of this Agreement (to the Person responsible for Fill/Finish) for reasons within Protalix's reasonable control (and, for clarity, not for reasons outside Protalix's reasonable control, i.e., a Force Majeure Event) at least [***] of the quantities of Drug Substance specified by Chiesi on Purchase Orders covering [***] (a "Supply Failure"), and such Supply Failure is not cured in the following [***] (whether by using Safety Stock or otherwise). For clarity, notwithstanding anything to the contrary herein, a failure to supply will not be treated as a Supply Failure under this Section 4.14(a) if such failure to supply was due to the failure to conduct Fill/Finish activities or Labeling and Packaging. For the sake of this Section 4.14(a), "cure" means supplying at least [***] of the quantities of Drug Substance specified by Chiesi on the applicable Purchase Orders that are the subject of the Supply Failure.

(b) Rights of Chiesi upon Failure to Supply. In the event of a Failure to Supply, at the option of Chiesi by giving written notice to Protalix, Chiesi shall have the right to, in compliance with applicable Laws and each Party's agreements with Third Parties, [***].

(c) Allocation of Costs. Protalix shall be responsible for [***].

(d) Right of Protalix to Resume Manufacturing. Should Protalix provide Chiesi with commercially reasonable evidence that it is ready, willing and able, directly or through subcontractors reasonably acceptable to Chiesi, to resume its supply obligations hereunder, Chiesi and Protalix will work together in good faith to [***].

(e) [***].

(f) [***]

Section 5. FINANCIAL PROVISIONS

5.1 Effective Date Payment. In consideration for and as reimbursement of the costs sustained by Protalix up to the Effective Date for the Development of the Compound, Drug Substance, Drug Product and Licensed Product (such costs hereby acknowledged and accepted by Chiesi, without any right of further review, challenge or audit with respect to such costs) and in a manner consistent with Section 5.3(a) and Section 5.3(h), Chiesi shall pay to Protalix within twenty (20) days after the Effective Date, the non-refundable, non-creditable amount of Twenty-Five Million Dollars (US $25,000,000). For the avoidance of doubt and notwithstanding the foregoing reference to Section 5.3(a), such amount shall not be included in or subject to the Development Costs Cap, Annual Cap, Required Studies Cap or any other cap on reimbursement provided for herein.

[***] Redacted pursuant to confidential treatment request.

5.2 Event Milestone Payments.

(a) Subject to the terms and conditions of this Agreement, Chiesi shall pay to Protalix the amount set forth in the table below opposite the corresponding event milestone (each an "Event Milestone") within thirty (30) days after the occurrence of such Event Milestone:

Event Milestone	Event Milestone Payment
[***] ("Event Milestone 1a")	[***]
[***] ("Event Milestone 1b")	[***]
Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of [***] ("Event Milestone 2")	[***]
Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of [***] ("Event Milestone 3")	[***]
Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of [***] ("Event Milestone 4")	[***]
Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of [***] ("Event Milestone 5")	[***]
Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of [***] ("Event Milestone 6")	[***]
Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of [***] ("Event Milestone 7")	[***]
Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of [***] ("Event Milestone 8")	[***]
Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of [***] ("Event Milestone 9")	[***]

[***] Redacted pursuant to confidential treatment request.

Annual Net Sales of the Licensed Product in the Territory (together with the Direct Sublicensee Revenue B) equal to or in excess of ("Event Milestone 10") [***]

(b) [***].

(c) For the avoidance of doubt: (i) subject to Section 5.2(d) below, each Event Milestone Payment shall be payable only on the first occurrence of the corresponding Event Milestone; and (ii) none of the Event Milestone Payments shall be payable more than once.

(d) In respect of Event Milestones 2 through 10, should more than one Event Milestone occur in any Commercial Year, then only the highest of such Event Milestone Payments shall be due and payable in such Commercial Year (however, any Deferred Milestones may also be due and payable in such Commercial Year, subject to the below). For example, if Protalix achieves Event Milestone 2, Event Milestone 3, Event Milestone 4, and Event Milestone 5 in the first Commercial Year of this Agreement, only the Event Milestone Payment for Event Milestone 5 shall be due and the Event Milestone Payments for Event Milestone 2, Event Milestone 3 and Event Milestone 4 shall be deferred as set forth below and not paid in that Commercial Year (each, a "Deferred Milestone"). Such Deferred Milestones shall become due and payable in any subsequent Commercial Year in which the corresponding Event Milestone for each such Deferred Milestone is again achieved (irrespective of whether a higher Event Milestone is also achieved in such Commercial Year); provided, that the aggregate Net Sales (together with Direct Sublicensee Revenue B) for such subsequent Commercial Year have not decreased, as compared to the highest amount of Net Sales (together with Direct Sublicensee Revenue B) achieved in any previous Commercial Year. If the aggregate Net Sales (together with Direct Sublicensee Revenue B) for such subsequent Commercial Year has decreased, than only the highest Event Milestone achieved in such year will be payable (i.e., any unpaid Deferred Milestones again shall be deferred to the next Commercial Year). Following on from the above example, if in the subsequent Commercial Year Protalix achieves Event Milestone 2 and Event Milestone 3 only (meaning that there has been a decrease), then in such Commercial Year, the Deferred Milestone for Event Milestone 3 shall be due and payable (being the highest unpaid Event Milestone achieved in such Commercial Year), but the Deferred Milestone for Event Milestone 4 shall remain unpaid (as the corresponding Event Milestone was not achieved in that Commercial Year), and the Deferred Milestone for Event Milestone 2 shall also remain unpaid (as there was a decrease in Net Sales (together with Direct Sublicensee Revenue B)). If instead, the Net Sales (together with Direct Sublicensee Revenue B) increased (for example, Event Milestone 6 had been achieved), than each of the Deferred Milestones for Event Milestone 2, Event Milestone 3 and Event Milestone 4 will be due and payable in such Commercial Year (in addition to the Event Milestone Payment for Event Milestone 6). Following the above example, and assuming that in that second Commercial Year there had been a decrease in aggregate Net Sales (together with Direct Sublicensee Revenue B), but that in the third Commercial Year, Protalix achieves each of Event Milestone 2, Event Milestone 3, Event Milestone 4, Event Milestone 5, and Event Milestone 6, then in such year, the Event Milestone Payment for Event Milestone 6 shall be due (as that is the highest of the Event Milestones achieved), as well as any unpaid Deferred Milestones (in the above example, the remaining Deferred Milestones would be Event Milestone 2 and Event Milestone 4).

[***] Redacted pursuant to confidential treatment request.

(e) Protalix acknowledges and agrees that the right to receive Event Milestone Payments is not a security, shall not be represented by a certificate or other instrument and shall not represent a security or ownership interest in Chiesi, its Affiliates or any of their respective assets.

(f) NOTWITHSTANDING THIS SECTION 5.2, PROTALIX MAKES NO REPRESENTATION, WARRANTY OR COVENANT, EITHER EXPRESS OR IMPLIED, THAT IT WILL BE ABLE TO SUCCESSFULLY DEVELOP AND CHIESI MAKES NO REPRESENTATION, WARRANTY OR COVENANT, EITHER EXPRESS OR IMPLIED, THAT IT WILL BE ABLE TO SUCCESSFULLY COMMERCIALIZE THE LICENSED PRODUCT.

5.3 Development Costs.

(a) Share of Costs. Subject to the Development Costs Cap and Annual Cap, and subject to Section 5.3(d), Chiesi shall reimburse Protalix for [***] of all Development Costs, within [***] of a receipt of an invoice therefor.

(b) Development Costs Cap. Notwithstanding Section 5.3(a), if Chiesi's reimbursement obligation in respect of its share of the Development Costs under Section 5.3(a) at any point during the Term exceeds twenty-five million dollars (US$25,000,000) in the aggregate during the Term (the "Development Costs Cap"), then Chiesi shall have the right but not the obligation to reimburse the amount exceeding the Development Costs Cap. If Chiesi decides to so reimburse, then Chiesi shall be entitled to credit any such amounts in excess of the Development Costs Cap that it pays to Protalix in accordance with Section 5.3(a) against any future payment obligations of Chiesi to Protalix in respect of the Event Milestone Payments and the Price to the extent applicable.

(c) Annual Cap. Notwithstanding Sections 5.3(a), and subject to Section 5.3(b) above, Chiesi's reimbursement obligation in respect of its share of the Development Costs under Section 5.3(a) shall not, in any single Calendar Year during the Term, exceed ten million dollars (US$10,000,000) (the "Annual Cap"); provided, however, that if in any Calendar Year during the Term Chiesi's reimbursement obligation in respect of its share of the Development Costs is less than the Annual Cap, the difference between Chiesi's actual reimbursement obligation for such Calendar Year and the Annual Cap for that Calendar Year shall carry forward to the next Calendar Year, such that the Annual Cap for that next Calendar Year shall increase by such amount (and in respect of such next Calendar Year, any references in this Agreement to Annual Cap shall be read as referring to such increased amount). If fifty percent (50%) of Development Costs for any Calendar Year exceeds the Annual Cap for that Calendar Year, then the difference between such actual Development Costs in that Calendar Year and twice the Annual Cap for such Calendar Year shall be deemed added to such Development Costs for the next Calendar Year (i.e., such amount will be subject to Chiesi's reimbursement obligation of [***] (per Section 5.3(a)) of such amount during the next Calendar Year, subject to the Annual Cap for such Calendar Year and the Development Costs Cap).

[***] Redacted pursuant to confidential treatment request.

(d) [***]. In the event that either Party is obligated to undertake one or more [***] under the terms of this Agreement, subject to this Section 5.3(d), [***] for such [***] ("[***]"), within [***] of a receipt of an invoice therefor. A separately established cap (the "Required Studies Cap") shall apply to any such [***], on the same terms and amounts set forth in Sections 5.3(b) and 5.3(c) (applying *mutatis mutandis*). For the avoidance of doubt, such Required Studies Cap for the [***] shall be calculated and accounted for separate from, and the [***] shall not in any event be included as a part of, the Development Costs Cap or Annual Cap under Sections 5.3(b) and 5.3(c).

(e) [***]. In the event that one or more Additional Studies are required by a Regulatory Authority in [***] for the purposes of obtaining (including, solely with respect to approvals granted upon specific conditions requiring the conduct of specified additional required studies to maintain such granted Regulatory Approval, maintaining) Regulatory Approval for the Licensed Product from a Regulatory Authority in [***], then, prior to proceeding with any such [***], both Parties must agree in writing (such agreement not to be unreasonably withheld, conditioned or delayed) whether to conduct such [***] and to any applicable terms thereto, including as to who will conduct such [***], the sharing or bearing of any costs and expenses associated with the conduct and completion of such [***] and the respective obligations of each Party in respect of the conduct of such [***]. With respect to any Country where a [***] is required by a Regulatory Authority, at the time the Parties agree on the conduct of, and cost-sharing (if any) between the Parties relating to, such [***] in accordance with the foregoing, the Parties shall also agree in writing in good faith on the appropriate financial provisions as between Chiesi and Protalix to apply to sublicensing in such Countries (including with respect to whether and to what extent, for such Country, the Other Sublicensee Revenue Payment (or some other method of addressing Other Sublicensee Revenue in such Country) should apply thereto, and how the Event Milestones and Applicable Rate provisions should apply thereto, with the understanding that if Protalix does not agree to share or bear at least [***] of the costs and expenses associated with the conduct and completion of the [***] for any such Country, such agreement [***].

(f) Clinical Studies Following Regulatory Approval and Additional Studies. Notwithstanding anything to the contrary herein, other than in respect of [***] as provided in Section 5.3(e), (i) Chiesi may only conduct Post-Approval Studies or Additional Studies with the prior written consent of Protalix, such consent not to be unreasonably delayed, withheld or conditioned; and (ii) Chiesi shall be responsible for paying [***], and to the extent Protalix is required to (or is requested by Chiesi to) provide assistance in relation to the conduct of such Post-Approval Studies or Additional Studies, Chiesi shall [***] incurred in providing such assistance (and such reimbursement shall not be subject to the Development Costs Cap, Annual Cap, Required Studies Cap or any other cap on reimbursement provided for herein).

[***] Redacted pursuant to confidential treatment request.

(g) Chiesi Step-in Rights. In the event that Chiesi exercises its step-in rights under Section 3.2(b), each of Sections 5.3(a) through 5.3(f), as applicable shall continue to apply with the obligation shifting to Protalix to reimburse Chiesi for [***] of all Development Costs and/or [***] (as applicable) incurred by Chiesi after the exercise of such step-in rights (i.e., replacing references to "Chiesi" with "Protalix" and vice-versa) in relation thereto, subject to the balances remaining under each of the Development Costs Cap, the Annual Cap, and the Required Studies Cap, as applicable, as of the date on which Chiesi first exercises such step-in rights; provided that any such reimbursement obligation of Protalix shall not be required to be paid by Protalix, but rather shall only be applied by deducting such amounts from immediately applicable future payment obligations of Chiesi to Protalix under this Agreement. For example, if one million dollars ($1,000,000) remains in the Development Costs Cap for the Ongoing Clinical Studies at the time Chiesi exercises its step-in rights, Protalix's responsibility to reimburse [***] of Chiesi's Development Costs in relation thereto shall be limited to a maximum of one million dollars ($1,000,000). In the event that the remaining amounts of the Development Costs Cap or [***] are exceeded during the course of Chiesi's exercise of its step-in rights, Chiesi shall be responsible for [***] of the Development Costs incurred in excess of either such cap. For the avoidance of doubt, [***].

(h) Reimbursement Payments. Where either Party is required to reimburse the other Party in accordance with the terms of this Agreement (including, for the avoidance of doubt, if Protalix has incurred certain Development Costs but Chiesi is responsible for paying such Development Costs pursuant to this Section 5.3), then the Party to whom such reimbursement is owed (the "Reimbursed Party") may, on a monthly basis, send an invoice to such other Party (the "Reimbursing Party") with respect to such reimbursable amounts, along with reasonable evidence thereof, and such Reimbursing Party shall issue payment against such invoices within forty five (45) days of the invoice date (other than as set forth in this Section 5.3 or elsewhere in this Agreement, including Section 5.1).

Section 6. ACCOUNTING AND PROCEDURES FOR PAYMENT

6.1 Periodic Reporting and Reconciliation Payments.

(a) Reports; Payments. Within [***], Chiesi shall provide Protalix with a report stating the Net Sales, Direct Sublicensee Revenue A, Direct Sublicensee Revenue B and Sublicensee Net Sales and computation thereof (including sales in units and in value of the Licensed Product made by or on behalf of Chiesi and its Affiliates and its Sublicensees (together with the calculation of Included Sublicensee Revenue) as applicable, in the Territory, and any permitted deductions from Net Sales and Sublicensee Net Sales), on a Country-by-Country basis, during such preceding Commercial Quarter, together with the calculation of the Price reconciliations as set out in Section 4.6(g) and, if applicable, Section 4.6(h) and the exchange rates used (together with any other supporting documentation reasonably requested by Protalix).

[***] Redacted pursuant to confidential treatment request.

(b) Disputes. In the event of a dispute regarding any amount reported by a Party pursuant to Section 6.1(a), the disputing Party shall provide a notice of the dispute to the other Party, and the Parties will promptly meet and negotiate in good faith a resolution to such dispute. In the event that the Parties are unable to resolve such dispute within thirty (30) days after notice by the disputing Party, the Parties will (i) use Commercially Reasonable Efforts to reach agreement on the appointment of one internationally-recognized independent accounting firm to determine the matter, or (ii) if the Parties cannot reach agreement on such accounting firm within sixty (60) days after notice by the disputing Party, then each Party will appoint one internationally-recognized accounting firm and such firms will choose a third internationally-recognized independent accounting firm to make the final determination, which shall be binding on the Parties.

6.2 Currency. All payments to be made hereunder by one Party to the other Party shall be computed and paid in United States dollars. For the purposes of determining Net Sales, Direct Sublicensee Revenue A, Direct Sublicensee Revenue B and Sublicensee Net Sales, amounts received in any foreign currency shall be converted into United States dollars using the average rate of exchange of the currency of such Country for the applicable calendar month in which such Net Sales, Direct Sublicensee Revenue A, Direct Sublicensee Revenue B or Sublicensee Net Sales occur, as published in the official Bank of Italy website (http://cambi.bancaditalia.it/cambi/cambi.do?lingua=en&to=cambiMedieMForm).

6.3 Method of Payments. Each payment to be made hereunder by either Party to the other Party shall be made by electronic transfer in immediately available funds via either a bank wire transfer, an ACH (automated clearing house) mechanism, or any other means of electronic funds transfer, at the other Party's election, to the account designated (in writing) by the other Party on or before the Effective Date. With respect to any payment invoiced by either Party to the other Party, the other Party may designate a different bank account on such invoice. With respect to any other payment, either Party may designate a different bank account at least thirty (30) days before such payment is due.

6.4 No Set-Off. All payments which either Party is required to make under this Agreement shall be made without any set-off, counterclaim or condition.

6.5 Interest for Late Payments. If either Party fails to make any payment due under this Agreement within [***] of the date upon which such payment is due, then interest shall accrue on such payment on a daily basis from the date such payment was originally due at a rate equal to weekly LIBOR (as published in The Wall Street Journal, New York edition and as officially confirmed by an officer of the respective Party) plus [***], or at the maximum rate permitted by applicable Law, whichever is the lower, and such interest shall be paid when such payment is made.

[***] Redacted pursuant to confidential treatment request.

6.6 Inspection of Records. Chiesi shall, and shall cause its Affiliates and Sublicensees to, keep accurate books and records with respect to the Commercialization of Licensed Product hereunder, setting forth gross sales of the Licensed Product and Net Sales, Direct Sublicensee Revenue A, Direct Sublicensee Revenue B and Sublicensee Net Sales sufficient to enable the calculation of amounts payable hereunder to be verified. Protalix shall, and shall cause its Affiliates and sublicensees to, keep accurate books and records setting forth the Price for the Licensed Products purchased by Chiesi from Protalix hereunder, sufficient to enable the calculation of the Price to be verified (the foregoing books and records of Chiesi and Protalix and their respective Affiliates and sublicensees, the "Financial Records"). Additionally, each Party shall keep sufficiently detailed books and records to enable the other Party to monitor such Party's compliance with the provisions of Sections 9.1(i) and 9.1(j) below (such additional books and records, "Compliance Records"). Each Party will retain such Financial Records and Compliance Records for [***] after the end of the Calendar Year, in which they are generated in order to enable audit of such records as set forth below. Each Party will have the right to request that an independent certified public accountant selected by it examine the other Party's Financial Records, or that such Party's nominated representative examine the other Party's Compliance Records, in each case, at any reasonable time, upon reasonable notice and at the facility(ies) where the other Party's Financial Records or Compliance Records are normally kept (an "Audit"). The foregoing rights of examination may be exercised only [***] during each twelve (12)-month period of the Term and only [***] during each twelve (12)-month period in the three (3) years after final payment has been made. The audited Party may require such accountants (or nominated representative) to enter into a reasonably acceptable confidentiality agreement. In respect of an Audit of a Party's Financial Records, the opinion of said independent accountants regarding such payments shall be binding on the Parties, other than in the case of manifest error. Except as set forth below, [***] shall bear the cost of any such examination and review. In respect of a Party's Financial Records, if such Audit by either Party of the other Party's books and records reveals that such other Party has made an underpayment (or received an overpayment) under this Agreement, then the Party in receipt of any such overpayment, or the Party responsible for any such underpayment, shall promptly reimburse the other Party in the amount of such overpayment or underpayment (as applicable) as was revealed by such Audit. If the discrepancy revealed by the Audit is greater than [***] of the amount due, then the Party responsible for the inaccurate reporting resulting in such overpayment or underpayment shall also promptly reimburse the other Party for any and all costs incurred in connection with such Audit.

6.7 Tax Matters.

(a) Taxes. Subject to Section 6.7(c) below, Chiesi shall assume and pay any and all taxes, customs, duties, assessments, excises and other charges levied upon the importation of or assessed against the Drug Product [***] supplied or rights licensed by Protalix hereunder, or for or on account of the Commercialization of the Licensed Product in the Territory. Prior to [***], Protalix shall assume and pay any and all taxes, customs, duties, assessments, excises and other charges levied upon the importation of or assessed against the Drug Substance in the EU with respect to the shipment of Drug Substance from Protalix to [***].

[***] Redacted pursuant to confidential treatment request.

(b) VAT. It is understood and agreed between the Parties that any payments made by Chiesi under this Agreement are exclusive of any value added or similar tax imposed upon such payments.

(c) Withholding Tax. Payments made by Chiesi to Protalix pursuant to this Agreement shall be made free and clear of any withholding in respect of taxes. [***]

(d) Cooperation. Each Party shall provide the other with reasonable assistance to enable a reduction in, elimination of, or the recovery, as permitted by applicable Law, of withholding taxes, VAT, or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the Party bearing such withholding tax or VAT. Chiesi shall provide reasonable notice to Protalix of its intent to withhold any amount in respect of taxes, and Protalix shall provide to Chiesi any tax forms that may be reasonably requested by and necessary for Chiesi not to withhold tax or to withhold tax at a reduced rate under applicable Law (including an applicable income tax treaty). Each Party further agrees to provide reasonable cooperation to the other Party, at the other Party's expense, in connection with any official or unofficial tax audit or contest relating to payments made by Chiesi to Protalix under this Agreement. Chiesi assumes the sole responsibility of procuring any required permits, authorizations, licenses or consents of Governmental Authorities for the export of funds as may be required in the Territory; provided, however, that to the extent that it is impossible to make such payments due to the "blocking" of funds by applicable Law, such "blocked" funds shall be deposited to the credit of Protalix in such depository as Protalix designates subject to such applicable Law or Chiesi or its Affiliates shall otherwise pay Protalix an amount equal to such "blocked" funds.

Section 7. PATENTS AND INFRINGEMENT

7.1 Filing and Prosecution. Protalix shall have the exclusive right, subject to Sections 7.2 through 7.5, to:

(a) file Patent Applications on any invention included in the Protalix Patent Rights;

(b) take all reasonable steps to prosecute all pending and new Patent Applications included within the Protalix Patent Rights;

(c) respond to oppositions, interferences, nullity actions, re-examinations, revocation actions and similar proceedings filed by Third Parties against the grant of Patents for such Patent Applications; and

(d) maintain in force any patents in the Territory included within the Protalix Patent Rights by duly filing all necessary papers and paying any fees required by the relevant patent Laws of the particular Country in which the patent was granted.

[***]

[***] Redacted pursuant to confidential treatment request.

7.2 Correspondence.

(a) Protalix will keep Chiesi informed of the status of the Protalix Patent Rights to the extent the Protalix Patent Rights [***].

(b) Protalix will, upon Chiesi's request, provide Chiesi with copies of all substantive documentation submitted to, or received from, the patent offices in the Territory in connection therewith. With respect to any Protalix Patent Rights that are not Protalix System Patent Rights, Protalix shall consider in good faith all comments provided by Chiesi with respect to a Protalix Patent Right in the Territory to the extent relating to the Compound or Licensed Product in the Field in the Territory or the Commercialization of the Licensed Product in the Field in the Territory. Protalix shall have final-decision making authority with respect to filings and prosecution of Protalix Patent Rights.

7.3 Maintenance. Protalix will [***] to maintain for the full life thereof all Patent Rights under the Protalix Patent Rights where the abandonment for non-payment [***]. Protalix will notify Chiesi of any decision (a) not to file applications for, or (b) not to enter the national phase for a PCT Patent Application (or not to validate a patent in a particular Country) for, or (c) to cease prosecution and/or maintenance (including the occurrences as set out in Section 7.2) of, or (d) not to pursue, or (e) to cease to pay the expenses of prosecution or maintenance of, any Protalix Patent Rights in any Country in the Territory. In such event, Chiesi shall have the right to make the filing, or to continue the prosecution and maintenance of such Patent Rights (other than Protalix System Patent Rights) in Protalix's name [***]. Notwithstanding the foregoing, Protalix shall have no obligation to provide such notice where the subject Protalix Patent Rights are directed [***] or otherwise where loss of the subject Protalix Patent Rights would not reasonably be expected to impair the Licensed Product in the Field in the Territory in any material respect.

7.4 Notices. Protalix agrees that it will, and will cause its Affiliates to execute and file those notices and other filings as Chiesi shall reasonably request be made, from time to time with any patent office in the Territory with respect to the rights granted under this Agreement, at Chiesi's sole cost and expense.

7.5 Interpretation of Patent Judgments. If any claim relating to a Patent under the Protalix Patent Rights becomes the subject of a judgment, decree or decision of a court, tribunal, or other authority of competent jurisdiction in any Country, which judgment, decree, or decision is or becomes final (there being no further right of review) and adjudicates the validity, enforceability, scope, or infringement of the same, the construction of such claim in such judgment, decree or decision shall be followed thereafter in such Country not only as to such claim but also as to all other claims in such Country to which such construction reasonably applies, in determining whether there are any Valid Claims in such Country. If at any time there are two or more conflicting final judgments, decrees, or decisions with respect to the same claim, the decision of the higher tribunal shall thereafter control, but if the tribunal be of equal rank, then the final judgment, decree, or decision more favorable to such claim shall control unless and until the majority of such tribunals of equal rank adopt or follow a less favorable final judgment, decree, or decision, in which event the latter shall control.

[***] Redacted pursuant to confidential treatment request.

7.6 Third Party Royalty Obligations.

(a) If either Party reasonably determines in good faith that in order to avoid infringement of any Patent Right not licensed hereunder, it is reasonably necessary to obtain a license or acquire the relevant Patent Right or Technology from a Third Party in order to make, use, sell, offer for sale, supply, cause to be supplied, or import the Licensed Product in a Country in the Territory and to pay a royalty or other consideration under such license or acquisition (including in connection with the settlement of a patent infringement claim), then the Steering Committee shall discuss the pertinent Third Party Patent Right and/or Technology and such Party's determination. If the Steering Committee decides (by mutual agreement of the Steering Committee members) that Chiesi should enter into such license or acquisition, Chiesi shall use Commercially Reasonable Efforts to negotiate and enter into a license or acquisition for such Third Party Patent Right and/or Technology. The Steering Committee (by mutual agreement of the Steering Committee members) shall determine each Party's respective share of any payments to the relevant Third Party, other than as provided in Section 13.2.

(b) Other than as provided in Section 13.2, if Chiesi is subject to a final court or other binding order or ruling requiring any payments, including the payment of a royalty to a Third Party Patent holder in respect of Commercialization of the Licensed Product in a Country in the Territory, then the amount of such payments made by Chiesi to the Third Party shall be in addition to, and separate from, any payments due to Protalix under this Agreement; provided that the Steering Committee (by mutual agreement of the Steering Committee members) shall determine each Party's respective share of any such payments to the relevant Third Party.

7.7 Third-Party Infringement. Each Party will promptly notify the other in the event of any actual, potential or suspected infringement of a Patent under the Protalix Patent Rights by any Third Party.

(a) Infringement of Protalix Patent Rights in the Field.

(i) Chiesi shall have the first right, but not the obligation, to institute litigation or take other remedial measures in connection with Third Party infringement of the Protalix Patent Rights occurring in the Field within the Territory [***], where such Third Party infringement would reasonably be expected to impair or has impaired the Commercialization of the Licensed Product in the Field in the Territory in any material respect. In order to establish standing, Protalix, upon request of Chiesi, agrees to timely commence or to join in any such litigation, at Chiesi's cost and expense, and in any event to reasonably cooperate with Chiesi at Chiesi's cost and expense. [***]

[***] Redacted pursuant to confidential treatment request.

(ii) Protalix shall have the sole right, but not the obligation, to institute litigation or take other remedial measures in connection with Third Party infringement of any Protalix Patent Rights occurring outside of the Territory and with respect to Third Party infringement of any Protalix Patent Rights directed solely to any Outside of the Scope Product or occurring outside the Field (within or outside of the Territory) [***].

7.8 Other Actions by a Third Party.

(a) Each Party shall promptly notify the other in the event of any (i) claims by a Third Party of alleged patent infringement by Chiesi or Protalix or any of their respective Affiliates with respect to the research, Development, Manufacture, use, sale, offer for sale or importation of a Compound (other than as used in New Use) or the Licensed Product or (ii) legal or administrative action by any Third Party involving a Protalix Patent Right [***] of which it becomes aware, including any nullity, revocation, reexamination or compulsory license proceeding. Unless subject to the indemnity provided by Protalix under Section 13.2 (in which case Protalix shall have sole control of such action and the defense thereof) or by Chiesi under Section 13.1 (in which case Chiesi shall have sole control of such action and the defense thereof), Chiesi shall have the first right, but no obligation, to defend against any such action involving such Protalix Patent Right in the Territory when the alleged patent infringement would reasonably be expected to impair the Commercialization of the Licensed Product in the Field in the Territory in any material respect [***]. Protalix, upon request of Chiesi, agrees to join in any such action [***] and in any event to reasonably cooperate with Chiesi [***]. If Chiesi declines to defend Protalix against any such action involving a Protalix Patent Right, then Protalix shall have the right to defend such action [***]. Chiesi, upon request of Protalix, shall reasonably cooperate with Protalix in any such action [***]. The Party defending against such action in accordance with this Section 7.8 shall assume direction and control of the defense, litigation, settlement, appeal or other disposition of such Claim (including the right to settle the Claim solely for monetary consideration for which such Party will be responsible) with counsel selected by such Party and reasonably acceptable to the other Party. The other Party shall have the right to join in (including the right to conduct discovery, interview and examine witnesses and participate in all settlement conferences), but not control, at its own expense, the defense of any Claim that such Party is defending as provided in this Section 7.8.

(b) Neither Party will enter into any settlement of any suit involving Licensed Products that materially affects the other Party's rights or obligations with respect to the Licensed Product without the other Party's prior written consent (which consent shall not be unreasonably withheld, delayed or conditioned). Without limiting the foregoing, neither Party shall, without the written consent of the other Party (which consent shall not be unreasonably withheld, delayed or conditioned), effect any settlement of any pending or threatened litigation in which the other Party has any potential liability, unless such settlement involves solely monetary damages and includes an unconditional release of such other Party from all liability on Claims that are the subject matter of such litigation.

[***] Redacted pursuant to confidential treatment request.

7.9 Patent Marking. Each Party shall comply with the patent marking statutes in each Country in which a Licensed Product in the Field is made, offered for sale, sold or imported by such Party, its Affiliates and sublicensees.

Section 8. CONFIDENTIALITY; PUBLICATION

8.1 Confidentiality. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, the Parties agree that for the Term and for [***] years thereafter, each Party shall keep confidential and shall not publish or otherwise disclose and shall not use for any purpose any Confidential Information furnished to it by the other Party pursuant to this Agreement, in a manner no less protective than the actions it would customarily take to preserve the confidentiality of its own similar types of confidential information.

8.2 Permitted Disclosures. Notwithstanding the foregoing, each Party may disclose the other Party's Confidential Information (a) to such Party's employees, consultants (including, for greater certainty, financial advisors), Affiliates, agents, contractors, or permitted sublicensees who are bound by obligations relating to confidentiality at least as restrictive of those contained herein and who have a need to know such information in connection with such Party's performance of its obligations or practice or enforcement of its rights under this Agreement, (b) to Regulatory Authorities in connection with any Regulatory Approvals required for Development of Licensed Product pursuant to the Development Plan or in compliance with applicable Law, including any requirements under or pursuant to the Food and Drug Administration Amendments Act of 2007, or (c) pursuant to Sections 8.3 and 8.4.

8.3 Terms of Agreement. The Parties agree that the material terms of this Agreement will be considered Confidential Information of both Parties. Subject to Section 8.4 below, no Party shall, without the prior written consent of the other Party, disclose in any manner to any Third Party the material terms and conditions of this Agreement, except for terms or subject matter which has been the subject of prior public disclosure or has been mutually approved for such disclosure and except as set forth below. Chiesi acknowledges that Protalix or its Affiliates may be legally required to file this Agreement as an exhibit to filings with the U.S. Securities and Exchange Commission. In addition: (a) either Party may disclose such terms as are required to be disclosed in its publicly-filed financial statements or other public statements, pursuant to applicable Laws, regulations and stock exchange rules (e.g., the rules of the U.S. Securities and Exchange Commission, the NYSE American, the NYSE, NASDAQ, or any other stock exchange on which securities issued by either Party may be listed); provided that such Party shall provide the other Party with a copy of the proposed text of such statements or disclosure (including any exhibits containing this Agreement) sufficiently in advance of the scheduled release or publication thereof to afford such other Party a reasonable opportunity to review and comment upon the proposed text (including redacted versions of this Agreement), (b) either Party shall have the further right to disclose the terms of this Agreement under a confidentiality obligation no less protective than those set forth in this Agreement, to any potential sublicensee, acquirer, merger partner, investor, business partner or potential providers of financing and their advisors or, in the case of Protalix, to the owner of any Protalix Patent Rights or Protalix Technology Controlled by Protalix, and (c) Protalix and Chiesi shall have the right to disclose information regarding the development or commercialization status of the Licensed Product in the Field in the Territory to the extent such disclosure by Protalix or Chiesi, as applicable, is required by applicable Laws or stock exchange rules.

[***] Redacted pursuant to confidential treatment request.

8.4 Mandatory Disclosure.

(a) Notification and Consultation. In the event that a Party is required by applicable Law (including rules of an applicable stock exchange), or pursuant to legal, governmental or self-regulatory organization proceedings (including by court order or judicial or administrative process) to disclose any part of the other Party's Confidential Information (including material terms or conditions of this Agreement), such Party shall (i) promptly notify the other Party of each such requirement and identify the documents so required thereby, so that the other Party may seek an appropriate protective order, confidential treatment or other remedy concerning any such disclosure and/or waive compliance by such Party with the provisions of this Agreement and (ii) consult with the other Party with respect to taking legally available steps to resist or narrow the scope of such requirement.

(b) Limited Disclosure. If, in the absence of such a protective order, confidential treatment request, other remedy or waiver by the other Party, such Party is nonetheless required to disclose any part of the other Party's Confidential Information or any material terms or conditions of this Agreement, such Party may disclose such Confidential Information or material terms or conditions without liability under this Agreement, except that such Party shall furnish only that portion of the Confidential Information or material terms or conditions that in its good faith judgment, after consultation with legal counsel, it is legally required to provide.

8.5 Publication. Subject to the restrictions set out below, nothing herein shall prevent Protalix and its Affiliates (and their respective employees, consultants, contractors, licensees and agents) from publishing or presenting information relating to the development or use of the System, Compound or Licensed Product or otherwise (a) limit the rights of Protalix's Third Party clinical investigators to publish the results of their studies or (b) prevent Protalix or its Affiliates from complying with applicable Law with respect to the disclosure of clinical study data and results or of any other material matter or information. Each Party recognizes that the publications regarding results of and other information regarding Development of Licensed Products in the Field in the Territory, including oral presentations and abstracts, may be beneficial to both Parties, provided that publications are subject to reasonable controls to protect Confidential Information and the Parties' mutual interest in obtaining rights in patent and protecting trade secret information. The Steering Committee shall appoint one referent person for each Party for reviewing and approving such publications ("Referent Person"). Accordingly, the Party proposing to submit any such publication or presentation shall first deliver to the Referent Person for review a copy of such Party's proposed publication or presentation that pertains to the Compound, Drug Substance, Drug Product or Licensed Product in the Field in the Territory prior to submitting the material to a publisher or initiating any such publication thereof. The Referent Person of the non-proposing Party must make a reasonable, good faith determination as to (solely in respect of publications to scientific journals or similar mediums and submission of abstracts to medical congresses) whether the proposing Party may submit such publication, and may (x) require modifications of such publication prior to it being submitted (i) to protect each Party's respective Confidential Information, or (ii) for trade secret reasons or other material commercial reasons; (y) request that the proposing Party delay such submission for an additional period as may be reasonably necessary to seek patent protection for the information disclosed in such proposed written submission; and (z) withhold its approval for such publication if it makes a reasonable, good faith determination that such publication will have an adverse effect on the non-publishing Party's ability to procure a patent or Develop or Commercialize any Licensed Product. The Referent Person of the non-publishing Party shall conduct its review and provide its approval as promptly as reasonably practicable, but in any event within [***] days in case of publications to scientific journals or similar medium and any abstracts to medical congresses (and the failure to provide any such response with such [***] day period shall be deemed approval hereunder). If the Parties are unable to reach agreement on whether the proposing Party may submit such publication, or on the scope of any reasonably necessary modifications or delay in respect of such publication, the issue shall be escalated to the Parties' respective Chief Executive Officers, who shall attempt to resolve the issue within [***] days. In respect of any oral or in-person presentations at medical conferences or medical congresses, posters, trade shows, or similar activities (but, for clarity, excluding business forums), the Referent Person of the non-publishing Party shall be afforded at least [***] Business Days to review and provide comment on any initial working draft thereto and [***] Business Days to review and provide comment on any revised draft (unless a working draft or revised draft is not available or, acting in good faith, the publishing Party considers such review period would risk delaying submission or missing a relevant deadline), and the publishing Party shall consider any such comments received during such [***] Business Day period in good faith; provided, however, that in respect of such oral or in-person presentations, the publishing Party shall not require the approval of the Referent Person of the non-publishing Party to proceed with such presentation.

8.6 Publicity. A draft public announcement of the execution of this Agreement is set forth on Exhibit C attached hereto and, subject to Protalix's further review and comment, shall be promptly disseminated as a press release following the execution of this Agreement by both Parties and the approval by Protalix of the final form thereof. Other than with respect to the matters addressed in Section 8.5 and disclosures required by applicable Law or stock exchange rules, each Party shall only issue press releases that contain material new information (i.e., material information that has not been previously disclosed) concerning the terms of, or events related to, this Agreement or concerning the Compound, Drug Substance, Drug Product or Licensed Product after having provided the other Party with an opportunity to review and approve (such approval not to be unreasonably withheld, conditioned or delayed) such statement; provided that failure to disapprove of such press release in writing within two (2) Business Days shall be deemed approval hereunder. Such Party shall give due consideration to any specific reasonable comments of the other Party on such text timely received from the other Party, subject to such Party's compliance with applicable Laws and stock exchange rules with respect to disclosure.

[***] Redacted pursuant to confidential treatment request.

8.7 Filing, Registration or Notification of the Agreement. Protalix shall provide Chiesi with a proposed form of redacted copy of this Agreement (the "Redacted Agreement") for Chiesi's review and comment as soon as reasonably practicable after the Effective Date, and Protalix shall consider any comments from Chiesi in good faith; provided, however, that the final form of such Redacted Agreement shall be determined by Protalix. If a Party determines that it is required by Law to publicly file, register or notify this Agreement with a Governmental Authority, such Party shall (a) initially file the Redacted Agreement, (b) request, and use Commercially Reasonable Efforts to obtain, confidential treatment of all terms redacted from this Agreement, as reflected in the Redacted Agreement, for a period of at least [***] years, (c) permit the other Party to review and approve such request for confidential treatment and any subsequent correspondence with respect thereto at least [***] Business Days prior to its submission to such Governmental Authority, (d) promptly deliver to the other Party any written correspondence received by it or its representatives from such Governmental Authority with respect to such confidential treatment request and promptly advise the other Party of any other communications between it or its representatives with such Governmental Authority with respect to such confidential treatment request, (e) upon the written request of the other Party, request an appropriate extension of the term of the confidential treatment period, and (f) if such Governmental Authority requests any changes to the redactions set forth in the Redacted Agreement, use Commercially Reasonable Efforts to support the redactions in the Redacted Agreement as originally filed and shall not agree to any changes to the Redacted Agreement without first discussing such changes with the other Party and taking the other Party's comments into consideration when deciding whether to agree to such changes. Each Party shall be responsible for its own legal and other external costs in connection with any such filing, registration or notification.

Section 9. REPRESENTATIONS, WARRANTIES AND COVENANTS

9.1 Mutual Representations, Warranties and Covenants. Each of Chiesi and Protalix hereby represents and warrants to the other Party as of the Effective Date (and covenants as set forth in Sections 9.1(h), 9.1(i), 9.1(j), 9.1(k), and 9.1(l) below) as follows:

(a) It is duly organized, validly existing and in good standing under the Laws of the jurisdiction of its incorporation or formation, as applicable. It has the requisite corporate power and authority to conduct its business as presently being conducted and as proposed to be conducted by it.

(b) It has the requisite corporate power and authority to enter into this Agreement and to perform its obligations hereunder. All corporate actions on its part, necessary for (i) the authorization, execution, delivery and performance by it of this Agreement, and (ii) the consummation of the transactions contemplated hereby, have been duly taken.

[***] Redacted pursuant to confidential treatment request.

(c) Assuming the due authorization, execution and delivery by the other Party, this Agreement constitutes a legally valid and binding obligation of such Party, enforceable against it in accordance with its terms (except in all cases as such enforceability may be limited by applicable bankruptcy, insolvency, reorganization, moratorium, or similar Laws affecting the enforcement of creditors' rights generally and except that the availability of the equitable remedy of specific performance or injunctive relief is subject to the discretion of the court or other tribunal before which any proceeding may be brought).

(d) There is no contractual restriction or obligation binding on such Party which would be materially contravened by execution and delivery of this Agreement or by the performance of its terms. Apart from expiration or termination of any applicable waiting periods (including any extensions thereof) required by any applicable Law or governmental entity for antitrust purposes in the Territory, there are no governmental filings or consents necessary for the consummation of this Agreement and the transactions contemplated hereby.

(e) Such Party is not debarred, and such Party in relation to the Licensed Product is not using, has not used, and will not use in any capacity the services of any person debarred, in each case under Subsection 306(a), (b) of the Generic Drug Enforcement Act of 1992, or any non-U.S. equivalent Law to the foregoing.

(f) To such Party's knowledge, no representation or warranty made by it in this Agreement, nor any statement contained in any schedule hereto furnished by it, contains any untrue statement of a material fact or omits any material fact necessary to make the statements contained herein or therein not misleading.

(g) There is no litigation, proceeding or investigation pending or, to such Party's knowledge, threatened against such Party in any court or before any agency or regulatory body which would reasonably be expected to materially adversely affect such Party's ability or right to carry out the transactions contemplated by this Agreement.

(h) During the Term, each Party shall promptly notify the other Party in writing upon learning of any actual or threatened investigation, inquiry, action or proceeding before the EMA or any other Regulatory Authority in the Territory with respect to the Compound, Drug Substance, Drug Product or Licensed Product.

(i) Each Party shall (i) comply in all material respects with applicable anti-bribery Laws and the Chiesi Anti-Bribery Policy, attached hereto as Exhibit D, and (ii) adopt, implement and keep for the Term, reasonably adequate measures aimed at preventing the commission, even attempted, of conduct in violation in any material respect of anti-bribery Laws by its Affiliates, directors, representatives, employees, and/or consultants involved in the performance of this Agreement.

(j) Each Party and its Affiliates, directors, representatives, employees, and/or consultants involved in the performance of this Agreement, in performing their obligations under this Agreement shall not, directly or indirectly:

(i) offer, transfer, promise or pay money, commissions, compensation or any other benefit (including gifts, entertainment, or any other similar benefit, even low value or non-material benefits, unless they can be considered as low value courtesy benefits) in favor of public or private parties, in violation of applicable anti-bribery Laws, the Chiesi Anti-Bribery Policy and/or with the intention of or as a condition to obtaining illegal benefits in favor of Chiesi or Protalix;

(ii) direct a Third Party to carry out the activities set out in subsection (i) above;

(iii) give, transfer or promise money, commissions, compensation and rewards in kind (including gifts, entertainment or any other similar benefit, even low value or non-material benefits, unless they can be considered as low value courtesy benefits) to the other Party's directors, legal representatives, employees or whoever acts on behalf of such other Party, in violation of any applicable anti-bribery Law and beyond the limits set forth within the Chiesi Anti-Bribery Policy.

(k) Unless to the extent this provision would be a violation of any applicable Laws, Protalix shall promptly notify Chiesi at the following Chiesi e-mail address: groupcompliance@chiesi.com, and Chiesi shall promptly notify Protalix at the following Protalix e-mail address: moshe.manor@protalix.com, if such Party becomes aware of:

(i) any request, promise, offer, or donation of money, commission, compensation or rewards in kind (including gifts, entertainments, or any other similar benefit, even low value or non-material benefits) made to public officers, private parties or the other Party's directors, legal representatives or employees (or whoever acts on behalf of such other Party), in relation to the activities prohibited under Section 9.1(j);

(ii) any gift, entertainment or any other similar benefit, even non-material benefits, carried out by either Party in breach of the provisions of Section 9.1(j); or

(iii) any investigation, administrative suit, law suit or other procedure involving such Party in relation to corruption, bribery or any other similar harmful act to the public treasury.

(l) Each Party shall conduct, and shall use reasonable efforts to cause its Affiliates to conduct, all its activities contemplated under this Agreement in accordance with all applicable Laws of the Country in which such activities are conducted.

9.2 Additional Representations, Warranties and Covenants of Protalix. Protalix hereby further represents and warrants to Chiesi as of the Effective Date (and covenants as set forth in Sections 9.2(f), 9.2(g), 9.2(h), 9.2(i), 9.2(n), 9.2(r) and 9.2(s) below), that, except as set forth in any publically available filings of Protalix or its Affiliates, and solely in respect of the Territory:

(a) Exhibit A contains a complete and correct list as of the Effective Date of all Patents and Patent Applications owned by Protalix covering the Compound, any Licensed Product and the System.

(b) Protalix is the sole and exclusive owner of, or has exclusive rights to, all of the Protalix Patent Rights in existence on the Effective Date that relate to the Compound and/or the Licensed Product in the Field, and the Protalix Patent Rights set forth on Exhibit A are in full force and effect and free and clear of all liens and other encumbrances, security interests or options (other than pursuant to any agreements, secured debt or other financing referenced in Protalix's or its Affiliates' publically available filings).

(c) Protalix has the right to grant the licenses and rights in the Protalix Technology it purports to grant to Chiesi hereunder. For the avoidance of doubt, the foregoing representation and warranty shall not be deemed a representation or warranty with respect to non-infringement, which representation and warranty is solely addressed in Section 9.2(k).

(d) The Protalix Patent Rights and Protalix Technology include all of the Patent and other intellectual property rights owned or Controlled by Protalix or its Affiliates that are necessary for the Commercialization of the Licensed Product. The Protalix Patent Rights have been prosecuted and maintained in accordance with all applicable Laws in all material respects.

(e) No government funding, facilities or resources of a university, college, other educational institution, research center or Regulatory Authority was used in the creation or development of any Protalix Patent Rights and Protalix Technology, other than grants received from the Office of Chief Scientist of the Israeli Ministry of Industry, Trade and Labor.

(f) Any Third Party License relating to the rights licensed to Chiesi under Section 2.1 (and, as a consequence, may also relate to other provisions of this Agreement) is a legal and valid obligation binding upon Protalix and, to Protalix's knowledge, the relevant Third Party licensor (in each case, subject to the effect of any applicable bankruptcy, reorganization, insolvency, moratorium or similar laws affecting creditors' rights generally and subject, as to enforceability, to the effect of general principles of equity (regardless of whether such enforceability is considered in a proceeding in equity or at law)), and authorizes, as necessary, Protalix to grant the sublicense(s) granted to Chiesi under this Agreement. As of the Effective Date, Protalix is in compliance in all material respects with any such Third Party License and Protalix covenants that during the Term it shall not modify or amend any Third Party License in a manner that would materially adversely affect Chiesi's access or rights hereunder without the prior written consent of Chiesi. Protalix has received no notices, whether written or oral, from any Third Party licensor alleging any past or present breach by Protalix of the terms of any such Third Party License. Protalix has issued no notices, whether written or oral, to any Third Party licensor alleging any past or present breach by any Third Party licensor of the terms of the relevant Third Party License. Protalix has provided Chiesi with true, correct and complete copy of any Third Party License, including any amendments thereto.

(g) Protalix shall not take any action that would materially adversely affect the rights granted to Chiesi hereunder with respect to any Third Party License, including selling, assigning or transferring the rights of Protalix under any Third Party License with respect to the Protalix Patent Rights and Protalix Technology, in each case, as relate to the Compound and/or the Licensed Product in the Field in the Territory, without Chiesi's prior written consent. Protalix shall: (i) comply in all material respects with and perform all of its material duties and obligations under any Third Party License relating to the Protalix Patent Rights and Protalix Technology, in each case, as relate to the Compound and/or the Licensed Product in the Field in the Territory; (ii) not intentionally take or fail to take any action within Protalix's reasonable control under any Third Party License that would materially adversely affect Chiesi's rights under this Agreement; (iii) use its Commercially Reasonable Efforts to enforce the provisions of any Third Party License against the relevant Third Party licensor; and (iv) not modify, amend or terminate any Third Party License with respect to the Protalix Patent Rights or Protalix Technology, in each case, as relate to the Compound and/or the Licensed Product in the Field in the Territory, in a manner that would materially adversely affect Chiesi's rights under this Agreement, without the prior written consent of Chiesi.

(h) Subject to Section 8, Protalix shall promptly notify Chiesi (other than to the extent Protalix, acting reasonably, determines that such notice could waive attorney-client privilege or any other legal privilege held by Protalix, or would otherwise breach a confidentiality provision or obligation) in writing of (i) any actual or threatened in writing default (including failure to pay royalties when due, if applicable), breach, suspension of compliance or performance, or termination (in whole or in part) under any Third Party License that relates to the Protalix Patent Rights or Protalix Technology, in each case, as relates to the Compound and/or the Licensed Product in the Field in the Territory, and which would materially adversely affect Chiesi's rights under this Agreement; and (ii) the actual or threatened in writing commencement of any dispute, claim, suit, litigation or arbitration proceeding related to the any Third Party License that relates to the Protalix Patent Rights or Protalix Technology, in each case, as relates to the Compound and/or the Licensed Product in the Field in the Territory, and which would materially adversely affect Chiesi's rights under this Agreement. Each such notification shall contain a summary of the event described therein. At the request of Chiesi, and subject to Section 8, Protalix shall (other than to the extent Protalix, acting reasonably, determines that to do so could waive attorney-client privilege or any other legal privilege held by Protalix, or would otherwise breach a confidentiality provision or obligation) (x) promptly provide to Chiesi full particulars, of which it is aware, in writing of the applicable matter; and (y) keep Chiesi reasonably informed as to the status and proposed resolution of each such matter.

(i) In the event that Protalix receives notice of any default (including failure to pay royalties or other amounts when due) or breach under any Third Party License that relates to the Protalix Patent Rights or Protalix Technology, in each case, as relates to the Compound and/or the Licensed Product in the Field in the Territory and which would materially adversely affect Chiesi's rights under this Agreement, and (i) has not cured such breach or default within ten (10) Business Days of receiving such notice, (ii) has not procured the entry by Chiesi into a Standby License as described in Section 2.2(d), and (iii) the amount of, and liability for, such breach or default is not disputed by Protalix (acting in good faith) or has been resolved in Chiesi's favor under Section 14.3, then Chiesi shall be entitled, but not obligated, to undertake payment or performance of the applicable underlying obligation on behalf of Protalix as necessary to cure such default or breach and to offset, against amounts payable to Protalix under this Agreement, any reasonable out-of-pocket costs and expenses incurred by Chiesi in the course thereof. In the event and to the extent that Protalix disputes the existence of such breach or default (acting in good faith), either Party may by written notice escalate the matter for discussions between the Chief Executive Officers of each Party to negotiate an agreed approach to the alleged breach or default and, to the extent the Parties cannot reach such agreement within thirty (30) days of the receipt of such notice, the Parties shall refer the matter for expert determination in accordance with Section 14.3.

(j) There is no material active, pending or, to Protalix's knowledge, threatened litigation or re-examination, pre- or post-grant or inter partes review, interference, derivation, opposition, claim of invalidity or other claim or proceeding (including in the form of any offer to obtain a license) alleging the invalidity, misuse, unregisterability, unenforceability or non-infringement of any Protalix Patent Rights, or challenging Protalix's ownership of, or Protalix's right to practice or license, any Protalix Patent Rights, or alleging any adverse right, title or interest with respect thereto (in each case, solely as relates to the Compound and/or the Licensed Product in the Field in the Territory).

(k) To the knowledge of Protalix after a reasonable internal inquiry of its executive officers and legal personnel, the practice of the Protalix Patent Rights and Protalix Technology in relation to the Compound and/or the Licensed Product in the Field in the Territory, and the Manufacture, use of the Compound, Drug Substance and/or Drug Product or Commercialization of Licensed Product (as now formulated) as contemplated under this Agreement, does not and will not infringe any issued Patent of any Third Party that exists on the Effective Date or, if and when issued, any Valid Claim within any Third Party Patent Application published before the Effective Date.

(l) Protalix and its Affiliates have complied in all material respects with all applicable Laws, with respect to the Development, Manufacture, use and handling of Compound, Drug Substance, Drug Product and Licensed Product.

(m) Protalix has not received any Form 483 observations, warning letters or other communications from a Regulatory Authority which would reasonably be expected to adversely impact the Development, Manufacture, use, handling of Compound, Drug Substance and/or Drug Product or the Commercialization of Licensed Product in any material respect.

(n) Drug Product (and Compound and Drug Substance) supplied by Protalix to Chiesi hereunder, prior to delivery by Protalix under Section 4.7: (i) will be Manufactured and stored in material compliance with the Product Specifications, GMP and all other provisions of this Agreement, the Quality Agreement and applicable Laws, including applicable environmental Laws, in force at the time of Manufacture, (ii) will not contain any material that would cause the Compound, Drug Substance and/or Drug Product to be adulterated or misbranded within the meaning of any applicable Laws and (iii) shall be free from defects in material and workmanship in all material respects.

(o) To Protalix's knowledge, there are no material investigations, inquiries, actions or other proceedings pending before FDA, EMA or any other Regulatory Authority with respect to the Compound, Drug Substance, Drug Product or Licensed Product.

(p) Protalix has not withheld any data or information known to Protalix related to the Compound, Drug Substance, Drug Product or Licensed Product, including, but not limited to, preclinical and clinical data, regulatory filings and regulatory communications, in each case, that would reasonably be expected to be material to Chiesi's decision to enter into this Agreement.

(q) The information contained in the excel file provided by Protalix to Chiesi via e-mail on October 10, 2017 relating to the costs sustained by Protalix through June 30, 2017 for the Development of the Compound, Drug Substance, Drug Product and Licensed Product is accurate in all material respects.

(r) During the Term, Protalix shall not grant any rights in violation of the rights and licenses granted herein, and Protalix shall not assign the Protalix Patent Rights and/or material Protalix Technology in the Territory except to a permitted assignee of this Agreement pursuant to Section 15.6.

(s) Protalix shall perform its obligations under this Agreement in compliance in all material respects with applicable provisions of the International Federal of Pharmaceutical Manufacturers & Associations Code of Practice and applicable provisions of the Chiesi Code of Ethics and Conduct, attached hereto as Exhibit E.

(t) Protalix has obtained the assignment from the inventors of all inventorship rights in the Protalix Patent Rights owned by Protalix.

9.3 Additional Representation and Warranty of Chiesi. Chiesi hereby further represents and warrants to Protalix as of the Effective Date, that to the knowledge of Chiesi, neither Chiesi nor any of its Affiliates (a) is engaged in the Development or Commercialization of a Competing Product on the Effective Date nor (b) has in effect on the Effective Date a written plan to Develop a Competing Product.

9.4 Disclaimer of Warranty. EXCEPT AS OTHERWISE EXPRESSLY STATED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY, AND EACH PARTY DISCLAIMS ALL, REPRESENTATIONS AND WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, WITH RESPECT TO THE COMPOUND, DRUG SUBSTANCE, LICENSED PRODUCT, SUCH PARTY'S TECHNOLOGY OR PATENT RIGHTS, OR ANY OTHER MATTER, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, AND NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES.

Section 10. NON-COMPETITION

10.1 Chiesi Non-Compete. In respect of each Country, other than to the extent this provision would be a violation of any applicable Laws in such Country, from the Effective Date and throughout the Term, neither Chiesi nor any of its Affiliates (including through any acquisition) shall, directly or indirectly, alone or in collaboration with any Third Party, Develop or Commercialize in any Country any Competing Product; provided that to the extent any of the foregoing restrictions are not permissible under applicable Law in a given Country, such restriction shall not apply only in such Country (and, if possible, shall be modified as necessary to conform to applicable Law in such Country in a manner intended to achieve the original intent of the Parties).

Section 11. TERM

This Agreement shall be effective as of the Effective Date and shall remain in effect until the later of (i) the expiration of the last enforceable Protalix Patent Right, or (ii) the 15th anniversary of Launch on a Country-by-Country basis, unless earlier terminated pursuant to Section 12 (the "Term"); [***].

Section 12. TERMINATION

12.1 Termination Rights. This Agreement may be terminated as follows:

(a) Mutual Agreement. This Agreement may be terminated in its entirety at any time upon mutual written agreement between the Parties.

(b) Material Breach. Either Party may terminate this Agreement at any time upon written notice to the other Party if the other Party is in material default or breach of this Agreement and such material default or breach is not cured within (i) thirty (30) days after written notice thereof is delivered to the defaulting or breaching Party, or (ii) in the case of a breach that cannot be cured within thirty (30) days, within a reasonable period not exceeding ninety (90) days after written notice thereof is delivered to the defaulting or breaching Party, so long as the breaching Party is making a good faith effort to cure such default. For the avoidance of doubt, a [***] does not constitute a material breach of this Agreement and shall not entitle Chiesi to terminate this Agreement. Termination shall not be the sole remedy for material breach of this Agreement, and a Party may choose to continue to perform hereunder and in response to any material breach may bring a claim for damages and other available remedies under this Agreement including, where applicable, a claim for injunctive relief, and bringing such a claim in good faith shall not constitute a breach of this agreement.

(c) Insolvency. Either Party may terminate this Agreement upon written notice to the other Party, if the other Party (i) files, or has filed against it, a petition for voluntary or involuntary bankruptcy or pursuant to any other insolvency Law, or (ii) applies for, or consents to, the appointment of a trustee, receiver or custodian for a substantial part of its property or business.

(d) Change of Control. Protalix may terminate this Agreement upon written notice, and agreement to pay the Buy-Back Payment, to Chiesi, upon the occurrence of a Change of Control in respect of Chiesi; provided, however, that such written notice must be provided within thirty (30) days of Protalix first becoming aware of the Change of Control. For purposes of this Section 12.1(d), "Buy-Back Payment" means [***]. Upon receipt of the termination notice from Protalix, Chiesi must within [***] issue an invoice for the applicable Buy-Back Payment. Such termination will take effect on the first Business Day following written agreement by Protalix to pay the applicable Buy-Back Payment, which must be delivered within [***] of receipt of an invoice provided by Chiesi for a Buy-Back Payment amount that is not disputed by Protalix in good faith. For the avoidance of doubt, until such dispute is resolved pursuant to Section 14.2, such termination will not take effect.

[***] Redacted pursuant to confidential treatment request.

(e) Patent Challenge. Protalix may terminate this Agreement as provided in and in accordance with Section 2.6(b).

(f) [***]. Without limiting its rights under Section 12.1(b):

(i) Protalix may terminate this Agreement (i) in its entirety, upon at least [***] written notice to Chiesi if within [***] of receipt of Regulatory Approval (and Price Approval and Governmental Authority or Third Party reimbursement approval where applicable and required) of the Licensed Product in the [***], Chiesi has not Launched for reasons within its reasonable control (and, for clarity, not for reasons outside Chiesi's reasonable control, i.e., a Force Majeure Event) the Licensed Product in at least one Country [***], or (ii) on a Country-by-Country basis, upon at least thirty (30) days' written notice to Chiesi, if for a period of [***] at any time following Launch of the Licensed Product in [***], Chiesi has [***].

(ii) Protalix may terminate this Agreement in its entirety (or, at Protalix's option, with respect to the applicable Country), in the event that Chiesi or any of its Affiliates (including through any acquisition), directly or indirectly, alone or in collaboration with any Third Party, Develop or Commercialize in any Country any Competing Product.

12.2 Continuing and Accrued Obligations. After notice of termination is given and, subject to the further provisions of this Section 12.2, prior to the effective date of termination, this Agreement, including all payment obligations hereunder, shall continue in full force and effect, and the Parties shall continue to carry out and perform their respective Development, Manufacturing and Commercialization activities in accordance with this Agreement through the effective date of termination. Without limitation of the foregoing, expiration or termination of this Agreement for any reason (i) shall be without prejudice to and shall not impair or limit in any manner (A) Protalix's right to receive payment from Chiesi of the Price (and any reconciliation amounts calculated in accordance with Section 4.6(h)) in respect of sales of Licensed Product in the Territory occurring prior to the effective date of such expiration or termination, whether or not the due date for such payment is after such effective date of expiration or termination, (B) Protalix's right to receive the applicable Event Milestone Payment in respect of any Event Milestone which occurs prior to the effective date of expiration or termination, whether or not the due date for such payment is after such effective date of expiration or termination, (C) Protalix's right to receive payment from Chiesi in accordance with this Agreement for any Licensed Product ordered by Chiesi pursuant to this Agreement prior to the effective date of such expiration or termination, whether or not the due date for such payment is after such effective date of expiration or termination, and (D) any remedies that either Party may have and (ii) shall not release a Party hereto from any indebtedness, liability, payment or other obligation incurred hereunder (including liability for breach of this Agreement) by such Party prior to the effective date of expiration or termination.

[***] Redacted pursuant to confidential treatment request.

12.3 Effects of Termination. Upon expiration or the earlier effective date of termination of this Agreement in accordance with this Section 12 or Section 4.14(e), all licenses and rights provided for herein, and all obligations of the Parties hereunder, shall terminate and this Agreement shall cease to be of further force or effect except as otherwise provided for in Section 15.5.

(a) Upon expiration or termination of this Agreement for any reason:

(i) Chiesi shall, promptly after such expiration or termination, provide to Protalix or its designee the following materials; provided that such materials shall be provided in the form and format in which such materials are maintained by Chiesi in the ordinary course of business (provided that Chiesi shall use Commercially Reasonable Efforts to provide such materials in a form and format useable by Protalix), and Chiesi shall not be required to prepare any new data, reports or information solely for purposes of transfer to Protalix:

(A) all regulatory filings, Regulatory Approvals, Price Approvals and Governmental Authority and Third Party reimbursement approvals to the extent related to the Drug Substance, Drug Product or Licensed Product;

(B) all pre-clinical and clinical data, reports and information (including drug master files) in Chiesi's possession or control to the extent relating to a Licensed Product, Drug Product or Drug Substance;

(C) all reports, records, regulatory correspondence and other materials in Chiesi's possession or control to the extent relating to the pre-clinical and clinical development of the Drug Substance, Drug Product or Licensed Product, and also including, if applicable, any information contained in the global safety database established and maintained by Chiesi for the Licensed Product; and

(D) all Product Marks actually used in commerce by Chiesi or its Affiliates for the Licensed Product, excluding the corporate or trade name or logo of Chiesi or its Affiliates.

(ii) Effective upon such expiration or termination:

(A) Chiesi hereby does (and shall) assign to Protalix, or a Protalix Affiliate identified by Protalix, all of Chiesi's right, title and interest in and to the materials transferred or delivered or deliverable by Chiesi pursuant to Section 12.3(a)(i), including the goodwill attendant to any Product Marks, to the extent Chiesi Controls such materials; with respect to the Product Marks, Chiesi shall execute an assignment of such Product Marks in favor of Protalix and Protalix shall be responsible for recording such assignment with the appropriate governmental trademark authorities. Chiesi shall cooperate in facilitating such assignment and recordation by timely executing all necessary documents provided to it by Protalix;

(B) Chiesi hereby does (and shall) assign to Protalix any applicable sublicenses to the extent related to the Licensed Product and/or Third Party agreements, with respect to significant services to be performed by Third Parties to the extent related to the Licensed Product in the Field, unless Protalix has advised Chiesi that it will not require such assignment.

(iii) Without limitation of the generality of the foregoing, the Parties shall use diligent efforts to complete the transition of the Commercialization of the Licensed Product in the Field in the Territory hereunder to Protalix (or its sublicensee or Third Party designee) as soon as is reasonably possible.

(b) Following any expiration or termination of this Agreement, each of Chiesi and Protalix shall, upon request of the other Party, return or destroy all Protalix Confidential Information and Chiesi Confidential Information, respectively, disclosed to it pursuant to this Agreement, including all copies and extracts of documents, as promptly as practicable following receipt of such request, except (i) that one (1) copy may be kept for the purpose of complying with continuing obligations under this Agreement and (ii) to the extent and for so long as necessary to perform its obligations or exercise its rights under this Section 12.2.

12.4 Following termination of this Agreement, other than termination by Protalix pursuant to Sections 12.1(b), 12.1(c), 12.1(d), 12.1(e), or 12.1(f), notwithstanding the termination of the licenses and rights granted by Protalix to Chiesi hereunder, Chiesi, its Affiliates and its Sublicensees shall have the right to continue to sell their existing inventories of the Licensed Product for a period not to exceed [***] after the effective date of such termination and Protalix shall continue to receive any amounts due hereunder in respect of such Net Sales, Direct Sublicensee Revenue A, Direct Sublicensee Revenue B and Sublicensee Net Sales, including any applicable Event Milestone Payments, or reconciliation amounts calculated in accordance with Section 4.6(h). Following termination of this Agreement (or, in the event of termination by Protalix pursuant to Sections 12.1(b), 12.1(c), 12.1(d), 12.1(e) or 12.1(f), following such [***] period), Chiesi, its Affiliates and its Sublicensees shall promptly return to Protalix or destroy (at Protalix's sole discretion) all inventory of Licensed Products in its possession as of the effective date of termination (or as of the end of such [***] period, as applicable).

Section 13. INDEMNIFICATION AND INSURANCE

13.1 Indemnification by Chiesi. Subject to Sections 13.3 and 13.4, Chiesi shall indemnify, defend and hold Protalix, its Affiliates, and their respective directors, officers, employees, consultants, contractors, sublicensees and agents (collectively, the "Protalix Indemnitees") harmless from and against any and all claims, suits, proceedings or causes of action ("Claims") brought by a Third Party against such Protalix Indemnitee, including any damages or other amounts payable to such Third Party and reasonable attorneys' fees and costs of litigation (collectively, "Damages"), in each case to the extent resulting from or based on: (a) the Commercialization of the Licensed Product or the performance of [***] activities after [***] or Commercial Medical Affairs and Pharmacovigilance activities by Chiesi or any of its Affiliates or Sublicensees; (b) any taxes for which Chiesi is responsible under Sections 4.6(b) and 6.7); (c) Chiesi's breach of this Agreement or of any of its representations, warranties or covenants herein; or (d) the negligence or willful misconduct of, or violation of applicable Law by, Chiesi, its Affiliates or its Sublicensees, or their respective employees, contractors or agents in the performance of this Agreement; in each case, to the extent not resulting from or related to Protalix's breach of its obligations under this Agreement or its negligence or willful misconduct.

[***] Redacted pursuant to confidential treatment request.

13.2 Indemnification by Protalix. Subject to Sections 13.3 and 13.4, Protalix shall indemnify, defend and hold Chiesi, its Affiliates, and their respective directors, officers, employees, consultants, contractors, Sublicensees and agents (collectively, the "Chiesi Indemnitees") harmless from and against any and all Claims brought by a Third Party against such Chiesi Indemnitee, including any Damages, in each case to the extent resulting from or based on: (a) any Development work conducted by Protalix for the Licensed Product; (b) Protalix's breach of this Agreement or of any of its representations, warranties or covenants herein; (c) any claim of infringement of an issued Patent or Technology to the extent such claim arises from a breach or alleged breach of Section 9.2(k); or (d) the negligence or willful misconduct of, or violation of applicable Law by, Protalix, its Affiliates or sublicensees, or their respective employees, contractors or agents in the performance of this Agreement; in each case, to the extent not resulting from or related to Chiesi's breach of its obligations under this Agreement or its negligence or willful misconduct.

13.3 Indemnification of Product Liability Claims. Notwithstanding any other provision of this Agreement, this Section 13.3 shall govern the allocation of liability with respect to any Third Party product liability Claim, including Claims of property injury, bodily injury or deaths related to the Licensed Product in the Territory (a "Third Party Product Claim").

(a) Subject to Section 13.4, Protalix shall indemnify and hold harmless the Chiesi Indemnitees from and against any and all Damages which a Chiesi Indemnitee may incur or suffer arising out of any Third Party Product Claim to the extent caused by or arisen from any defect in the Manufacturing of the Licensed Product by Protalix.

(b) Subject to Section 13.4 and except to the extent provided in subsection (a) above, Chiesi shall defend, indemnify and hold harmless the Protalix Indemnitees from and against any and all Damages arising out of any Third Party Product Claims to the extent caused by or arising out of any sale, use, importation, storage, handling, distribution, offer for sale (or other Commercialization) or sale of Licensed Product in the Territory.

13.4 Defense Procedures; Procedures for Third Party Claims.

(a) For purposes of this Agreement, "Third Party Claim" means a Claim asserted by a Third Party (in no event to include any Affiliate of either Party) against a Party or any of its Affiliates, or any of their respective directors, officers, employees, consultants, contractors, sublicensees and agents. In the event a Third Party Claim is asserted with respect to any matter for which a Party or any of its Affiliates, or any of their respective directors, officers, employees, consultants, contractors, sublicensees and agents (the "Indemnified Party") is entitled to indemnification hereunder, then the Indemnified Party shall promptly notify in writing the Party obligated to indemnify the Indemnified Party hereunder (the "Indemnifying Party") thereof; provided, however, that no delay on the part of the Indemnified Party in notifying the Indemnifying Party shall relieve the Indemnifying Party from any obligation hereunder unless (and then only to the extent that) the Indemnifying Party is prejudiced thereby.

(b) The Indemnifying Party shall assume direction and control of the defense, litigation, settlement, appeal or other disposition of the Third Party Claim (including the right to settle the Claim solely for monetary consideration) with counsel selected by the Indemnifying Party and reasonably acceptable to the Indemnified Party. The Indemnified Party shall have the right to join in (including the right to conduct discovery, interview and examine witnesses and participate in all settlement conferences), but not control, at its own expense, the defense of any Third Party Claim that the Indemnifying Party is defending as provided in this Agreement. Notwithstanding anything to the contrary contained herein, an Indemnified Party shall be entitled to assume the defense of any Third Party Claim with respect to the Indemnified Party, upon written notice to the Indemnifying Party, in which case the Indemnifying Party shall be relieved of liability under Section 13.1, as applicable, solely for such Third Party Claim and related Damages.

(c) Neither Party will enter into any settlement of any suit involving Licensed Products that materially affects the other Party's rights or obligations with respect to the Licensed Product without the other Party's prior written consent (which consent shall not be unreasonably withheld, delayed or conditioned). Without limiting the foregoing, the Indemnifying Party shall not, without the written consent of the Indemnified Party (which consent shall not be unreasonably withheld, delayed or conditioned), effect any settlement of any pending or threatened litigation in which the Indemnified Party has sought indemnification hereunder by the Indemnifying Party, unless such settlement involves solely monetary damages and includes an unconditional release of the Indemnified Party from all liability on Claims that are the subject matter of such litigation.

13.5 Insurance. The Parties shall maintain insurance with creditworthy insurance companies in full force and effect during the Term and, with respect to "claims made" policies, for a period of [***] after expiration or termination of this Agreement as follows: worker's compensation (if applicable), general liability, employers liability, clinical trial liability and product liability insurance coverage in such amounts and with such scope of coverages as are adequate to cover such Party's obligations under this Agreement and as are customary in the industry for companies of like size and activities. Upon written request, each Party shall provide evidence of such insurance to the other Party and ensure that the other Party will receive no less than thirty (30) days' notice of any cancellation or material change in such coverage.

13.6 Disclaimer of Liability for Consequential Damages. IN NO EVENT SHALL EITHER PARTY OR ANY OF ITS RESPECTIVE AFFILIATES BE LIABLE UNDER THIS AGREEMENT FOR SPECIAL, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES, WHETHER IN CONTRACT, WARRANTY, TORT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE, INCLUDING LOSS OF PROFITS OR REVENUE, SUFFERED BY CHIESI, PROTALIX OR ANY OF THEIR RESPECTIVE AFFILIATES. THE FOREGOING SENTENCE SHALL NOT LIMIT THE OBLIGATIONS OF EITHER PARTY TO INDEMNIFY THE OTHER PARTY FROM AND AGAINST THIRD PARTY CLAIMS UNDER SECTION 13 OR LIABILITIES RESULTING FROM A BREACH OF THE CONFIDENTIALITY OBLIGATIONS UNDER Section 8 ABOVE, OR ANY LIABILITY ARISING OUT OF THE INFRINGEMENT OF THE PROTALIX PATENT RIGHTS OR PROTALIX TECHNOLOGY INCLUDING, FOR CLARITY, ANY USE BY CHIESI, ITS AFFILIATES OR ITS SUBLICENSEES OF THE PROTALIX PATENT RIGHTS OR PROTALIX TECHNOLOGY OTHER THAN AS EXPRESSLY PROVIDED FOR IN Section 2 AND PROVIDED THAT THIS SECTION 13.6 SHALL NOT RELIEVE EITHER PARTY FROM ITS PAYMENT OBLIGATIONS UNDER THIS AGREEMENT.

[***] Redacted pursuant to confidential treatment request.

13.7 Sole Remedy. EXCEPT AS EXPRESSLY PROVIDED IN THIS AGREEMENT AND EXCEPT FOR ANY EQUITABLE REMEDIES THAT MAY BE AVAILABLE TO A PARTY, INDEMNIFICATION PURSUANT TO SECTION 13 SHALL BE THE SOLE AND EXCLUSIVE REMEDY (WHETHER BASED ON CONTRACT, TORT OR ANY OTHER LEGAL THEORY) AVAILABLE TO PROTALIX OR CHIESI FOR THE MATTERS COVERED THEREIN.

Section 14. GOVERNING LAW AND JURISDICTION

14.1 Governing Law. This Agreement shall be governed by and construed in accordance with the substantive Laws of the State of New York, without regard to conflicts of law rules. The provisions of the U.N. Convention on Contracts for the International Sale of Goods shall not apply to this Agreement.

14.2 Jurisdiction and Dispute Resolution Process. With the exception of those matters referred for resolution by independent accountants under Section 6.1(b), Section 6.6 or Section 6.7(c) or by independent consultants under Section 4.8(c) or by Joint Legal Counsel under Section 14.3, any dispute, controversy or claim arising out of or relating to this Agreement, or the interpretation or breach thereof, including disputes regarding the existence, validity or termination of this Agreement or the scope of the agreement to arbitrate herein (each, a "Dispute"), shall be determined in accordance with the provisions of this Section 14.2:

(a) If any Dispute arises, either Party may provide written notice of the Dispute to the other Party and request negotiation between the executive officers of each Party ("Dispute Notice"). Within fifteen (15) days after the delivery of a Dispute Notice, the executive officers shall confer in person or by teleconference to attempt to settle the Dispute. All communication between such executive officers shall not be construed as an admission or agreement as to the liability of any Party, nor be admitted in evidence in any related arbitration, litigation, or other adversary proceeding.

(b) If, within thirty (30) days after the delivery of a Dispute Notice, the Parties are unable to resolve the Dispute in writing, upon written notice by any Party to the other Party, such Dispute shall be determined exclusively by arbitration in London, England, before a panel of three (3) arbitrators in accordance with the Rules of Arbitration of the International Chamber of Commerce ("ICC Rules"), except as modified herein.

(c) In any arbitration commenced pursuant to this Section 14.2:

(i) There shall be three arbitrators, one of which shall be nominated by Protalix and another of which shall be nominated by Chiesi, as provided in the ICC Rules. The third arbitrator, who shall serve as the president of the tribunal, shall be jointly nominated by the two Party-nominated arbitrators within twenty (20) days of the date of confirmation of the second arbitrator by the ICC. Any arbitrator not timely nominated as provided herein shall be appointed by the ICC Court.

(ii) The seat of arbitration shall be London, England. The language of the arbitration shall be English. The Parties agree that the award rendered by the arbitral tribunal shall be final and binding and enforceable against the Parties and their respective assets in any court of competent jurisdiction. Unless determined otherwise by the arbitral tribunal, [***]. The arbitral tribunal shall not award any damages excluded by Section 13.6.

(iii) Any arbitration hereunder shall be confidential, and neither the Parties nor their agents shall disclose to any Third Party the existence or status of the arbitration, any information made known or documents produced in the arbitration not otherwise available to them or in the public domain, or any awards arising from the arbitration, except and to the extent that disclosure is required by applicable Law or is required to protect or pursue a legal right.

(iv) For any proceeding in aid of arbitration or for preliminary relief to preserve the status quo or avoid irreparable harm prior to the appointment of an arbitral tribunal, each Party irrevocably and unconditionally consents and submits to the exclusive jurisdiction and venue of the courts located in England, and waives, to the fullest extent possible, any objection to the laying of venue in such courts. The arbitral tribunal also shall have full authority to grant provisional remedies and to direct the Parties to request that any court modify or vacate any provisional, temporary or preliminary relief issued by a court hereunder.

(v) In any action pursuant to Section 14.2 and in any action with respect to any arbitration award obtained pursuant to this Agreement or to the enforcement of such an award, the Parties agree to accept service of process in the manner provided for notices in this Agreement, and to waive any other requirements for service of process in any jurisdiction to the fullest extent permitted by Law.

(vi) Each Party shall continue to perform obligations hereunder, when any bona fide Dispute is pending.

14.3 Expert Legal Determination.

(a) In the event that the Parties are unable to agree on an approach to an alleged breach or default by Protalix of a Third Party License (in accordance with Section 9.2(i)), the Parties shall jointly engage an agreed-upon, independent law firm of reputable stature with relevant licensing expertise (specifically in respect of life science agreements) in the relevant jurisdiction ("Joint Legal Counsel") to provide its legal opinion as to existence of, and liability in respect of, such alleged breach or default of such Third Party License ("Joint Legal Opinion").

[***] Redacted pursuant to confidential treatment request.

(b) [***]. Communications with Joint Legal Counsel, its work product, and the Joint Legal Opinion shall be privileged and confidential and shall not be disclosed to anyone other than the Parties, who will be Joint Legal Counsel's joint clients, except that a Party may disclose the Joint Legal Opinion in confidence to a court or arbitration tribunal if necessary to enforce its rights under this Agreement.

(c) If the Joint Legal Counsel takes the position in the Joint Legal Opinion that the alleged breach or default exists and is able to quantify the amount of liability relating to such breach or default, Chiesi shall be entitled to (but not obligated to) exercise the right set out in Section 9.2(i) to undertake payment or performance of the underlying obligation on behalf of Protalix as necessary to cure such default or breach and to offset, against amounts payable to Protalix under this Agreement, any reasonable out-of-pocket costs and expenses incurred by Chiesi in the course thereof.

(d) If the Joint Legal Counsel takes the position in the Joint Legal Opinion that the alleged breach or default does not exist (or if the Joint Legal Counsel is unable to reach a conclusion in the Joint Legal Opinion as to the existence or otherwise of the alleged breach or default), then Chiesi may not exercise the right set out in Section 9.2(i), and such alleged breach or default may not be again referred for determination under this Section 14.3.

Section 15. MISCELLANEOUS

15.1 Force Majeure. Neither Party hereto shall be liable to the other Party for any losses or damages attributable to a default under or breach of this Agreement that is the result of war (whether declared or undeclared), acts of God, revolution, acts of terror, fire, earthquake, flood, pestilence, riot, enactment or change of Law (following the Effective Date), accident(s), labor trouble, shortage of or inability to obtain material equipment or transport or any other cause beyond the reasonable control of such Party (each, a "Force Majeure Event"); provided that if such a cause occurs, then the Party affected will promptly notify the other Party of the nature and likely result and duration (if known) of such cause and use its Commercially Reasonable Efforts to avoid or remove such causes of nonperformance as soon as is reasonably practicable. Upon termination of the Force Majeure Event, the performance of any suspended obligation or duty shall promptly recommence. If the event lasts for a period of longer than one (1) month, the Parties shall meet and work diligently to implement appropriate remedial measures.

15.2 Severability. If and solely to the extent that any provision of this Agreement shall be invalid or unenforceable, or shall render this entire Agreement to be unenforceable or invalid, such offending provision shall be of no effect and shall not affect the enforceability or validity of the remainder of this Agreement or any of its provisions; provided, however, the Parties shall use their respective reasonable efforts to mutually agree to replace the invalid provisions in a manner that best accomplishes the original intentions of the Parties.

[***] Redacted pursuant to confidential treatment request.

15.3 Waivers. Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver shall be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. Neither the waiver by any Party of any term or condition of this Agreement nor the failure on the part of any Party, in one or more instances, to enforce any of the provisions of this Agreement or to exercise any right or privilege, shall be deemed or construed to be a waiver of such term or condition for any similar instance in the future or of any subsequent breach hereof. All rights, remedies, undertakings, obligations and agreements contained in this Agreement shall be cumulative and none of them shall be a limitation of any other remedy, right, undertaking, obligation or agreement.

15.4 Entire Agreements; Amendments. This Agreement, together with the Quality Agreement(s), sets forth the entire agreement and understanding between the Parties as to the subject matter hereof and supersedes all agreements or understandings, verbal or written, made between Protalix and Chiesi before the date hereof with respect to the subject matter hereof, including the Confidential Disclosure Agreement between the Parties, dated May 24, 2017. All Confidential Information disclosed by either Party to the other Party prior to the Effective Date will be deemed to have been disclosed pursuant to this Agreement. None of the terms of this Agreement shall be amended, supplemented or modified except in writing signed by the Parties.

15.5 Survival. The provisions of Section 2.3 (Non-Assertion of Rights), Section 6.6 (Inspection of Records), Sections 8.1-8.6 and 8.7 (Confidentiality), Section 9.4 (Disclaimer of Warranty), Sections 12.2 and 12.3 (Continuing and Accrued Obligations; Effects of Termination), Section 13.1-13.4, 13.6 and 13.7 (Indemnification; Disclaimer of Liability for Consequential Damages; Sole Remedy), Section 14 (Governing Law and Jurisdiction), and Section 15 (Miscellaneous), as well as (x) any other Sections or defined terms referred to in such Sections or necessary to give them effect and (y) any other provision that by its terms expressly survives termination of this Agreement, shall survive termination of this Agreement and remain in force until discharged in full. Furthermore, any other provisions required to interpret and enforce the Parties' rights and obligations or to wind up their outstanding obligations under this Agreement shall survive to the extent required.

15.6 Assignment; Binding Effect.

(a) Neither this Agreement nor any rights or obligations of either Party to this Agreement may be assigned or otherwise transferred by either Party without the consent of the other Party; provided, however, either Party may, without such consent, assign this Agreement, in whole or in part: (i) to any of its respective Affiliates; provided that such assigning Party shall remain jointly and severally liable with such Affiliate in respect of all obligations so assigned, or (ii) to a Third Party successor to all or substantially all of the assets of such Party whether by merger, sale of stock, all or substantially all of a Party's assets or other similar transaction, so long as such Third Party agrees in writing to be bound by the terms of this Agreement. Notwithstanding anything to the contrary herein, nothing herein shall prevent Protalix or Protalix Parent from engaging in any merger, consolidation, reorganization, sale or purchase of stock, or sale or purchase of assets, or undergoing any Change of Control.

(b) Any purported assignment in violation of this Section 15.6 shall be void. Any permitted assignee shall assume all obligations of its assignor under this Agreement.

15.7 Independent Contractor. The relationship between Protalix and Chiesi is that of independent contractors. Protalix and Chiesi are not joint venturers, partners, principal and agent, employer and employee, and have no other relationship other than independent contracting parties.

15.8 Notices. Each communication and document made or delivered by one Party to another under this Agreement shall be made in the English language. All notices, consents, approvals, requests or other communications required hereunder given by one Party to the other hereunder shall be in writing and made by registered or certified air mail, facsimile, express overnight courier or delivered personally to the following addresses of the respective Parties:

If to Protalix:
Moshe Manor
P.O. Box 455,
Carmiel 20100, Israel
with a copy to:
Yossi Maimon

If to Chiesi:
Chief Executive Officer
Largo F. Belloli, 11/A -
43122 Parma, Italy
with a copy to:
General Counsel; and
Head of Global Corporate Development

Notices hereunder shall be deemed to be effective (a) upon receipt if personally delivered, (b) on the tenth (10th) Business Day following the date of mailing if sent by registered or certified air mail and (c) on the second (2nd) Business Day following the date of transmission or delivery to the overnight courier if sent by facsimile or overnight courier. A Party may change its address listed above by sending notice to the other Party in accordance with this Section 15.8.

15.9 Third-Party Beneficiaries. None of the provisions of this Agreement shall be for the benefit of or enforceable by any Third Party, including any creditor of either Party. No Third Party shall obtain any right under any provision of this Agreement or shall by reason of any such provision make any claim in respect of any debt, liability or obligation (or otherwise) against either Party.

15.10 Binding Effect. This Agreement shall be binding upon and inure to the benefit of the Parties hereto and their respective heirs, successors and permitted assigns.

15.11 Performance by Affiliates. To the extent that this Agreement imposes obligations on Affiliates of a Party, such Party agrees to cause its Affiliates to perform such obligations. Chiesi may use one or more of its Affiliates to exercise its rights or perform its obligations and duties hereunder, provided that Chiesi shall remain liable hereunder for the prompt payment and performance of all of its obligations hereunder, including, for the avoidance of doubt, in respect of any Net Sales, Direct Sublicensee Revenue A, or Direct Sublicense Revenue B (or, as applicable, Sublicensee Net Sales) of Licensed Products attributable to the Commercialization activities of any of Chiesi's Affiliates or Sublicensees.

15.12 Counterparts. This Agreement may be executed in any counterparts, each of which, when executed, shall be deemed to be an original and which together shall constitute one and the same document. Signatures provided by facsimile transmission or in Adobe™ Portable Document Format (PDF) sent by electronic mail shall be deemed to be original signatures.

15.13 Headings. Headings in this Agreement are included herein for ease of reference only and shall have no legal effect.

15.14 Equitable Remedies. The Parties agree that irreparable damage may occur in the event that any of the provisions of this Agreement were not performed in accordance with their specific terms or were otherwise breached. It is accordingly agreed that, without limitation of other remedies which may be available to a Party for breach of this Agreement by the other Party, the Parties shall be entitled to seek an injunction or injunctions to prevent breaches of this Agreement and to enforce specifically the terms and provisions of this Agreement.

[Signature Page Follows]

IN WITNESS WHEREOF the Parties hereto have caused this Agreement to be executed by their duly authorized officers upon the date set out below.

CHIESI FARMACEUTICI S.p.A.

By: /s/ Alberto Chiesi
Name: Alberto Chiesi
Title: President

CHIESI FARMACEUTICI S.p.A.

By: /s/ Ugo Di Francesco
Name: Ugo Di Francesco
Title: Chief Executive Officer

PROTALIX LTD.

By: /s/ Moshe Manor
Name:
Title:

EXHIBIT A

PROTALIX PATENT RIGHTS

[***]

[***] Redacted pursuant to confidential treatment request.

EXHIBIT B

THIRD PARTY LICENSES

[***]

[***] Redacted pursuant to confidential treatment request.

EXHIBIT C

PRESS RELEASE

[***]

[***] Redacted pursuant to confidential treatment request.

EXHIBIT D

CHIESI ANTI-BRIBERY POLICY

[***]

[***] Redacted pursuant to confidential treatment request.

EXHIBIT E

CHIESI CODE OF ETHICS AND CONDUCT

[***]

[***] Redacted pursuant to confidential treatment request.

EXHIBIT F

SELECT MATTERS

[***]

[***] Redacted pursuant to confidential treatment request.

SCHEDULE 3.1

CONFIDENTIAL DRAFT DEVELOPMENT PLAN

[***]

[***] Redacted pursuant to confidential treatment request.

SCHEDULE 3.7

CONFIDENTIAL INITIAL DRAFT COMMERCIALIZATION PLAN

[***]

[***] Redacted pursuant to confidential treatment request.

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-208004) and on Form S-8 (No. 333-148983, No. 333-182677 and No. 333-203960) of Protalix BioTherapeutics, Inc. of our report dated March 6, 2018, relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ Kesselman & Kesselman

Kesselman & Kesselman
Certified Public Accountants (lsr.)
A member firm of PricewaterhouseCoopers International Limited

Tel-Aviv, Israel
March 6, 2018

EXHIBIT 31.1

CERTIFICATION

I, Moshe Manor, certify that:

1. I have reviewed this Annual Report on Form 10-K of Protalix BioTherapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)**)** for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 6, 2018

/s/ Moshe Manor
Moshe Manor
President and Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION

I, Yossi Maimon, certify that:

1. I have reviewed this Annual Report on Form 10-K of Protalix BioTherapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)**)** for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 6, 2018

/s/ Yossi Maimon
Yossi Maimon
Chief Financial Officer, Treasurer

EXHIBIT 32.1

PROTALIX BIOTHERAPEUTICS, INC.

CERTIFICATION

In connection with the Annual Report of Protalix BioTherapeutics, Inc. (the "Company") on Form 10-K for the period ended December 31, 2017 as filed with the Securities and Exchange Commission (the "Report"), I, Moshe Manor, President and Chief Executive Officer of the Company, hereby certify as of the date hereof, solely for purposes of Title 18, Chapter 63, Section 1350 of the United States Code, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company at the dates and for the periods indicated.

This Certificate is being furnished to the Securities and Exchange Commission as an exhibit to the Report.

Dated: March 6, 2018

/s/ Moshe Manor
Moshe Manor
President and Chief Executive Officer

EXHIBIT 32.2

PROTALIX BIOTHERAPEUTICS, INC.

CERTIFICATION

In connection with the Annual Report of Protalix BioTherapeutics, Inc. (the "Company") on Form 10-K for the period ended December 31, 2017 as filed with the Securities and Exchange Commission (the "Report"), I, Yossi Maimon, Vice President and Chief Financial Officer of the Company, hereby certify as of the date hereof, solely for the purposes of Title 18, Chapter 63, Section 1350 of the United States Code, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company at the dates and for the periods indicated.

This Certificate is being furnished to the Securities and Exchange Commission as an exhibit to the Report.

Dated: March 6, 2018

/s/ Yossi Maimon
Yossi Maimon
Vice President and Chief Financial Officer