

\$20,000,000



Common Stock

On July 2, 2021, we entered into an At The Market Offering Agreement, as amended (the "Sales Agreement") with H.C. Wainwright & Co., LLC, as sales agent (the "Sales Agent"), relating to shares of our common stock, par value \$0.001 per share, offered under this prospectus supplement and the accompanying prospectus having an aggregate offering price of up to \$20,000,000. Prior to the date hereof, such shares were offered and sold under a different registration statement on Form S-3 which has since expired. This prospectus supplement and the accompanying prospectus were filed as part of the registration statement on Form S-3 we filed to replace the expired registration statement. Prior to the expiration, we offered and sold shares of common stock under the Sales Agreement for aggregate gross proceeds equal to \$90,777.56; accordingly, we are offering shares of common stock for gross proceeds equal to \$19,909,222.44 under this prospectus supplement and the accompanying prospectus.

In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock at any time and from time to time through the Sales Agent. Sales of the shares, if any, will be made by means of transactions that are deemed to be "at the market" offerings as defined in Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), including block trades and sales made in ordinary brokers' transactions on the NYSE American LLC ("NYSE American") or otherwise at market prices prevailing at the time of the sale, at prices related to prevailing market prices or at negotiated prices. If we and the Sales Agent agree on any method of distribution other than sales of shares of our common stock into the NYSE American or another existing trading market in the United States at market prices, we will file a prospectus supplement providing all information about such offering as required by Rule 424(b) under the Securities Act.

The Sales Agent will receive from us a commission of 3.0% of the gross sales price per share for any shares sold through it under the Sales Agreement. The net proceeds we receive from the sale of our common stock in this offering will be the gross proceeds received from such sales less the commissions and any other costs we may incur in issuing the shares. Subject to the terms and conditions of the Sales Agreement, the Sales Agent is not required to sell any specific number or dollar amount of shares but will use its commercially reasonable efforts to sell on our behalf any shares to be offered under the Sales Agreement. Under the terms of the Sales Agreement, we also may sell shares to the Sales Agent as principal for its own account, at a price agreed upon at the time of sale. If we sell shares to the Sales Agent as principal, we will enter into a separate terms agreement with the Sales Agent setting forth the terms of such transaction, and we will describe this agreement in a separate pricing supplement.

Our common stock is listed on the NYSE American under the symbol "PLX" and on the Tel Aviv Stock Exchange ("TASE") under the symbol "PLX." On April 29, 2022, the last reported sale price of our common stock was \$1.16 per share on the NYSE American and on April 28, 2022, the last reported sale price of our common stock was NIS 3.735 per share on the TASE.

Investing in our common stock involves certain risks. See "Risk Factors" beginning on page S-8 of this prospectus supplement and in the reports we file with the Securities and Exchange Commission ("SEC") pursuant to the Securities Exchange Act of 1934, as amended (the "Exchange Act"), incorporated by reference in this prospectus supplement and the accompanying prospectus to read about factors you should consider before making an investment in our common stock.

Neither the SEC, the Israeli Securities Authority nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

H.C. Wainwright & Co.

The date of this prospectus supplement is May 2, 2022.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying base prospectus are part of a registration statement that we filed with the SEC utilizing a “shelf” registration process. By using a shelf registration statement, we may offer shares of our common stock having an aggregate offering price of up to \$20,000,000 from time to time under this prospectus supplement at prices and on terms to be determined by market conditions at the time of offering.

This document is in two parts. The first part is the prospectus supplement, which describes the specific terms of this offering and certain other matters relating to us. The second part, the accompanying base prospectus, provides more general information, some of which may not apply to this offering. You should read both this prospectus supplement and the accompanying base prospectus as well as the additional information described in this prospectus supplement under the headings “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference” before investing in our common stock.

If information varies between this prospectus supplement and the accompanying base prospectus, you should rely only on the information in this prospectus supplement. To the extent that any statement that we make in this prospectus supplement is inconsistent with the statements made in the accompanying base prospectus or in any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, the statements made in the accompanying base prospectus, or such earlier filing, as applicable, are deemed modified or superseded by the statements made in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

In this prospectus supplement, unless the context indicates otherwise, references to “Company,” “we,” “us” and “our” refer to Protalix BioTherapeutics, Inc. and its consolidated subsidiaries.

YOU SHOULD RELY ONLY ON THE INFORMATION CONTAINED OR INCORPORATED BY REFERENCE IN THIS PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING BASE PROSPECTUS. WE HAVE NOT, AND THE SALES AGENT HAS NOT, AUTHORIZED ANY OTHER PERSON TO PROVIDE YOU WITH DIFFERENT OR ADDITIONAL INFORMATION. IF ANYONE PROVIDES YOU WITH DIFFERENT OR ADDITIONAL INFORMATION, YOU SHOULD NOT RELY ON IT. WE ARE NOT, AND THE SALES AGENT IS NOT, MAKING AN OFFER TO SELL THESE SECURITIES IN ANY JURISDICTION WHERE THE OFFER OR SALE IS NOT PERMITTED. YOU SHOULD ASSUME THAT THE INFORMATION APPEARING IN THIS PROSPECTUS SUPPLEMENT, THE ACCOMPANYING BASE PROSPECTUS AND ANY DOCUMENTS INCORPORATED BY REFERENCE HEREIN OR THEREIN IS ACCURATE ONLY AS OF THE RESPECTIVE DATES OF SUCH INFORMATION, REGARDLESS OF THE TIME OF DELIVERY OF THIS PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING BASE PROSPECTUS OR ANY SALES OF THE SHARES OF COMMON STOCK. OUR BUSINESS, FINANCIAL CONDITION, RESULTS OF OPERATIONS AND PROSPECTS MAY HAVE CHANGED SINCE THOSE DATES.

CAUTIONARY NOTE CONCERNING FORWARD LOOKING STATEMENTS

This prospectus supplement, the accompanying base prospectus and the documents incorporated herein and therein by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, including statements regarding the expectations, beliefs, intentions or strategies for the future. These forward-looking statements are intended to provide management's current expectations or plans for future operating and financial performance based on assumptions currently believed to be valid. Forward-looking statements can be identified by the use of words such as "anticipate," "believe," "estimate," "expect," "can," "continue," "could," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" and words or phrases of similar meaning in connection with a discussion of future operating or financial performance. We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. The statements made in this prospectus supplement, the accompanying base prospectus, and the documents incorporated by reference into this prospectus supplement and the accompanying base prospectus, regarding the following subject matters are forward-looking by their nature:

- the use of proceeds from this offering;
- risks related to the timing and progress of the preparation of an updated Biologics License Application ("BLA") for pegunigalsidase alfa ("PRX-102") addressing the Complete Response Letter ("CRL") we received from the U.S. Food and Drug Administration (the "FDA") on April 27, 2021;
- risks related to the timing, progress and likelihood of final approval by the FDA and the European Medicines Agency ("EMA"), of a resubmitted BLA and of a Marketing Authorization Application ("MAA"), respectively, for PRX-102, and, if approved, whether the use of PRX-102 will be commercially successful;
- the risk that the FDA, the European Medicines Agency (the "EMA") or other foreign regulatory authorities may not accept or approve a marketing application we file for any of our other product candidates;
- 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 FDA, the EMA or other foreign regulatory authorities may not accept or approve a marketing application we file for any of our product candidates, and other risks relating to the review process;
- risks associated with the novel coronavirus disease ("COVID-19") outbreak, which may adversely impact our business, preclinical studies and clinical trials;
- risks related to any transactions we may effect in the public or private equity and debt markets to raise capital to finance future research and development activities, general and administrative expenses and working capital;
- risks relating to our evaluation and pursuit of strategic alternatives;
- the risk that the results of our clinical trials will not support the applicable claims of 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 our collaborators, distributors or partners, including, but not limited to, Pfizer Inc. ("Pfizer") and Chiesi Farmaceutici S.p.A. ("Chiesi");
- risks relating to changes to interim, topline or preliminary data from clinical trials that we announce or publish;
- risks relating to our ability to make required payments under our outstanding convertible notes or any other indebtedness as they come due and our ability to obtain additional financing and raise capital as necessary should the regulatory approval process become more extended;

- risk of significant lawsuits, including, stockholder litigation, which is common in the life sciences sector;
- our dependence on performance by third-party providers of services and supplies;
- the impact of development of competing therapies and/or technologies by other companies;
- risks related to our supply of drug product to Pfizer Inc. (“Pfizer”);
- risks related to our expectations with respect to the potential commercial value of our product and product candidates;
- risks relating to the compliance by Fundação Oswaldo Cruz, an arm of the Brazilian Ministry of Health, with its purchase obligations under our supply and technology transfer agreement, which may have a material adverse effect on us and may also result in the termination of such agreement;
- potential product liability risks, and risks of securing adequate levels of related insurance coverage;
- the possibility of infringing a third-party’s patents or other intellectual property rights and the uncertainty of obtaining patents covering our products and processes and 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.

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. 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 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 and other risks and uncertainties are detailed under the heading “Risk Factors” in this prospectus supplement, in our Annual Report on Form 10-K for the year ended December 31, 2021, and are described from time to time in the reports we file with the SEC.

All forward-looking statements speak only as of the date they are made. New risks and uncertainties arise over time and it is not possible to predict those events or how they may affect us. Except as required by law, we are not obligated to, and we do not intend to, update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

SUMMARY

This summary description of our business highlights selected information about us contained elsewhere in this prospectus supplement or the accompanying base prospectus or the documents incorporated by reference herein or therein. This summary does not contain all the information that you should consider before investing in our securities. You should carefully read the entire prospectus supplement and the accompanying base prospectus, including all documents incorporated by reference herein and therein, before making an investment decision.

We are a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins primarily based on our proprietary ProCellEx[®] protein expression system. We developed our first commercial drug product, Eleyso[®], using our ProCellEx system and we are now focused on utilizing the system to develop a pipeline of proprietary, clinically superior versions of complex 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 most advanced investigational drug in our product pipeline is pegunigalsidase alfa, or PRX-102, a therapeutic protein candidate for the treatment of Fabry disease, a rare, genetic lysosomal disorder, which is the subject of a phase III clinical program. The PRX-102 phase III clinical program includes three separate studies which are referred to as the BALANCE study, the BRIDGE study and the BRIGHT study. The BRIDGE and BRIGHT studies have been completed, and the last patient from the BALANCE study received the final dose of the study in October 2021. In addition, the phase III clinical program includes two extension studies in which subjects that participated in our phase I/II clinical trials and our phase III clinical trials may enroll and continue to be treated with PRX-102. The studies are designed to evaluate the potential superiority of PRX-102 over current therapies in a head-to-head study and a switch-over study, evaluate the potential for improved efficacy and better quality of life for patients with Fabry disease and evaluate the safety of our drug/therapy.

On February 7, 2022, an MAA for PRX-102 was submitted to, and subsequently validated by, the EMA. The submission was made after the October 8, 2021 meeting we held, together with Chiesi, with the Rapporteur and Co-Rapporteur of the EMA regarding PRX-102. At the meeting, we and Chiesi discussed the scope of the then anticipated MAA submission for the European Union, and the Rapporteur and Co-Rapporteur were generally supportive of the planned MAA submission for PRX-102.

On April 28, 2021, we, together with Chiesi, our development and commercialization partner for PRX-102, announced that the receipt of a CRL from the FDA regarding the BLA for PRX-102 for the treatment of adult patients with Fabry disease, which had been submitted in May 2020. The CRL did not report any concerns relating to the potential safety or efficacy of PRX-102 in the submitted data package. In the CRL, the FDA noted that an inspection of our manufacturing facility in Carmiel, Israel, including the FDA's subsequent assessment of any related FDA findings, is required before the FDA can approve a resubmitted BLA. Due to travel restrictions, the FDA was unable to conduct the required inspection during the review cycle. The FDA explained in the letter that it will continue to monitor the public health situation as well as travel restrictions, and is actively working to define an approach for scheduling outstanding inspections. With respect to the third-party facility in Europe at which fill and finish processes are performed for PRX-102, due to COVID-19, the FDA reviewed records under Section 704(a)(4) of the U.S. Federal Food, Drug, and Cosmetic Act in lieu of a pre-licensing inspection. In the CRL, the FDA stated that it will communicate remaining issues to the facility in order to seek prompt resolution of any pending items. In addition to the foregoing, in the CRL, the FDA noted that Fabrazyme[®] (agalsidase beta), a therapy used to treat Fabry patients (marketed by Sanofi after the acquisition of Genzyme), was recently converted to full approval and is now an "available therapy," which must be addressed in the context of any potential resubmission of a BLA for PRX-102.

We and Chiesi participated in a Type A (End of Review) meeting with the FDA on September 9, 2021. As part of the meeting minutes provided by the FDA, which included the preliminary comments and meeting discussion, the FDA, in principle, agreed that the data package proposed to the FDA for a BLA resubmission has the potential to support a traditional approval of PRX-102 for the treatment of Fabry disease. The planned data package for the BLA resubmission, given the changed regulatory landscape in the United States, will include the final two-year analyses of the BALANCE study. We intend to continue to work collaboratively with the FDA to resolve the issues noted in the CRL and provide a new, alternative drug to Fabry patients.

In addition to PRX-102, our product pipeline currently includes, among other candidates:

(1) alidornase alfa, or PRX-110, a proprietary plant cell recombinant human Deoxyribonuclease 1, or DNase, which has successfully completed a phase II efficacy and safety study; we are continuing to evaluate potential strategic marketing partnerships and collaboration programs with biotechnology and pharmaceutical companies for this product candidate for various respiratory indications;

(2) PRX-115, our plant cell-expressed recombinant PEGylated uricase (urate oxidase) – a chemically modified enzyme to treat refractory gout; and

(3) PRX-119, our plant cell-expressed PEGylated recombinant human DNase I product candidate being designed to elongate half-life in the circulation for NETs-related diseases.

Obtaining marketing approval with respect to any product candidate in any country is 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.

We have licensed the rights to commercialize taliglucerase alfa, an enzyme replacement therapy for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease, worldwide (other than Brazil) to Pfizer and the rights to commercialize PRX-102 worldwide to Chiesi. Otherwise, we hold the worldwide commercialization rights to our other 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 institutions. Our common stock is listed on both the NYSE American and the TASE under the symbol "PLX." Our principal executive offices are located at 2 Snunit Street, Science Park, P.O. Box 455, Carmiel 2161401, Israel, our telephone number is 972-4-988-9488 and our corporate website address is www.protalix.com. Our website and the information contained on or accessible through our website are not part of this document. We have included our website address in this prospectus supplement solely as an inactive textual reference.

THE OFFERING

Issuer	Protalix BioTherapeutics, Inc.
Common Stock Being Offered	Shares of our common stock, \$0.001 par value, having an aggregate offering price of up to \$20,000,000.
Common Stock Outstanding Prior to the Offering	46,366,832
Plan of Distribution	“At-the-market” offering that may be made from time to time through our Sales Agent, H.C. Wainwright & Co., LLC. We may also sell shares to the Sales Agent as principal for its own account. See “Plan of Distribution” on page S-15.
Use of Proceeds	We intend to use the net proceeds from the sale of shares for general corporate purposes. See “Use of Proceeds” below.
Risk Factors	See “Risk Factors” on page S-8 of this prospectus supplement for a discussion of factors you should carefully consider before investing in shares of our common stock.
Exchange Listing	Our common stock issued hereunder will be listed for trading on NYSE American. Our common stock is listed on the NYSE American under the symbol “PLX” and on the TASE under the symbol “PLX.”

RISK FACTORS

An investment in our common stock involves risks. We urge you to carefully consider all of the information contained in or incorporated by reference in this prospectus supplement and the accompanying base prospectus and other information which may be incorporated by reference in this prospectus supplement and the accompanying base prospectus as provided under “Incorporation of Certain Documents by Reference.” In particular, you should consider the risk factors under the heading “Risk Factors” in our [Annual Report on Form 10-K for the year ended December 31, 2021](#) which are incorporated by reference in this prospectus supplement and the accompanying base prospectus, as those risk factors are amended or supplemented by our subsequent filings with the SEC. This prospectus supplement also contains forward-looking statements that involve risks and uncertainties. Please read “Cautionary Note Concerning Forward Looking Statements.” Our actual results could differ materially from those anticipated in the forward-looking statements as a result of certain factors, including the risks described in the documents incorporated by reference into this prospectus supplement and the accompanying base prospectus. There may be additional risks that we do not presently know of or that we currently believe are immaterial, which could also impair our business and financial position. If any of these risks occur, this could expose us to liability, and our business, financial condition or results of operation could be adversely affected. As a result, you could lose all or part of your investment.

Risks Related to this Offering

The common stock offered hereby will be sold in “at-the-market” offerings, and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

The actual number of shares we will issue under the Sales Agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the Sales Agreement and compliance with applicable law, we have the discretion to deliver a sales notice to the Sales Agent at any time throughout the term of the Sales Agreement. The number of shares sold by the Sales Agent after delivering a sales notice will fluctuate based on the market price of the shares of common stock during the sales period and limits we set with the Sales Agent. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares that will be ultimately issued.

Sales of our common stock in this offering or otherwise, or the perception that such sales may occur, could cause the market price of our common stock to fall.

We may issue and sell shares of our common stock for aggregate gross proceeds of up to \$20,000,000 from time to time in connection with this offering. The issuance and sale from time to time of these new shares of common stock, or our ability to issue these new shares of common stock in this offering, could have the effect of depressing the market price of our common stock.

In addition, we may issue additional shares of our common stock in subsequent public offerings or private placements for general corporate purposes, to conduct research and development, to make new investments or for other purposes. We are not required to offer any such shares to existing stockholders on a preemptive basis. Therefore, it may not be possible for existing stockholders to participate in such future share issuances, which may dilute the existing stockholders' interests in us.

Management has broad discretion as to the use of net proceeds of this offering, and may not use these net proceeds in a manner desired by our stockholders.

Our management will have broad discretion as to the use of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Our needs may change as our business evolves. As a result, the net proceeds to be received in this offering may be used in a manner significantly different from our current expectations. It is possible that the net proceeds will be invested in a way that does not yield a favorable, or any, return.

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 trading 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 in 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.

There is no certainty regarding the net proceeds to our Company.

There is no certainty that gross proceeds of \$20,000,000 will be raised in this offering. The Sales Agent has agreed to use its commercially reasonable efforts to sell the shares on our behalf if and as instructed by us, or to purchase the shares as principal from time to time, if agreed pursuant to a separate terms agreement. However, we are not required to request the sale of the maximum amount offered or any amount and, if we request a sale, the Sales Agent is not obligated to purchase any shares that are not sold. As a result of the offering being made on a commercially reasonable efforts basis with no minimum, and only as requested by us, we may raise substantially less than the maximum total offering amount or nothing at all.

The common stock is equity and is subordinate to our existing and future indebtedness, including our outstanding convertible notes.

Shares of the common stock are equity interests in our Company and do not constitute indebtedness. As such, shares of the common stock will rank junior to all indebtedness, including our outstanding 7.5% Secured Convertible Promissory Notes due 2024, and other non-equity claims on our Company with respect to assets available to satisfy claims on our Company, including in a liquidation of our Company. Additionally, our board of directors is authorized to issue up to 100,000,000 shares of preferred stock without any action on the part of the holders of our common stock. Holders of our common stock are subject to the prior dividend, liquidation preferences, terms of redemption, conversion rights and voting rights, if any, of any holders of our preferred stock or depositary shares representing such preferred stock then outstanding.

USE OF PROCEEDS

The net proceeds from this offering will depend upon the number of shares of common stock sold and the market price at which they are sold. We intend to use any net proceeds from the sales of shares of our common stock pursuant to this prospectus supplement for general corporate purposes, which may include but are not limited to working capital and funding clinical trials. The amounts and timing of our use of the net proceeds will vary depending on a number of factors, including the progress of our clinical trials. As a result, we will retain broad discretion in the allocation of the net proceeds of this offering, if any.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES

The following is a general summary of the material U.S. federal income tax consequences of the purchase, ownership, and disposition of common stock by a non-U.S. holder (as defined below) that acquires our common stock in this offering and holds it as a capital asset (generally, property held for investment). This discussion is based upon the Internal Revenue Code of 1986, as amended, which we refer to as the Code, effective U.S. Treasury regulations, and judicial decisions and administrative interpretations thereof, all as of the date hereof and all of which are subject to change, possibly with retroactive effect. The foregoing are subject to differing interpretations which could affect the tax consequences described herein. This discussion does not address all aspects of U.S. federal income taxation that may be applicable to investors in light of their particular circumstances, or to investors subject to special treatment under U.S. federal income tax laws, such as financial institutions, insurance companies, tax-exempt organizations, entities or arrangements that are treated as partnerships for U.S. federal income tax purposes, dealers in securities or currencies, expatriates and certain former citizens or long-term residents of the United States, controlled foreign corporations, passive foreign investment companies, persons deemed to sell common stock under the constructive sale provisions of the Code, and persons that hold common stock as part of a straddle, hedge, conversion transaction, or other integrated investment. Furthermore, this discussion does not address any state, local or foreign tax laws or any U.S. federal tax laws other than income tax laws, such as estate and gift tax laws.

This discussion is for informational purposes only and is not tax advice. You are urged to consult your tax advisors regarding the U.S. federal, state, local, and foreign income and other tax consequences of the purchase, ownership, and disposition of our common stock, including the consequences under any applicable income tax treaty.

For purposes of this summary, you are a “non-U.S. holder” if you are a beneficial owner of common stock that, for U.S. federal income tax purposes, is not:

- an individual who is a citizen or resident of the United States;
- a corporation, other entity treated as a corporation for U.S. federal income tax purposes, or partnership that is created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, provided that, (1) a court within the United States is able to exercise primary supervision over its administration or one or more U.S. persons (as defined in the Code) have the authority to control all substantial decisions of that trust, or (2) the trust was in existence on August 20, 1996 and has made an election under the applicable Treasury regulations to be treated as a U.S. person.

If a partnership (including any entity or arrangement treated as a partnership for U.S. federal income tax purposes) owns our common stock, the U.S. federal income tax treatment of a partner in the partnership generally will depend upon the status of the partner, the activities of the partnership, and certain determinations made at the partner level. Accordingly, partners in a partnership that owns our common stock should consult their tax advisors as to the particular U.S. federal income tax consequences applicable to them.

Distributions

Except as described below, if you are a non-U.S. holder of common stock, distributions made to you out of our current or accumulated earnings and profits, as determined for U.S. federal income tax purposes, will be treated as dividends and will be subject to withholding of U.S. federal income tax at a 30% rate or at a lower rate if you are eligible for the benefits of an income tax treaty that provides for a lower rate. Even if you are eligible for a lower treaty rate, we and other payors will generally be required to withhold at a 30% rate (rather than the lower treaty rate) on dividend payments to you, unless you have furnished to us or another payor valid documentation required to claim the benefits under such tax treaty (generally, an Internal Revenue Service Form W-8BEN or W-8BEN-E or a suitable successor or an acceptable substitute form) upon which you certify, under penalties of perjury, your status as (or, in the case of a non-U.S. holder that is a partnership or an estate or trust, such forms certifying the status of each partner in the partnership or beneficiary of the estate or trust as) a non-U.S. person and your entitlement to the lower treaty rate with respect to such payments.

Special certification and other requirements apply to certain non-U.S. holders that are pass-through entities rather than companies or individuals.

If you are eligible for a reduced rate of U.S. withholding tax under an income tax treaty, you may obtain a refund of any amounts withheld in excess of that rate by timely filing a refund claim with the Internal Revenue Service.

If dividends paid to you are effectively connected with your conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that you maintain in the United States), we and other payors generally are not required to withhold tax from the dividends, provided that you have furnished to us or such other payor a valid Internal Revenue Service Form W-8ECI or a suitable successor or an acceptable substitute form upon which you certify, under penalties of perjury, that you are a non-U.S. person and that the dividends are effectively connected with your conduct of a trade or business within the United States and are includible in your gross income. Effectively connected dividends are taxed at rates applicable to U.S. persons on a net income basis. If you are a corporate non-U.S. holder, effectively connected dividends that you receive may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate, or at a lower rate if you are eligible for the benefits of an income tax treaty that provides for a lower rate, as adjusted for certain items.

Distributions in excess of our current and accumulated earnings and profits will not be taxable to the extent that the distributions do not exceed your adjusted tax basis in the shares, but rather will reduce the adjusted tax basis of such shares. To the extent that distributions in excess of our current and accumulated earnings and profits exceed your adjusted tax basis in the shares, such distributions will be included in income as capital gain and will be treated as described below under "Disposition of Common Stock."

Disposition of Common Stock

Except as described below, if you are a non-U.S. holder, you generally will not be subject to U.S. federal income tax on gain from U.S. sources that you recognize on a disposition of our common stock unless:

- the gain is effectively connected with your conduct of a trade or business in the United States (or, if required by an applicable income tax treaty, you maintain a permanent establishment in the United States to which such gain is attributed);

- you are a nonresident alien individual present in the United States for 183 or more days in the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period ending on the date of your disposition of our common stock or your holding period for our common stock.

Effectively connected gains are taxed at rates applicable to U.S. persons on a net income tax basis. If you are a corporate non-U.S. holder, effectively connected gains that you recognize may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate, or at a lower rate if you are eligible for the benefits of an income tax treaty that provides for a lower rate, as adjusted for certain items.

If you are an individual non-U.S. holder described in the second bullet point above, and your tax home is in the United States, then you may be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the disposition, which may be offset by your U.S.-source capital losses provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

We believe we currently are not, and we do not anticipate becoming, a USRPHC for U.S. federal income tax purposes. However, because the determination of whether we are a USRPHC depends on the fair market value of our USRPIs relative to the fair market value of our other trade or business assets and our foreign real property interests, there can be no assurance that we will not become a USRPHC in the future. Even if we are or become a USRPHC, as long as our common stock is “regularly traded” on an “established securities market” (as such terms are defined by applicable U.S. Treasury regulations), such common stock will be treated as a USRPI with respect to you only if you actually or constructively held more than 5% of such regularly traded common stock during the applicable period. If we are determined to be a USRPHC and the foregoing exception does not apply, you generally will be taxed on your net gains derived from the disposition on a net income tax basis. No assurance can be provided that our common stock will be regularly traded on an established securities market for purpose of the rules described above.

Information Reporting and Backup Withholding

We must generally report annually to the Internal Revenue Service and to each non-U.S. holder the amount of dividends paid to such holder, if any, and the tax withheld with respect to such dividends, regardless of whether withholding was required. Copies of the information returns reporting such dividends and withholding may also be made available to the tax authorities in the country in which the non-U.S. holder resides under the provisions of an applicable income tax treaty.

A non-U.S. holder may be subject to backup withholding for dividends paid to such holder unless such holder certifies under penalty of perjury that it is a non-U.S. holder (generally, by furnishing a valid Internal Revenue Service Form W-8BEN, W-8BEN-E, W-8ECI, W-8EXP, or other applicable Internal Revenue Service Form) or such holder otherwise establishes an exemption and we do not have actual knowledge or reason to know that such holder is a U.S. person as defined under the Code.

Information reporting and, depending on the circumstances, backup withholding will apply to the proceeds of a sale of our common stock within the United States or conducted through certain U.S.-related financial intermediaries, unless we receive the certification described above or such holder otherwise establishes an exemption and we do not have actual knowledge or reason to know that such holder is a U.S. person as defined under the Code.

Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's U.S. federal income tax liability provided the required information is timely furnished to the Internal Revenue Service.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code, U.S. Treasury regulations promulgated thereunder, and other official guidance (commonly referred to as FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code and whether such institution or entity is the beneficial owner or an intermediary), unless those entities comply with certain requirements under the Code and applicable U.S. Treasury regulations, which requirements may be modified by an "intergovernmental agreement" entered into between the United States and an applicable foreign country. Future U.S. Treasury regulations or other official guidance may modify these requirements.

Pursuant to proposed regulations, the Treasury Department has indicated its intent to eliminate the requirements under FATCA of withholding on gross proceeds from the sale or other disposition of certain financial instruments (which would include our stock). The Treasury Department has indicated that taxpayers may rely on these proposed regulations pending their finalization.

Any applicable FATCA withholding tax will apply to all withholdable payments without regard to whether the beneficial owner of the payment would otherwise be entitled to an exemption from imposition of withholding tax pursuant to an applicable income tax treaty with the United States or U.S. domestic law.

Investors are urged to consult their own tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

DILUTION

If you purchase shares of our common stock in this offering, you will experience dilution to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share after giving effect to this offering. We calculate net tangible book value (deficit) per share by dividing the net tangible book value (deficit), which is tangible assets less total liabilities, by the number of outstanding shares of our common stock. Dilution represents the difference between the public offering price per share paid by purchasers in this offering and the as adjusted net tangible book value (deficit) per share of our common stock immediately after giving effect to this offering. Our net tangible book value (deficit) as of December 31, 2021 was approximately \$(6.04) million, or \$(0.13) per share.

After giving further effect to the assumed sale in this offering of \$19.9 million of our common stock, at an assumed public offering price of \$1.16 per share, the last reported sale price of our common stock on the NYSE American on April 29, 2022, and after deducting the commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2021 would have been \$13.2 million, or \$0.21 per share of common stock. This represents an immediate increase in the as adjusted net tangible book value of \$0.34 per share to our existing stockholders and an immediate dilution per share of \$0.95 to new investors. The following table illustrates this per share dilution:

Assumed public offering price per share		\$	1.16
Net tangible book value (deficit) per share as of December 31, 2021	\$	(0.13)	
Increase in net tangible book value per share attributable to this offering	\$	0.34	
As adjusted net tangible book value per share after giving effect to this offering		\$	0.21
Dilution per share to new investors participating in this offering		\$	0.95

The above table and discussion is based on 45,556,647 shares of common stock outstanding as of December 31, 2021.

PLAN OF DISTRIBUTION

We have entered into the Sales Agreement with H.C. Wainwright & Co., LLC, as the sales agent, under which we may, over a period of time and from time to time, offer and sell shares of our common stock having an aggregate sales price of up to \$20,000,000 through the Sales Agent or to the Sales Agent. We will file a copy of the Sales Agreement as an exhibit to the Current Report on Form 8-K to be incorporated by reference in the registration statement of which this prospectus supplement forms a part. The sales, if any, of our common stock made under the Sales Agreement, and to which this prospectus supplement relates, will be made in “at the market” offerings as defined in Rule 415 under the Securities Act, including block trades and sales made in ordinary brokers’ transactions on the NYSE American or otherwise at market prices prevailing at the time of the sale, at prices related to prevailing market prices or at negotiated prices. If we and the Sales Agent agree on any method of distribution other than sales of shares of our common stock into the NYSE American or another existing trading market in the United States at market prices, we will file a prospectus supplement providing all information about such offering as required by Rule 424(b) under the Securities Act.

The offering of common stock pursuant to the Sales Agreement will terminate upon the earlier of (1) the sale of common stock having an aggregate sales price of \$20,000,000, (2) the expiration date of the registration statement of which this prospectus supplement and the accompanying prospectus are a part and (3) the termination by us or the Sales Agent of the Sales Agreement pursuant to its terms.

We also may sell shares of our common stock to the Sales Agent, as principal for its own account, at a price per share agreed upon at the time of sale. If we sell shares of our common stock to the Sales Agent, as principal, we will enter into a separate terms agreement with such Sales Agent, and we will describe the agreement in a separate prospectus supplement.

From time to time during the term of the Sales Agreement, we may deliver a placement notice to the Sales Agent specifying the length of the selling period, the amount of shares of common stock to be sold and the minimum price below which sales may not be made.

The Sales Agent has agreed that, upon receipt of a placement notice from us that is accepted by the Sales Agent, and is subject to the terms and conditions of the Sales Agreement, the Sales Agent will use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares of our common stock on such terms. We or the Sales Agent may suspend the offering of the shares of common stock at any time upon proper notice to the other party, upon which the selling period will immediately terminate. Settlement for sales of the shares of our common stock is expected to occur on the second business day following the date on which any sales were made. The obligation of the Sales Agent under the Sales Agreement to sell common shares pursuant to any placement notice is subject to a number of conditions, which the Sales Agent reserves the right to waive in its sole discretion.

If acting as sales agent, the Sales Agent will provide to us written confirmation following the close of trading on the NYSE American on each trading day on which shares are sold under the Sales Agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross sales proceeds of the shares, the net proceeds to us (after deduction of any transaction fees, transfer taxes or similar taxes or fees imposed by any governmental entity or self-regulatory organization in respect of such sales) and the aggregate compensation payable by us to the Sales Agent with respect to such sales. We will report, on a quarterly basis, the number of shares sold by or through the Sales Agent during such quarterly fiscal period, the net proceeds received by the Company and the aggregate compensation paid by the Company to the Sales Agent with respect to such sales.

We will pay the Sales Agent a commission of 3.0% of the gross sales price per share for any shares sold through it as an agent under the Sales Agreement. We have agreed to reimburse the Sales Agent for certain fees and expenses in connection with this offering, including the fees and disbursements of counsel to the Sales Agent, up to an amount not to exceed \$50,000.

In connection with the sale of our common stock on our behalf, the Sales Agent may be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to the Sales Agent may be deemed to be underwriting commissions or discounts. We have agreed in the Sales Agreement to provide indemnification and contribution to the Sales Agent against certain civil liabilities, including liabilities under the Securities Act.

Sales of our common stock, which are the subject of this offering, may be issued from shares that we hold as treasury shares. Sales of the common stock as contemplated by this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and the Sales Agent may agree upon.

The offering of the common stock pursuant to the Sales Agreement will terminate upon the earliest of (1) the sale of the maximum aggregate amount of our common stock subject to the Sales Agreement, (2) the expiration date of the registration statement of which this prospectus supplement and the accompanying base prospectus are a part, and (3) the termination of the Sales Agreement by either party at any time upon three days’ notice, or by the Sales Agent, upon notice to the Company, in certain circumstances, including certain bankruptcy events relating to us or any material subsidiary, our failure to maintain a listing of our common stock on the NYSE American or the occurrence of a material adverse effect on our Company.

We estimate that the total expenses of this offering payable by us, excluding commissions payable to the Sales Agent under the Sales Agreement, will be approximately \$150,000.

The Sales Agent and its affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. The Sales Agent and its affiliates have provided, and may in the future provide, a variety of these services to us and to persons and entities with relationships with us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the Sales Agent and its affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to our assets, securities and/or instruments (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The Sales Agent and its affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

No Public Offering Outside of the United States

Other than in the United States, no action has been taken that would permit a public offering of the securities offered by this prospectus supplement and the accompanying base prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement and the accompanying base prospectus may not be offered or sold, directly or indirectly, nor may this prospectus supplement and the accompanying base prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement and the accompanying base prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement and the accompanying base prospectus. This prospectus supplement and the accompanying base prospectus do not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement and the accompanying base prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Mayer Brown LLP, New York, New York. Ellenoff Grossman & Schole LLP, New York, New York, is acting as counsel to the Sales Agent in connection with this offering.

EXPERTS

The financial statements incorporated in this prospectus supplement by reference to the [Annual Report on Form 10-K for the year ended December 31, 2021](#) have been so incorporated in reliance on the report of Kesselman & Kesselman, Certified Public Accountants (Isr.), a member firm of PricewaterhouseCoopers International Limited, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC in connection with this offering. In addition, we file annual, quarterly, current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public at the SEC's Internet site at <http://www.sec.gov>. Our reference to the SEC's Internet site is intended to be an inactive textual reference only.

In addition, since we are also listed on the TASE, we submit copies of all our filings with the SEC 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).

Copies of certain information filed by us with the SEC are also available on our website at www.protalix.com. Information contained in or accessible through our website does not constitute a part of this prospectus supplement and is not incorporated by reference in this prospectus supplement.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference information into this document. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is an important part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Section 13(a), 13(c), 14, or 15(d) of the Exchange Act made subsequent to the date of this prospectus supplement until the termination of the offering of the securities described in this prospectus supplement (other than information in such filings that was “furnished,” under applicable SEC rules, rather than “filed”).

We incorporate by reference the following documents or information that we have filed with the SEC:

- [our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on March 31, 2022;](#)
- our Current Reports on Form 8-K filed with the SEC on [February 24, 2022](#), [March 31, 2022](#); and [April 4, 2022](#) (other than Items 2.02 and 9.01);
- [our Definitive Proxy Statement, filed on April 29, 2022, for our Annual Meeting of Stockholders scheduled to be held on June 30, 2022;](#) and
- [the description of our common stock included in our registration statement on Form 8-A12B \(File No. 001-33357\) filed with the Commission on March 9, 2007, including any amendment or reports filed for the purpose of updating such description.](#)

Copies of these filings are available at no cost on our website, www.protalix.com. In addition, you may request a copy of these filings at no cost by writing or telephoning us at the following address:

Eyal Rubin
2 Snunit Street, Science Park
P.O. Box 455
Carmiel 2161401, Israel
+972-4-988-9488

You should rely only on the information incorporated by reference or provided in this prospectus supplement or the accompanying base prospectus. We have not authorized anyone else to provide you with different or additional information. An offer of these securities is not being made in any jurisdiction where the offer or sale is not permitted. You should not assume that the information in this prospectus supplement or the accompanying base prospectus is accurate as of any date other than the date on the front of those documents.

\$100,000,000
PROTALIX
Biotherapeutics

Common Stock
Preferred Stock
Debt Securities
Warrants

We may from time to time offer, in one or more series, separately or together, the following:

- our common stock;
- our preferred stock in one or more series;
- debt securities in one or more series; and
- warrants to purchase our common stock.

The aggregate public offering price of the securities that we may offer through this prospectus will be up to \$100,000,000.

We will provide the specific terms of the securities offered by us in supplements to this prospectus, which we will deliver together with the prospectus at the time of sale. This prospectus may not be used to sell securities unless accompanied by a prospectus supplement. Please read this prospectus and the applicable prospectus supplement carefully before you invest in any of our securities.

We may, from time to time, offer and sell these securities directly or through one or more underwriters, agents or dealers, through underwriting syndicates managed or co-managed by one or more underwriters, or directly to purchasers, on or off the NYSE American at prevailing market prices or at privately negotiated prices, on a continuous or delayed basis.

Our common stock is listed on the NYSE American under the symbol "PLX" and on the Tel Aviv Stock Exchange under the symbol "PLX." On April 19, 2022, the last reported sale price of our common stock was \$1.33 per share on the NYSE American and NIS 4.27 per share on the Tel Aviv Stock Exchange.

Investing in our securities involves risks. Risks associated with an investment in our securities will be described in the applicable prospectus supplement and certain of our filings with the Securities and Exchange Commission, as described under the caption "Risk Factors" on page 4.

None of the Securities and Exchange Commission, the Israeli Securities Authority or any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is April 29, 2022

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No dealer, salesman or other person has been authorized to give any information or to make any representations in connection with the offer made by this prospectus or any prospectus supplement other than those contained in, or incorporated by reference in, this prospectus or any prospectus supplement, and if given or made, such information or representations must not be relied upon as having been authorized by us or any underwriter, agent or dealer. We or an authorized underwriter, agent or dealer may also furnish you with a free writing prospectus relating to the applicable securities. This prospectus, any prospectus supplement or any free writing prospectus does not constitute an offer to sell or a solicitation of any offer to buy any securities in any jurisdiction to any person to whom it is unlawful to make an offer or solicitation in such jurisdiction. The delivery of this prospectus, any prospectus supplement or any free writing prospectus at any time does not imply that the information contained herein or therein is correct as of any time subsequent to their respective dates.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

The statements set forth and incorporated by reference in this prospectus, which are not historical, constitute “forward- looking statements” within the meaning 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 the expectations, beliefs, intentions or strategies for the future. When used in this prospectus, or in any document incorporated by reference in this prospectus, the terms “anticipate,” “believe,” “estimate,” “expect,” “can,” “continue,” “could,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” and 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. 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. We intend that all forward-looking statements be subject to the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995. 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:

- risks related to the timing and progress of the preparation of an updated Biologics License Application, or BLA, for PRX-102 addressing the Complete Response Letter, or CRL;
- risks related to the timing, progress and likelihood of final approval by the U.S. Food and Drug Administration, or the FDA, and the European Medicines Agency, or the EMA, of a resubmitted Biologics License Application, or BLA, and of a Marketing Authorization Application, or an MAA, respectively, for PRX-102, and, if approved, whether the use of PRX-102 will be commercially successful;
- 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 FDA, the EMA, or other foreign regulatory authorities may not accept or approve a marketing application we file for any of our product candidates, and other risks relating to the review process;
- risks associated with the novel coronavirus disease, or COVID-19, outbreak and variants, which may adversely impact our business;
- risks related to any transactions we may effect in the public or private equity markets to raise capital to finance future research and development activities, general and administrative expenses and working capital;
- risks relating to our evaluation and pursuit of strategic alternatives;
- the risk that the results of our clinical trials will not support the applicable claims of safety or efficacy and that our product candidates will not have the desired effects or will be associated with undesirable side effects or other unexpected characteristics;
- risks relating to our ability to manage our relationship with our collaborators, distributors or partners, including, but not limited to, Pfizer Inc., or Pfizer, and Chiesi Farmaceutici S.p.A., or Chiesi;
- risks relating to changes to interim, topline or preliminary data from clinical trials that we announce or publish;
- risk of significant lawsuits, including stockholder litigation, which is common in the life sciences sector;

- our dependence on performance by third-party providers of services and supplies, including without limitation, clinical trial services;
- the impact of development of competing therapies and/or technologies by other companies;
- risks related to our supply of drug product to Pfizer;
- risks related to our expectations with respect to the potential commercial value of our product and product candidates;
- 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 us and may also result in the termination of such agreement;
- potential product liability risks, and risks of securing adequate levels of related insurance coverage;
- the possibility of infringing a third-party's patents or other intellectual property rights and the uncertainty of obtaining patents covering our products and processes and successfully enforcing our intellectual property rights against third-parties;
- risks relating to changes in healthcare laws, rules and regulations in the United States, the European Union 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 certain regulatory authorities and of certain of our suppliers, collaborative partners, licensees, clinical trial sites, distributors and customers.

Given these uncertainties, you should not place undue reliance on these forward-looking statements. 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 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 and other risks and uncertainties are detailed under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021, and are described from time to time in the reports we file with the U.S. Securities and Exchange Commission, or the Commission.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Commission using a “shelf” registration process. Under this shelf registration process, we may sell shares of common stock and preferred stock, debt securities and/or warrants in one or more offerings, up to a total dollar amount of \$100,000,000.

This prospectus provides you with a general description of the securities we may offer under this prospectus. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus.

The Commission allows us to “incorporate by reference” certain information that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the Commission will update automatically, supplement and/or supersede this information. Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other document that also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. You should read the detailed information regarding our company, our securities and our financial statements and the notes to those statements appearing elsewhere in this prospectus or incorporated herein by reference.

You should read both this prospectus and the applicable prospectus supplement together with additional information from the sources described under the caption “Where You Can Find More Information” in this prospectus. You should not assume that the information in this prospectus, the prospectus supplements, any free writing prospectus or any document incorporated by reference is accurate as of any date subsequent to their respective dates.

You should rely only on the information provided or incorporated by reference in this prospectus, any free writing prospectus and any prospectus supplement, if applicable. We have not authorized anyone to provide you with different information.

References in this prospectus to “our company,” “we,” “our,” and “us” refer to Protalix BioTherapeutics, Inc.

OUR BUSINESS

We are a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins primarily 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 complex 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.

Pegunigalsidase alfa (PRX-102), our proprietary plant cell culture expressed enzyme in development for the treatment of Fabry disease, is our most advanced product candidate. Our PRX-102 phase III clinical program of PRX-102 for the treatment of Fabry disease includes three separate studies: the *BALANCE*, *BRIDGE* and *BRIGHT* studies. The *BRIDGE* and *BRIGHT* studies have been completed, and the last patient in the *BALANCE* study received the final dose in the study in October 2021. The studies were designed to evaluate the potential superiority of PRX-102 over current therapies, demonstrate the potential for improved efficacy and better quality of life for patients with Fabry disease and demonstrate the safety of our drug/therapy. We are also evaluating the potential of a once-monthly treatment regimen with a higher dose of PRX-102. In addition, the phase III clinical program includes two extension studies in which subjects that participated in our phase I/II clinical trials and our phase III clinical trials may enroll and continue to be treated with PRX-102.

On April 4, 2022, we, together with our development and commercialization partner for PRX-102, Chiesi, announced positive topline results from our *BALANCE* study, a pivotal phase III clinical trial evaluating PRX-102, 1 mg/kg, administered every two weeks, compared to agalsidase beta (Fabrazyme[®]) for the treatment of Fabry disease.

On February 7, 2022, an MAA for PRX-102 was submitted to, and subsequently validated by, the EMA. The submission was made after the October 8, 2021 meeting we held, together with Chiesi, with the Rapporteur and Co-Rapporteur of the EMA regarding PRX-102. At the meeting, Chiesi and the Company discussed the scope of the then anticipated MAA submission for the European Union, and the Rapporteur and Co-Rapporteur were generally supportive of the planned MAA submission for PRX-102.

On April 28, 2021, we, together with Chiesi, announced the receipt of a CRL from the FDA regarding the PRX-102 BLA. The CRL did not report any concerns relating to the potential safety or efficacy of PRX-102 in the submitted data package. In the CRL, the FDA noted that an inspection of our manufacturing facility in Carmiel, Israel, including the FDA's subsequent assessment of any related FDA findings, is required before the FDA can approve a resubmitted BLA. Due to travel restrictions, the FDA was unable to conduct the required inspection during the review cycle. The FDA explained in the letter that it will continue to monitor the public health situation as well as travel restrictions, and is actively working to define an approach for scheduling outstanding inspections. With respect to the third-party facility in Europe at which fill and finish processes are performed for PRX-102, due to COVID-19, the FDA reviewed records under Section 704(a)(4) of the FDCA in lieu of a pre-licensing inspection. In the CRL, the FDA stated that it will communicate remaining issues to the facility in order to seek prompt resolution of any pending items. In addition to the foregoing, in the CRL, the FDA noted that agalsidase beta, a therapy used to treat Fabry patients, was recently converted to full approval and is now an "available therapy," which must be addressed in the context of any potential resubmission of a BLA for PRX-102.

We and Chiesi participated in a Type A (End of Review) meeting with the FDA on September 9, 2021. As part of the meeting minutes provided by the FDA, which included the preliminary comments and meeting discussion, the FDA, in principle, agreed that the data package proposed to the FDA for a BLA resubmission has the potential to support a traditional approval of PRX-102 for the treatment of Fabry disease. The planned data package for the BLA resubmission, given the changed regulatory landscape in the United States, will include the final two-year analyses of the *BALANCE* study. We intend to continue to work collaboratively with the FDA to resolve the issues noted in the CRL and provide a new, alternative drug to Fabry patients.

We have entered into two exclusive global licensing and supply agreements (ex-U.S. and U.S.) with Chiesi for PRX-102; on October 19, 2017, Protalix Ltd., our wholly-owned subsidiary, entered into an Exclusive License and Supply Agreement with Chiesi, or the Chiesi Ex-US Agreement, pursuant to which Chiesi was granted an exclusive license for all markets outside of the United States to commercialize PRX-102 and on July 23, 2018, Protalix Ltd. entered into an Exclusive License and Supply Agreement with Chiesi, or the Chiesi US Agreement, with respect to the commercialization of PRX-102 in the United States.

In addition to PRX-102, our product pipeline currently includes, among other candidates:

- 1) alidornase alfa, or PRX-110, a proprietary plant cell recombinant human DNase, which has successfully completed a phase II efficacy and safety study; we are continuing to evaluate potential strategic marketing partnerships and collaboration programs with biotechnology and pharmaceutical companies for this product candidate for various respiratory indications;
- 2) PRX-115, our plant cell-expressed recombinant PEGylated uricase (urate oxidase) – a chemically modified enzyme to treat refractory gout; and
- 3) PRX-119, our plant cell-expressed PEGylated recombinant human DNase I product candidate being designed to elongate half-life in the circulation for NETs-related diseases.

We have licensed the rights to commercialize taliglucerase alfa worldwide (other than Brazil) to Pfizer, and the rights to commercialize pegunigalsidase alfa worldwide to Chiesi. Otherwise, we hold the worldwide commercialization rights to our other 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.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the specific risks sets forth under the caption “Risk Factors” in the applicable prospectus supplement and under the captions “Risk Factors” in any of our filings with the Commission, including our Annual Report on Form 10-K for the year ended December 31, 2021 before making an investment decision. For additional information, please see the sources described under the caption “Where You Can Find More Information.”

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds of the securities we offer hereby. Unless the applicable prospectus supplement states otherwise, the net proceeds from the securities we sell will be added to our general corporate funds and may be used for research and development expenses, clinical trials, establishing an internal sales force for selected territories, acquisitions of new technologies or businesses, and general corporate and administrative purposes. Until the net proceeds have been used, they will be invested primarily in short-term bank deposits or marketable securities. If we elect at the time of the issuance of the securities to make different or more specific uses of proceeds other than as described in this prospectus, the change in use of proceeds will be described in the applicable prospectus supplement.

DILUTION

We will set forth in a prospectus supplement the following information regarding any material dilution of the equity interests of investors purchasing securities in an offering under this prospectus:

- the net tangible book value per share of our equity securities before and after the offering;
- the amount of the increase in such net tangible book value per share attributable to the cash payments made by purchasers in the offering; and
- the amount of the immediate dilution from the public offering price that will be absorbed by such purchasers.

SECURITIES WE MAY OFFER

Types of Securities

The securities we may offer from time to time by this prospectus are:

- common stock;
- preferred stock, which we may issue in one or more series;
- debt securities, which we may issue in one or more series; and
- warrants entitling the holders to purchase common stock.

We will describe in a prospectus supplement, which we will deliver with this prospectus at the time of sale, the terms of the particular securities that we may offer in the future.

The aggregate initial offering price of all securities sold will not exceed \$100,000,000. When we sell securities, we will determine the amounts of securities we will sell and the prices and other terms on which we will sell them. We may sell securities to or through underwriters, through agents or dealers or directly to purchasers.

Additional Information

We will describe in a prospectus supplement, which we will deliver with this prospectus, the terms of particular securities that we may offer in the future. In each prospectus supplement we will include the following information:

- the type and amount of securities that we propose to sell;
- the initial public offering price of the securities;
- the names of the underwriters, agents or dealers, if any, through or to which we will sell the securities;
- the compensation, if any, of those underwriters, agents or dealers;
- if applicable, information about any securities exchange or automated quotation system on which the securities will be listed or traded;
- material U.S. federal income tax considerations applicable to the securities;
- any material risk factors associated with the securities;
- maturity, if any;
- original issue discount, if any;
- rates and times of payment of interest, dividends or other payments, if any;
- redemption, conversion, exercise, exchange, settlement or sinking fund terms, if any;
- ranking, if applicable;
- voting or other rights, if any;
- conversion, exchange or settlement prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion, exchange or settlement prices or rates and in the securities or other property receivable upon conversion, exchange or settlement; and
- any other material information about the offer and sale of the securities.

In addition, the prospectus supplement may add, update or change the information contained in this prospectus.

DESCRIPTION OF EQUITY SECURITIES

We are a Delaware corporation. The rights of our stockholders are governed by the Delaware General Corporation Law, our Certificate of Incorporation, as amended, and our bylaws. The following summary of the material terms, rights and preferences of our capital stock is not complete. You should read our Certificate of Incorporation, as amended, and our bylaws, which we refer to as our charter, for more complete information before you purchase any of our securities. You should read these documents, copies of which are available from us upon request at the address set forth under the caption "Where You Can Find More Information," in order to more fully understand the terms of our common stock.

Common Stock

General. Our charter provides that we may issue up to 120,000,000 shares of common stock, par value \$0.001 per share, and 100,000,000 shares of preferred stock, par value \$0.0001 per share, all of which preferred stock are undesignated. As of April 15, 2022, 46,365,832 shares of our common stock were issued and outstanding and no shares of preferred stock were issued and outstanding.

Holders of common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Holders of common stock are entitled to receive dividends when, as and if declared by our board of directors out of funds legally available therefor.

In the event of our liquidation, dissolution or winding-up, after payment of all of our debts and liabilities, the holders of our common stock are entitled to share ratably in all remaining assets available for distribution after the payment of debts and liabilities and after provision has been made for each class of stock, if any, having preferences over our common stock. Holders of our common stock, as such, have no preemptive or other rights and there are no redemption provisions applicable to our common stock. All of our outstanding shares of common stock are fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. In accordance with the rules of the Tel Aviv Stock Exchange Ltd., or the TASE, and as long as our securities are listed for trading on the TASE, we are allowed to issue securities with preferential rights relating to dividends, but such securities may not have voting rights.

Dividend Policy. We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings to finance the growth and development of our business and therefore do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our board of directors and will depend upon our financial condition, operating results, capital requirements, covenants in our debt instruments (if any), and such other factors as our board of directors deems relevant.

Transfer Agent and Registrar. The transfer agent and registrar of our common stock is American Stock Transfer & Trust Company.

Preferred Stock

Our restated articles of incorporation, as amended, authorizes the issuance of up to 100,000,000 shares of preferred stock with such voting rights, rights of redemption and other relative rights and preferences as may be determined from time to time by our board of directors. Accordingly, our board of directors is empowered, without shareholder approval, to issue preferred stock with dividend, liquidation, conversion, voting or other rights which could adversely affect the voting power or other rights of the holders of our common stock. The preferred stock could be utilized, under certain circumstances, as a method of discouraging, delaying or preventing a change in control of our company. We currently have no plan to issue any shares of preferred stock.

Terms. You should refer to the prospectus supplement relating to the offering of any preferred stock for specific terms of the shares, including the following terms:

- title and stated or liquidation value;
- number of shares offered and initial offering price;
- voting rights and other protective provisions;

- any dividend rate(s), payment period(s) and/or payment date(s) or method(s) of calculation of any of those terms that apply to those shares;
- date from which dividends will accumulate, if applicable;
- terms and amount of a sinking fund, if any, for purchase or redemption;
- redemption rights, including conditions and the redemption price(s), if applicable;
- listing on any national securities exchange;
- terms and conditions upon which shares will be convertible into common stock or any other securities, including the conversion price, rate or other manner of calculation and anti-dilution provisions, if applicable;
- the relative ranking and preference as to dividend rights and rights upon liquidation, dissolution or the winding-up of our affairs, including liquidation preference amount;
- any limitation on issuance of any series of preferred stock ranking senior to or on a parity with that series of preferred stock as to dividend rights and rights upon liquidation, dissolution or the winding-up of our affairs;
- any other specific terms, preferences, rights, limitations or restrictions; and
- a discussion of applicable material U.S. federal income tax consequences.

The terms of any preferred stock we issue under this prospectus will be set forth in a certificate of designation. We will file a form of the certificate of designation as an exhibit to the registration statement that includes this prospectus, or as an exhibit to a filing with the Commission that is incorporated by reference into this prospectus. The description of preferred stock in any prospectus supplement will not necessarily describe all of the terms of the preferred stock in detail. You should read the applicable certificate of designation for a complete description of all of the terms.

Ranking. Unless we provide otherwise in a prospectus supplement, the preferred stock offered through that supplement will, with respect to dividend rights and rights upon our liquidation, dissolution or winding-up, rank:

- senior to all classes or series of our common stock, and to all other equity securities ranking junior to the offered shares of preferred stock;
- on a parity with all of our equity securities ranking on a parity with the offered shares of preferred stock; and
- junior to all of our equity securities ranking senior to the offered shares of preferred stock.

The term “equity securities” does not include convertible debt securities.

Dividends. Subject to any preferential rights of any outstanding stock or series of stock, our preferred stockholders may be entitled to receive dividends, when and as authorized by our board of directors, out of legally available funds, as specified in the applicable prospectus supplement.

Redemption. If we provide for a redemption right in a prospectus supplement, the preferred stock offered through that prospectus supplement may be subject to mandatory redemption or redemption at our option, in whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in that prospectus supplement.

Liquidation Preference. In the event of our voluntary or involuntary dissolution, liquidation or winding-up, the holders of any series of our preferred stock may be entitled to receive, after distributions to holders of any series or class of our capital stock ranking senior, an amount equal to the stated or liquidation value of the shares of the series plus, if applicable, an amount equal to accrued and unpaid dividends. If the assets and funds to be distributed among the holders of our preferred stock will be insufficient to permit full payment to the holders, then the holders of our preferred stock may share ratably in any distribution of our assets in proportion to the amounts that they otherwise would receive on their shares of our preferred stock if the shares were paid in full.

Voting Rights. Unless otherwise indicated in the applicable prospectus supplement, holders of our preferred stock will not have any voting rights, except as may be required by applicable law.

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into common stock or other securities will be set forth in the prospectus supplement relating to the offering of those shares of preferred stock. These terms typically will include:

- the number of shares of common stock or other securities into which the preferred stock is convertible;
- the conversion price (or manner of calculation);
- the conversion period;
- provisions as to whether conversion will be at the option of the holders of the preferred stock or at our option;
- the events, if any, requiring an adjustment of the conversion price; and
- provisions affecting conversion in the event of the redemption of that series of preferred stock.

Transfer Agent and Registrar. We will identify the transfer agent and registrar for any series of preferred stock offered by this prospectus in a prospectus supplement.

Warrants

We may issue warrants for the purchase of common stock. If we offer warrants, we will describe the terms of the warrants in a prospectus supplement. Warrants may be offered independently, together with other securities offered by any prospectus supplement, or through a dividend or other distribution to stockholders and may be attached to or separate from other securities. Warrants may be issued under a written warrant agreement to be entered into between us or the holder or beneficial owner, or we may issue warrants under a written warrant agreement with a warrant agent specified in a prospectus supplement. A warrant agent would act solely as our agent in connection with the warrants of a particular series and would not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of those warrants.

The following are some of the warrant terms that could be described in a prospectus supplement:

- the title of the warrants;
- the aggregate number of warrants;
- the price or prices at which the warrants will be issued;
- the designation, number and terms of the shares of common stock that may be purchased upon exercise of the warrants;
- the date, if any, on and after which the warrants and the securities offered with the warrants, if any, will be separately transferable;
- the purchase price for each security purchasable on exercise of the warrants;
- the dates on which the right to purchase certain securities upon exercise of the warrants will begin and end;
- the minimum or maximum number of shares of common stock that may be purchased at any one time upon exercise of the warrants;
- any anti-dilution provisions or other adjustments to the exercise price of the warrants;
- the terms of any right that we may have to redeem the warrants;
- the effect of any merger, consolidation, sale or other transfer of our business on the warrants and the applicable warrant agreement, if any;
- information with respect to book-entry procedures, if any;
- a discussion of material U.S. federal income tax considerations; and
- other material terms, including terms relating to transferability, exchange, exercise or amendments of the warrants.

Unless otherwise provided in the applicable prospectus supplement, the warrants and the warrant agreements will be governed by the laws of the State of New York.

Options

As of December 31, 2021, options to purchase 2,259,020 shares of our common stock at a weighted average exercise price equal to approximately \$4.42 per share were outstanding.

Convertible Notes

On August 25, 2021, we completed exchanges, or the Exchanges, of our outstanding 7.50% Senior Secured Convertible Notes due 2021, or the 2021 Notes, with institutional note holders of a substantial majority of the 2021 Notes. The Exchanges involved the exchange of an aggregate of \$54.65 million principal amount of our outstanding 2021 Notes for an aggregate of \$28.75 million principal amount of newly issued 7.50% Senior Secured Convertible Notes due 2024, or the 2024 Notes, \$25.90 million in cash, and approximately \$1.1 million in cash representing accrued and unpaid interest through the closing date. The initial conversion rate for the 2024 Notes is 563.2216 shares of our common stock for each \$1,000 principal amount of 2024 Notes (equivalent to an initial conversion price of approximately \$1.7755 per share of our common stock), subject to adjustment in certain circumstances. This initial conversion price represents a premium of approximately 32.5% relative to the closing price of our common stock on the NYSE American on August 13, 2021.

Delaware Anti-Takeover Law Governance and Certain Charter Provisions

We have elected not to be subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a “business combination” with any “interested stockholder” for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A “business combination” includes, among other things, a merger or consolidation involving us and the “interested stockholder” and the sale of more than 10% of our assets. In general, an “interested stockholder” is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

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. 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.

NYSE American and Tel Aviv Stock Exchange

Our common stock is listed on both the NYSE American and the TASE under the symbol “PLX.”

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsubordinated debt that we may have and may be secured or unsecured. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all or some portion of our senior indebtedness. Any convertible debt securities that we may issue will be convertible into or exchangeable for common stock, preferred stock or other securities of ours or of a third party. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

The debt securities will be issued under one or more indentures, which are contracts between us and a national banking association or other eligible party, as trustee. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in a prospectus supplement (and any free writing prospectus).

We will issue the senior notes under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue the subordinated notes under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We will file forms of these documents as exhibits to an amendment to the registration statement of which this prospectus is a part. We use the term “indentures” to refer to both the senior indenture and the subordinated indenture.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term “indenture trustee” to refer to either the senior trustee or the subordinated trustee, as applicable.

The following summaries of the material provisions of the senior notes, the subordinated notes and the indentures are not complete and are qualified in their entirety by reference to all of the provisions of the indenture applicable to a particular series of debt securities. You should read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. Forms of indentures will be filed as exhibits to an amendment to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to an amendment to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the Commission. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

The following are some of the terms relating to a series of debt securities that could be described in a prospectus supplement:

- title;
- principal amount being offered, and, if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether we will issue the series of debt securities in global form and, if so, the terms and who the depository will be;
- maturity date;
- principal amount due at maturity, and whether the debt securities will be issued with any original issue discount;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- annual interest rate, which may be fixed or variable, or the method for determining the rate, the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- whether the debt securities will be secured or unsecured, and the terms of any secured debt;
- terms of the subordination of any series of subordinated debt;
- place where payments will be payable;
- restrictions on transfer, sale or other assignment, if any;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- date, if any, after which, the conditions upon which, and the price at which we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions, and any other applicable terms of those redemption provisions;
- provisions for a sinking fund, purchase or other analogous fund, if any;

- date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder’s option to purchase, the series of debt securities;
- whether the indenture will restrict our ability or the ability of our subsidiaries to:
 - incur additional indebtedness;
 - issue additional securities;
 - create liens;
 - pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;
 - redeem capital stock;
 - place restrictions on our subsidiaries’ ability to pay dividends, make distributions or transfer assets;
 - make investments or other restricted payments;
 - sell or otherwise dispose of assets;
 - enter into sale-leaseback transactions;
 - engage in transactions with shareholders or affiliates;
 - issue or sell stock of our subsidiaries; or
 - effect a consolidation or merger;
- whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;
- a discussion of any material or special U.S. federal income tax considerations applicable to the debt securities;
- information describing any book-entry features;
- procedures for any auction or remarketing, if any;
- whether the debt securities are to be offered at a price such that they will be deemed to be offered at an “original issue discount” as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;
- denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- if other than dollars, the currency in which the series of debt securities will be denominated; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any events of default that are in addition to those described in this prospectus or any covenants provided with respect to the debt securities that are in addition to those described above, and any terms that may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement or free writing prospectus the terms on which a series of debt securities may be convertible into or exchangeable for common stock, preferred stock or other securities of ours, including the conversion or exchange rate, as applicable, or how it will be calculated, and the applicable conversion or exchange period. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of our securities that the holders of the series of debt securities receive upon conversion or exchange would, under the circumstances described in those provisions, be subject to adjustment, or pursuant to which those holders would, under those circumstances, receive other property upon conversion or exchange, for example in the event of our merger or consolidation with another entity.

Consolidation, Merger or Sale

The indentures in the forms to be filed as exhibits to an amendment to the registration statement of which this prospectus is a part will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor of ours or acquiror of such assets would have to assume all of our obligations under the indentures and the debt securities, as appropriate. In addition, the terms of any securities that we may offer pursuant to this prospectus may limit our ability to merge or consolidate or otherwise sell, convey, transfer or otherwise dispose of all or substantially all of our assets, which terms would be set forth in the applicable prospectus supplement and supplemental indenture.

If the debt securities are convertible for our other securities, the person with whom we consolidate or merge or to whom we sell all of our property would have to make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

The following are events of default under the indentures to be filed as exhibits to an amendment to the registration statement with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 30 days and the time for payment has not been extended or deferred;
- if we fail to pay the principal or premium, if any, when due and payable and the time for payment has not been extended or deferred;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures and our failure continues for 90 days after we receive notice from the indenture trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the indenture trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the indenture trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding would be due and payable without any notice or other action on the part of the indenture trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture occurs and continues, the indenture trustee would be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the indenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the indenture trustee, or exercising any trust or power conferred on the indenture trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the indenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the indenture trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the indenture trustee to institute the proceeding as trustee; and
- the indenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 60 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on the debt securities.

We will periodically file statements with the indenture trustee regarding our compliance with specified covenants in the indentures.

Supplemental Indenture

We and the indenture trustee may from time to time and at any time enter into an indenture or supplemental indenture without the consent of any holders for one or more of the following purposes:

- to evidence the succession of another corporation, and the assumption by the successor corporation of our covenants, agreements and obligations under the indenture and debt securities;
- to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any of such additional covenants, restrictions, conditions or provisions an event of default;
- to add to or change any of the provisions of the indenture to provide that bearer securities may be registrable as to principal, to change or eliminate any restrictions on the payment of principal of or any premium or interest on bearer securities, to permit bearer securities to be issued in exchange for registered securities, to permit bearer securities to be issued in exchange for bearer securities of other authorized denominations or to permit or facilitate the issuance of securities in uncertificated form, provided that such action shall not adversely affect the interests of the holders of the securities or any related coupons, including provisions necessary or desirable to provide for or facilitate the administration of the trusts hereunder;
- to modify, eliminate or add to any of the provisions of the indenture to such extent as necessary to effect the qualification of the indenture under the Trust Indenture Act, and to add to the indenture such other provisions as may be expressly permitted by the trust indenture act, excluding however, the provisions referred to in Section 316(a)(2) of the Trust Indenture Act;
- to modify, eliminate or add to any of the provisions of the indenture;
- to cure any ambiguity or to correct or supplement any provision contained in the indenture or in any supplemental indenture that may be defective or inconsistent with other provisions;
- to convey, transfer, assign, mortgage or pledge any property to or with the trustee;
- to make provisions in regard to matters or questions arising under the indenture, so long such other provisions do not materially affect the interest of any other holder of debt securities;
- to secure any series of security; and
- to evidence and provide for the acceptance and appointment of a successor trustee and to add or change any provisions of the indenture as necessary to provide for or facilitate the administration of the trust by more than one trustee.

In addition, we and the trustee, with the consent of the holders of not less than 66-2/3% in aggregate principal of the outstanding debt securities of each series that is affected, may from time to time and at any time enter into an indenture or supplemental indenture for the purpose of adding any provisions to or changing in any manner the rights of the holders of the securities of such series and any related coupons of the indenture, provided that no such supplemental indenture shall:

- extend the fixed maturity of any securities, or reduce the principal amount thereof or premium, if any, or reduce the rate or extend the time of payment of interest, without the consent of the holder so affected;
- reduce the aforesaid percentage of securities, the consent of the holders of which is required for any such supplemental indenture, without the consent of all holders of outstanding series of debt securities; or
- modify any of the above provisions.

Discharge

Each indenture to be filed as an exhibit to an amendment to the registration statement will provide that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;

- recover excess money held by the indenture trustee;
- compensate and indemnify the indenture trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the indenture trustee money or government obligations, or a combination thereof, sufficient to pay all the principal of, any premium and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement or free writing prospectus, in denominations of \$1,000 and any integral multiple thereof. The indentures will provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement or free writing prospectus with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement or free writing prospectus, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement or free writing prospectus, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement or free writing prospectus the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of or exchange any debt securities of any series being redeemed in part during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Indenture Trustee

The indenture trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the indenture trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the indenture trustee is under no obligation to exercise any of the powers given it by an indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that, unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we may make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in a prospectus supplement or free writing prospectus, we will designate an office or agency of the indenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement or free writing prospectus any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the indenture trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement or free writing prospectus. The indentures in the forms initially filed as exhibits to the registration statement of which this prospectus is a part do not limit the amount of indebtedness which we may incur, including senior indebtedness or subordinated indebtedness, and do not limit us from issuing any other debt, including secured debt or unsecured debt.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, at the market offerings, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents or directly to one or more purchasers.

We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Unless stated otherwise in the applicable prospectus supplement, the obligations of any underwriter to purchase securities will be subject to certain conditions, and the underwriter will be obligated to purchase all of the applicable securities if any are purchased. If a dealer is used in a sale, we may sell the securities to the dealer as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

We or our agents may solicit offers to purchase securities from time to time. Unless stated otherwise in the applicable prospectus supplement, any agent will be acting on a best-efforts basis for the period of its appointment.

In connection with the sale of securities, underwriters or agents may receive compensation (in the form of discounts, concessions or commissions) from us or from purchasers of securities for whom they may act as agents. Underwriters may sell securities to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agents. Underwriters, dealers and agents that participate in the distribution of securities may be deemed to be underwriters, as that term is defined in the Securities Act, and any discounts or commissions received by them from us and any profits on the resale of the securities by them may be deemed to be underwriting discounts and commissions under the Securities Act. We will identify any such underwriter or agent, and we will describe any compensation paid to them, in the related prospectus supplement.

Underwriters, dealers and agents may be entitled under agreements with us to indemnification against and contribution toward certain civil liabilities, including liabilities under the Securities Act.

If stated in the applicable prospectus supplement, we will authorize agents and underwriters to solicit offers by certain specified institutions or other persons to purchase securities at the public offering price set forth in the prospectus supplement under delayed delivery contracts providing for payment and delivery on a specified date in the future. Institutions with whom these contracts may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions, and other institutions, but shall in all cases be subject to our approval. These contracts will be subject only to those conditions set forth in the applicable prospectus supplement and the applicable prospectus supplement will set forth the commission payable for solicitation of these contracts. The obligations of any purchaser under any such contract will be subject to the condition that the purchase of the securities shall not be prohibited at the time of delivery under the laws of the jurisdiction to which the purchaser is subject. The underwriters and other agents will not have any responsibility in respect of the validity or performance of these contracts.

The securities may or may not be listed on a national securities exchange or traded in the over-the-counter market, as set forth in the applicable prospectus supplement. No assurance can be given as to the liquidity of the trading market for any of our securities. Any underwriter may make a market in these securities. However, no underwriter will be obligated to do so, and any underwriter may discontinue any market-making at any time, without prior notice.

If underwriters or dealers are used in the sale, until the distribution of the securities is completed, Commission rules may limit the ability of any underwriters and selling group members to bid for and purchase the securities. As an exception to these rules, representatives of any underwriters are permitted to engage in certain transactions that stabilize the price of the securities. These transactions may consist of bids or purchases for the purpose of pegging, fixing or maintaining the price of the securities. If the underwriters create a short position in the applicable securities in connection with any offering (in other words, if they sell more securities than are set forth on the cover page of the applicable prospectus supplement) the representatives of the underwriters may reduce that short position by purchasing securities in the open market. The representatives of the underwriters may also elect to reduce any short position by exercising all or part of any overallotment option we may grant to the underwriters, as described in the prospectus supplement. The representatives of the underwriters may also impose a penalty bid on certain underwriters and selling group members. This means that if the representatives purchase securities in the open market to reduce the underwriters' short position or to stabilize the price of the securities, they may reclaim the amount of the selling concession from the underwriters and selling group members who sold those shares as part of the offering.

In general, purchases of a security for the purpose of stabilization or to reduce a short position could cause the price of the security to be higher than it might be in the absence of those purchases. The imposition of a penalty bid might also have an effect on the price of the securities to the extent that it discourages resales of the securities. The transactions described above may have the effect of causing the price of the securities to be higher than it would otherwise be. If commenced, the representatives of the underwriters may discontinue any of the transactions at any time. In addition, the representatives of any underwriters may determine not to engage in those transactions or that those transactions, once commenced, may be discontinued without notice.

Certain of the underwriters or agents and their associates may engage in transactions with and perform services for us or our affiliates in the ordinary course of their respective businesses.

In no event will the commission or discount received by any Financial Industry Regulatory Authority, or FINRA, member or independent broker-dealer participating in a distribution of securities exceed 8% of the aggregate principal amount of the offering of securities in which that FINRA member or independent broker-dealer participates.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 that we filed with the Commission under the Securities Act. You should rely only on the information contained in this prospectus or incorporated by reference in this prospectus. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or any sale of securities.

We file annual, quarterly and current reports, proxy statements and other information with the Commission. Our Commission filings, including the registration statement and exhibits, are available to the public at the Commission's website at <http://www.sec.gov>. You can request copies of these documents by writing to the Commission and paying a fee for the copying cost. In addition, since we are also listed on the TASE, 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).

We maintain an Internet site at www.protalix.com. Webcasts of presentations we make at certain conferences may also be available on our website from time to time. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

This prospectus does not contain all of the information included in the registration statement. We have omitted certain parts of the registration statement in accordance with the rules and regulations of the Commission. For further information, we refer you to the registration statement, including its exhibits and schedules, that may be found at the Commission's website at <http://www.sec.gov>. Statements contained in this prospectus and any accompanying prospectus supplement about the provisions or contents of any contract, agreement or any other document referred to are not necessarily complete. Please refer to the actual exhibit for a more complete description of the matters involved.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The Commission allows us to “incorporate by reference” the information we file with the Commission, which means we can disclose important information to you by referring you to those documents. The information we incorporate by reference is an important part of this prospectus, and certain information that we will later file with the Commission will automatically update and supersede this information. We incorporate by reference the documents listed below as well as any future filings we make with the Commission pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (excluding, unless otherwise provided therein or herein, documents not deemed “filed” with the Commission and information furnished pursuant to Item 2.02 and Item 7.01 on any Current Report on Form 8-K or certain exhibits furnished pursuant to Item 9.01 of Form 8-K) after the date of the initial registration statement and prior to the effectiveness of this registration statement, and any filings made after the date of this prospectus until we sell all of the securities under this prospectus. The following documents filed with the Commission are incorporated by reference in this prospectus:

- [our Annual Report on Form 10-K for the year ended December 31, 2021;](#)
- our Current Reports on Form 8-K filed with the Commission on [February 24, 2022, March 31, 2022; and April 4, 2022](#) (other than Items 2.02 and 9.01);
- [our Definitive Proxy Statement, filed on April 29, 2022, for our Annual Meeting of Stockholders scheduled to be held on June 30, 2022; and](#)
- [the description of our common stock included in our registration statement on Form 8-A12B \(File No. 001-33357\) filed with the Commission on March 9, 2007, including any amendment or reports filed for the purpose of updating such description.](#)

Copies of these filings are available at no cost on our website, www.protalix.com. In addition, you may request a copy of these filings and any amendments thereto at no cost, by writing or telephoning us. Those copies will not include exhibits to those documents unless the exhibits are specifically incorporated by reference in the documents or unless you specifically request them. You may also request copies of any exhibits to the registration statement at no cost. Please direct your request to:

Eyal Rubin
Sr. Vice President and Chief Financial Officer
Protalix BioTherapeutics, Inc.
2 University Plaza, Suite 100
Hackensack, NJ 07601
(201) 696-9345

You should rely only on the information in this prospectus, any prospectus supplement, any applicable free writing prospectus and the documents that are incorporated by reference. We have not authorized anyone else to provide you with different information. We are not offering these securities in any state where the offering is prohibited by law. You should not assume that the information in this prospectus, any prospectus supplement, any applicable free writing prospectus or any incorporated document is accurate as of any date other than the date of the document.

LEGAL MATTERS

The validity of the issuance of the shares of common stock offered hereby will be passed upon for us by Mayer Brown LLP, New York, New York.

EXPERTS

The financial statements incorporated in this prospectus by reference to the [Annual Report on Form 10-K for the year ended December 31, 2021](#) have been so incorporated in reliance on the report of Kesselman & Kesselman, Certified Public Accountants (Isr.), a member firm of PricewaterhouseCoopers International Limited, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

\$20,000,000

PROTALIX
Biotherapeutics

COMMON STOCK

PROSPECTUS SUPPLEMENT

H.C. Wainwright & Co.

May 2, 2022
