

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM S-3  
REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

**PROTALIX BIOTHERAPEUTICS, INC.**  
(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**65-0643773**  
(I.R.S. Employer  
Identification No.)

**2 Snunit Street, Science Park**  
**P.O. Box 455**  
**Carmiel 2161401, Israel**  
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**CT Corporation System**  
**111 Eighth Avenue**  
**New York, NY 10011**  
**(212) 894-8400**  
(Name, address, including zip code, and telephone number, including area code, of agent for service)

*Please send copies of all communications to:*

**Anna T. Pinedo, Esq.**  
**Brian D. Hirshberg, Esq.**  
**Mayer Brown LLP**  
**1221 Avenue of the Americas**  
**New York, NY 10020**  
**Telephone: (212) 506-2500**

**Approximate date of commencement of proposed sale to the public:**  
**From time to time after the effective date of this registration statement.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: ☐

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box: ☐

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box: ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐  
Non-accelerated filer ☐

Accelerated filer ☒  
Smaller reporting company ☒  
Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of Securities Act. ☐

**CALCULATION OF REGISTRATION FEE**

| <b>Title of each class of Securities to be registered</b> | <b>Amount to be registered (1)</b> | <b>Proposed maximum offering price per share (2)</b> | <b>Proposed maximum aggregate offering price (2)</b> | <b>Amount of registration fee</b> |
|---|------------------------------------|--|--|-----------------------------------|
| Common stock, par value \$0.001 per share                 | 35,208,846                         | \$ 2.73  | \$ 96,120,149.58                                     | \$ 12,476.40                      |

- (1) Consists of 17,604,423 shares of common stock and 17,604,423 shares of common stock issuable upon the exercise of warrants to purchase shares of common stock at an initial exercise price of \$2.36 per share, or the Warrants. Pursuant to Rule 416 under the Securities Act of 1933, as amended, or the Securities Act, the shares of common stock being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares of common stock being registered hereunder as a result of stock splits, stock dividends or similar transactions.
- (2) Estimated in accordance with Rule 457(c) solely for purposes of calculating the registration fee. The maximum price per share and the maximum aggregate offering price are based on the average of the \$2.45 (high) and \$2.64 (low) sale price of the Registrant's common stock as reported on the NYSE American on April 9, 2020, which date is within five business days prior to filing this Registration Statement.

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The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

**SUBJECT TO COMPLETION, DATED APRIL 17, 2020**

**PROSPECTUS**



**35,208,846 Shares of Common Stock**

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This prospectus relates to the offer and sale from time to time by the selling stockholders identified in the section entitled "Selling Stockholders" of up to an aggregate of 35,208,846 shares of our common stock, including 17,604,423 shares held by the selling stockholders and 17,604,423 shares issuable to the selling stockholders upon exercise of the warrants to purchase shares of our common stock at an initial exercise price of \$2.36 per share, or the Warrants.

The shares of common stock described in this prospectus or in any supplement to this prospectus may be sold from time to time pursuant to this prospectus by the selling stockholders in ordinary brokerage transactions, in transactions in which brokers solicit purchases, in negotiated transactions, or in a combination of such methods of sale, at market prices prevailing at the time of sale, at prices related to such prevailing market prices, at fixed prices or prices subject to change, or at negotiated prices. See "Selling Stockholders" and "Plan of Distribution." We cannot predict when or in what amounts the selling stockholders may sell any of the shares offered by this prospectus.

We are not selling any shares of our common stock, and we will not receive any of the proceeds from the sale of shares by the selling stockholders. The selling stockholders will pay all brokerage fees and commissions and similar sale-related expenses. We are only paying expenses relating to the registration of the shares with the U.S. Securities and Exchange Commission, or the SEC. The registration of the shares of our common stock does not necessarily mean that any of such shares will be offered or sold by the selling stockholders.

A supplement to this prospectus may add, update or change information contained in this prospectus. You should read this prospectus and any prospectus supplement, together with the documents we incorporate by reference, carefully before you invest.

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 16, 2020, the last reported sale price of our common stock was \$3.45 per share on the NYSE American and NIS 12.66 per share on the Tel Aviv Stock Exchange.

**INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" BEGINNING ON PAGE 30 OF OUR ANNUAL REPORT ON FORM 10-K FOR THE YEAR ENDED DECEMBER 31, 2019 AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT OR ANY DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS BEFORE INVESTING IN OUR SECURITIES.**

Neither the SEC, the Israeli Securities Authority nor 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                      , 2020.**

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC, using a “shelf” registration process for the delayed offering and sale of securities pursuant to Rule 415 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration process, the selling stockholders named in this prospectus or any supplement to this prospectus may sell the securities described in this prospectus in one or more offerings. This prospectus provides you with a general description of our common stock. The selling stockholders are required to provide you with this prospectus and, in certain cases, a prospectus supplement containing specific information about the selling stockholders and the terms upon which the securities are being offered. A prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the additional information described under the headings “Incorporation by Reference” and “Where You Can Find More Information” below.

We may also add, update or change information contained in this prospectus by means of a prospectus supplement or by incorporating by reference information that we file or furnish to the SEC. The registration statement that we filed with the SEC includes exhibits that provide more detail on the matters discussed in this prospectus. If the information in this prospectus is inconsistent with a prospectus supplement, you should rely on the information in that prospectus supplement. Please carefully read this prospectus and any prospectus supplement, together with the additional information described under the headings “Incorporation by Reference” and “Where You Can Find More Information” before purchasing any securities.

**You should rely only on the information contained or incorporated by reference in this prospectus, any prospectus supplement and any issuer free writing prospectus. “Incorporated by reference” means that we can disclose important information to you by referring you to another document filed separately with the SEC. We have not authorized any other person to provide you with different information. If anyone provides you with different information, you should not rely on it. We are not making an offer of these securities in any state or jurisdiction where the offer is not permitted. You should only assume that the information in this prospectus or in any prospectus supplement or issuer free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.**

In this prospectus, the “Company,” “we,” “us” and “our” refer to Protalix BioTherapeutics, Inc. and its consolidated subsidiaries, except where the context otherwise requires.

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## CAUTIONARY NOTE CONCERNING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, including the documents incorporated by reference into this prospectus and any accompanying prospectus supplement, contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. 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 "believe," "expect," "assume," "expectations," "plans," "strategy," "prospects," "estimate," "project," "target," "anticipate," "will," "may," "should," "see," "guidance," "confident" and other words of similar meaning in connection with a discussion of future operating or financial performance. All forward-looking statements involve risks, uncertainties and other factors that may cause actual results to differ materially from those expressed or implied in the forward-looking statements. Risks, uncertainties and other factors that could cause actual results to differ from these forward-looking statements include, but are not limited to, risks and uncertainties detailed in the section titled "Risk Factors" beginning on page 30 of our Annual Report on Form 10-K for the year ended December 31, 2019. The statements made in this prospectus and any accompanying prospectus supplement, including the documents incorporated by reference into this prospectus and any accompanying prospectus supplement, regarding the following subject matters are forward-looking by their nature:

- the risk that the U.S. Food and Drug Administration, or the FDA, will not accept an application for Accelerated Approval of PRX-102 with the data generated to date or will request additional data or other conditions of the submission, or that the FDA, the European Medicines Agency, or other foreign regulatory authorities may not accept or approve a marketing application we file for any of our other product candidates;
- risks relating to our evaluation and pursuit of strategic alternatives;
- risks related to our ability to identify and obtain financing on attractive terms or at all within the time period required to regain compliance with the continued listing standards of the NYSE American LLC, or the NYSE American, or to otherwise maintain compliance with its continued listing standards;
- failure or delay in the commencement or completion of our preclinical studies and clinical trials, which may be caused by several factors, including: slower than expected rates of patient recruitment; unforeseen safety issues; determination of dosing issues; lack of effectiveness during clinical trials; inability or unwillingness of medical investigators and institutional review boards to follow our clinical protocols; inability to monitor patients adequately during or after treatment; and or lack of sufficient funding to finance our clinical trials;
- the risk that the results of our clinical trials will not support the applicable claims of 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;
- risks relating to our ability to make required payments under our outstanding convertible notes or any other indebtedness;
- 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;
- 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., or Pfizer;
- risks related to our expectations with respect to the potential commercial value of our product and product candidates;
- 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.

The preceding list is not intended to be an exhaustive list of all forward-looking statements in this prospectus and any accompanying prospectus supplement. You should read this prospectus and any accompanying prospectus supplement with the understanding that actual future results, levels of activity, performance and achievements may be materially different from what is currently expected. We qualify all of the forward-looking statements by these cautionary statements. Additional factors that could cause results to differ materially from those described above can be found in the reports and information that we file with the SEC from time to time.

## SUMMARY INFORMATION

*This summary does not contain all the information that you should consider before investing in our Company. You should carefully read the entire prospectus and any accompanying prospectus supplement, including all documents incorporated by reference herein and therein.*

We are a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins primarily based on our proprietary ProCellEx<sup>®</sup> protein expression system. We developed our first commercial drug product, Elelyso<sup>®</sup>, 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* Study, the *BRIDGE* Study and the *BRIGHT* Study. The studies are 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. Enrollment has been completed in each of the *BALANCE*, *BRIDGE* and *BRIGHT* Studies.

On February 5, 2019, we announced preliminary pharmacokinetic (PK) data from our phase III *BRIGHT* study. Data showed PRX-102 to be well-tolerated; and infusion of 2 mg/kg PRX-102 administered every 4 weeks resulted in the presence of continuous active enzyme throughout the entire infusion interval.

On October 17, 2019, we announced positive 12-month interim data from our *BRIDGE* study. Data from the first 16 of the 22 adult patients (9 males and 7 females) demonstrated a mean improvement in kidney function in both male and female patients when switched from agalsidase alfa (Replagal<sup>®</sup>) to PRX-102.

We anticipate that, in coordination with Chiesi Farmaceutici S.p.A., or Chiesi, a biologics license application, or a BLA, for pegunigalsidase alfa for the treatment of Fabry disease will be filed with the FDA under the FDA's Accelerated Approval Pathway based on the completed phase I/II clinical trials of PRX-102, and safety and efficacy data from the ongoing *BRIDGE* Study. In October 2019, we met, together with Chiesi, with the FDA to discuss key information on PRX-102 to be included in the proposed BLA filing and reached alignment with the FDA on the Accelerated Approval pathway 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. Under each of the Chiesi Ex-US Agreement and the Chiesi US Agreement, or collectively, the Chiesi Agreements, Chiesi made an upfront payment to Protalix Ltd. of \$25.0 million. In addition, under the Chiesi Ex-US Agreement, Protalix Ltd. was entitled to additional payments of up to \$25.0 million in PRX-102 development costs, capped at \$10.0 million per year, and is entitled to receive additional payments of up to \$320.0 million, in the aggregate, in regulatory and commercial milestone payments. Under the Chiesi US Agreement, Protalix Ltd. was entitled to payments of up to a maximum of \$20.0 million to cover development costs for PRX-102, subject to a maximum of \$7.5 million per year, and is eligible to receive additional payments of up to a maximum of \$760.0 million, in the aggregate, in regulatory and commercial milestone payments.

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

Since its approval by the FDA, taliglucerase alfa has been marketed by Pfizer as provided in the Exclusive License and Supply Agreement dated as of November 30, 2009 between Protalix Ltd. and Pfizer Inc., which was amended and restated by the Amended and Restated Exclusive License and Supply Agreement by and between Pfizer Inc. and Protalix Ltd., dated October 12, 2015, or the Amended Pfizer Agreement. Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso in exchange for a cash payment equal to \$36.0 million. Under the Amended Pfizer Agreement, Pfizer has an exclusive license to commercialize Elelyso worldwide other than Brazil; we maintain full rights to BioManguinhos alfatiglicerase in Brazil. We will continue to manufacture drug substance for Pfizer, subject to certain terms and conditions. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all revenues globally for Elelyso, excluding Brazil, where we are responsible for all expenses and retain all revenues.

On June 18, 2013, we entered into a Supply and Technology Transfer Agreement, or the Brazil Agreement, with Fiocruz, an arm of the Brazilian MoH for BioManguinhos alfatiglicerase. Fiocruz's purchases of BioManguinhos alfatiglicerase to date have been significantly below certain agreed-upon purchase milestones. We are continuing to supply BioManguinhos alfatiglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with BioManguinhos alfatiglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in our best interest.

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

- (1) pegunigalsidase alfa, or PRX-102, a therapeutic protein candidate for the treatment of Fabry disease, a rare, genetic lysosomal disorder in humans, currently in ongoing phase III clinical trials.
- (2) OPRX-106, our oral anti-TNF product candidate which is being developed as an orally-delivered anti-inflammatory treatment using plant cells as a natural capsule for the expressed protein. We released final data generated in our phase IIa clinical trial of OPRX-106 for the treatment of ulcerative colitis in March 2018. Additional data was released in June 2018.
- (3) alidornase alfa, or PRX-110, a plant cell expressed recombinant human DNase I chemically modified to resist inhibition by actin, thus enhancing enzymatic activity. We have completed a phase IIa efficacy and safety study of alidornase alfa for the treatment of Cystic Fibrosis.
- (4) PRX-115, our plant cell-expressed recombinant PEGylated Uricase (Urate Oxidase) – a chemically modified enzyme to treat Gout.

We have licensed the rights to commercialize taliglucerase alfa 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 institutes.

Our common stock trades on the NYSE American and the Tel Aviv Stock Exchange 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](http://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 solely as an inactive textual reference.

## **RISK FACTORS**

An investment in our shares involves risks. Before acquiring our shares from a selling stockholder, you should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K, our subsequent Quarterly Reports on Form 10-Q and the other information contained in this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in any accompanying prospectus supplement. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered shares.

## USE OF PROCEEDS

This prospectus relates to the offer and sale from time to time of up to an aggregate of 35,208,846 shares of common stock for the account of the selling stockholders referred to in this prospectus, including 17,604,423 shares held by the selling stockholders and 17,604,423 shares issuable to the selling stockholders upon exercise of the Warrants. We will not receive any of the proceeds from the sale of any shares of common stock offered by the selling stockholders under this prospectus. Any proceeds from the sale of shares of common stock under this prospectus will be received by the selling stockholders. Please see “Selling Stockholders.”

## SELLING STOCKHOLDERS

This prospectus relates to the offer and sale from time to time by the selling stockholders identified below of up to an aggregate 35,208,846 shares of our common stock. The shares of our common stock issued and sold (and to be issued and sold upon exercise of the Warrants) to the selling stockholders were offered and sold pursuant to the exemption from the registration requirements of the Securities Act afforded by Section 4(a)(2) of the Securities Act.

We do not know how long the selling stockholders will hold the shares before selling them or how many shares the selling stockholders will sell and we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares of common stock registered under the registration statement of which this prospectus is a part.

The following table sets forth the maximum number of shares of our common stock to be sold by the selling stockholders. The table also sets forth the name of the selling stockholders, the nature of any position, office, or other material relationship which the selling stockholders has had, within the past three years, with us or with any of our predecessors or affiliates, and the number of shares of our common stock to be owned by each selling stockholder after completion of the offering.

We prepared the table based on information provided to us by the selling stockholders. We have not sought to verify such information. Additionally, the selling stockholders may have sold or transferred some or all of their shares of our common stock in transactions exempt from the registration requirements of the Securities Act since the date on which the information in the table was provided to us. Other information about the selling stockholders may also change over time.

Except as otherwise indicated, each selling stockholder has sole voting and dispositive power with respect to such shares.

| Name of Selling Stockholder                           | Shares of Common Stock<br>Beneficially Owned Prior to<br>the Offering(1)(2) |            | Shares of<br>Common Stock<br>Being Offered<br>Hereby(4) | Shares of Common Stock<br>Beneficially Owned After<br>Completion of the<br>Offering(5) |            |
|---|---|------------|---|--|------------|
|   | Number  | Percent(3) | Number  | Number   | Percent(3) |
| Psagot Provident Funds and Pension Ltd.               | 3,223,156   | 9.93%      | 5,633,802   | 406,255  | *          |
| Angels Investments in Hi-Tech Ltd.                    | 2,816,901   | 8.68%      | 5,633,802   | -  | -          |
| Dexcel Pharma Technologies Ltd.                       | 2,816,901   | 8.68%      | 5,633,802   | -  | -          |
| Highbridge Tactical Credit Master Fund, L.P.          | 3,332,754   | 10.27%     | 4,828,974   | 918,267  | 1.83%      |
| Alrov Properties & Lodgings Ltd.                      | 2,503,615   | 7.72%      | 4,024,144   | 491,543  | *          |
| HIR Investments Ltd.                                  | 2,196,651   | 6.77%      | 4,024,144   | 184,579  | *          |
| Nineteen77 Global Multi-Strategy Alpha Master Limited | 1,746,005   | 5.38%      | 1,609,658   | 941,176  | 1.88%      |
| More Provident Funds Ltd.                             | 600,000   | 1.85%      | 1,200,000   | -  | -          |
| Matag Investment Ltd.                                 | 402,414   | 1.24%      | 804,828   | -  | -          |
| Rosalind Master Fund L.P.                             | 301,810   | *          | 603,620   | -  | -          |
| More Alternative Investments, Limited Partnership     | 216,036   | *          | 432,072   | -  | -          |
| S.H.N Financial Investments Ltd.                      | 200,000   | *          | 400,000   | -  | -          |
| More Investment House Portfolio Management Ltd.       | 190,000   | *          | 380,000   | -  | -          |

\* Less than 1%

- (1) Beneficial ownership is determined in accordance with Rule 13d-3 under the Exchange Act. In computing the number of shares beneficially owned by a person and the percentage ownership of each selling stockholder, securities that are currently exercisable into shares of our common stock, or exercisable into shares of our common stock within 60 days of the date hereof, are deemed outstanding.
- (2) Ownership prior to the offering consists of shares of common stock directly owned by each selling stockholder and does not include shares of common stock underlying the Warrants held by such selling stockholder because the Warrants are not exercisable until the six-month anniversary of the Closing Date, which is more than 60 days from the date of this prospectus.
- (3) Calculated based on 32,442,636 shares of our common stock outstanding on April 15, 2020.
- (4) The number of shares being offered hereby includes the shares issuable to each selling stockholder upon exercise of the Warrants held by each selling stockholder.
- (5) Because the selling stockholders are not obligated to sell all or any portion of the shares of our common stock shown as offered by them, we cannot estimate the actual number or percentage of shares of our common stock that will be held by the selling stockholders upon completion of this offering. However, for purposes of this table, we have assumed that all shares of common stock being registered under the registration statement of which this prospectus forms a part are sold in this offering, and that the selling stockholders do not acquire additional shares of our common stock after the date of this prospectus and prior to completion of this offering.

## PLAN OF DISTRIBUTION

The shares of common stock listed in the table appearing under “Selling Stockholders” are being registered to permit the resale of the shares by the selling stockholders from time to time after the date of this prospectus. There can be no assurance that the selling stockholders will sell any or all of the common stock offered hereby. We will not receive any of the proceeds from the sale of the common stock by the selling stockholders. We will pay substantially all of the expenses incident to this offering of the shares by the selling stockholders to the public other than commissions and discounts of underwriters, brokers, dealers or agents.

The selling stockholders may sell all or a portion of the shares of common stock beneficially owned by them and offered hereby from time to time directly to purchasers or through one or more underwriters, broker-dealers or agents, at market prices prevailing at the time of sale, at prices related to such market prices, at a fixed price or prices subject to change or at negotiated prices, by a variety of methods including the following:

- on any national securities exchange or over-the-counter market on which the shares of common stock may be listed or quoted at the time of sale;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which a broker-dealer may attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer, as principal, and a subsequent resale by the broker-dealer for its account;
- in “at the market” offerings to or through market makers into an existing market for the shares;
- privately negotiated transactions;
- in transactions otherwise than on such exchanges or in the over-the-counter market;
- through a combination of any such methods; or
- through any other method permitted under applicable law.

In addition, the selling stockholders may enter into option, derivative or hedging transactions with respect to the shares, and any related offers or sales of shares may be made pursuant to this prospectus. For example, the selling stockholders may:

- enter into transactions involving short sales of the shares by broker-dealers in the course of hedging the positions they assume with the selling stockholders;
- sell shares short itself and deliver the shares registered hereby to settle such short sales or to close out stock loans incurred in connection with their short positions;
- write call options, put options or other derivative instruments (including exchange-traded options or privately negotiated options) with respect to the shares, or which they settle through delivery of the shares;
- enter into option transactions or other types of transactions that require the selling stockholders to deliver shares to a broker, dealer or other financial institution, who may then resell or transfer the shares under this prospectus; or
- lend or pledge the shares to a broker, dealer or other financial institution, which may sell the shares under this prospectus.

In effecting sales, broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate. If the selling stockholders effect such transactions by selling the common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholder or commissions from purchasers of the common stock for whom they may act as agent or to whom they may sell as principal. Underwriters may sell securities to or through dealers, and 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 agent.

The selling stockholders and any underwriters, brokers, dealers or agents that participate in such distribution may be deemed to be “underwriters” within the meaning of the Securities Act, and any discounts, commissions or concessions received by any underwriters, brokers, dealers or agents might be deemed to be underwriting discounts and commissions under the Securities Act. Any selling stockholder who is an “underwriter” within the meaning of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act and the provisions of the Exchange Act and the rules thereunder relating to stock manipulation.

In order to comply with the securities laws of some states, the shares sold in those jurisdictions may only be sold through registered or licensed brokers or dealers. In addition, in some states, the shares may not be sold unless the shares have been registered or qualified for sale in that state or an exemption from registration or qualification is available and is complied with.

Underwriters, dealers and agents who participate in the distribution of securities and their controlling persons may be entitled, under agreements that may be entered into with us, to indemnification by us and the selling stockholders against certain liabilities, including liabilities under the Securities Act, or to contribution with respect to payments that the underwriters, dealers or agents and their controlling persons may be required to make in respect of those liabilities.

## INFORMATION INCORPORATED 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, 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 Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act made subsequent to the date of this prospectus until the termination of the offering of the securities described in this prospectus (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, 2019](#); and
- our Current Reports on Form 8-K filed with the SEC on [February 6, 2020](#), [March 12, 2020](#) and [March 18, 2020](#).

Any statement contained in this prospectus or contained in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded to the extent that a statement contained in this prospectus or any subsequently filed supplement to this prospectus, or document deemed to be incorporated by reference into this prospectus, modifies or supersedes such statement.

Copies of these filings are available at no cost on our website, [www.protalix.com](http://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 or in any prospectus supplement. 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 or any prospectus supplement is accurate as of any date other than the date on the front of those documents.

## WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. 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. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public from commercial document retrieval services and over the Internet at the SEC’s website at <http://www.sec.gov>. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. In addition, since we are also listed on the Tel Aviv Stock Exchange, we submit copies of all our filings with the SEC to the Israeli Securities Authority and the Tel Aviv Stock Exchange. Such copies can be retrieved electronically through the Tel Aviv Stock Exchange’s internet messaging system ([www.maya.tase.co.il](http://www.maya.tase.co.il)) and through the MAGNA distribution site of the Israeli Securities Authority ([www.magna.isa.gov.il](http://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](http://www.protalix.com). Information contained in or accessible through our website does not constitute a part of this prospectus and is not incorporated by reference in this prospectus.

## **LEGAL MATTERS**

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

## **EXPERTS**

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2019 have been so incorporated in reliance on the report of Kesselman & Kesselman, 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.



**35,208,846 Shares of Common Stock**

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**PROSPECTUS**

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**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 14. Other Expenses of Issuance and Distribution.**

The following table sets forth the costs and expenses, other than underwriting discounts and commissions, payable by us in connection with the sale and distribution of the securities being registered. All of the amounts shown are estimates:

|                              | <b>Amount to<br/>be paid</b> |
|------------------------------|------------------------------|
| SEC registration fee         | \$ 12,476.40                 |
| Printing expenses            | 5,000.00*                    |
| Legal fees and expenses      | 50,000.00*                   |
| Accounting fees and expenses | 15,000.00*                   |
| Miscellaneous                | —                            |
| Total                        | \$ 82,476.40*                |

\* Estimates.

**Item 15. Indemnification of Directors and Officers.**

**General Corporation Law**

We indemnify our directors and officers to the maximum extent permitted by Delaware law for the costs and liabilities of acting or failing to act in an official capacity. In addition, we have entered into indemnification agreements with each of our executive officers and directors to provide them with the maximum indemnification allowed under our amended and restated bylaws and applicable Delaware law, including indemnification for all judgments and expenses incurred as the result of any lawsuit in which such person is named as a defendant by reason of being our director, officer or employee, to the extent indemnification is permitted by the laws of Delaware. We believe that the indemnification agreements will enhance our ability to continue to attract and retain qualified individuals to serve as directors and officers.

The articles of association of Protalix Ltd., our wholly owned subsidiary, allow it to exculpate, indemnify, and insure its office holders to the fullest extent permitted by Israeli law, as described below. Accordingly, Protalix Ltd. has entered into indemnification agreements with each of its officers and directors undertaking to indemnify them to the fullest extent permitted by Israeli law. As required by law, the indemnification is limited to events determined as foreseeable by the board of directors of Protalix Ltd. based on the activities of Protalix Ltd. upon adoption of the form of indemnification in 2016, and to an amount determined by the board of directors as reasonable under the circumstances.

We purchase and maintain a directors and officers liability insurance policy that covers the liability of our directors and officers on a “claims made” basis for their ongoing activity since December 28, 2006, with a limit of \$20,000,000 for any one claim and in the aggregate for the period of insurance with the addition of 20% of the above limit for legal defense costs (in Israel).

Furthermore, we purchase and maintain a Side A Excess and Difference In Conditions insurance that covers the non-indemnifiable liability of our directors and officers on a “claims made” basis for their ongoing activity since December 28, 2006, with a limit of \$15,000,000 for any one claim and in the aggregate for the period of insurance with the addition of 20% of the above limit for legal defense costs (in Israel).

As of the date of hereof, no claims for directors’ and officers’ liability insurance have been filed under those policies and neither we nor Protalix Ltd. is aware of any pending or threatened litigation or proceeding involving any of our directors or officers, or those of Protalix Ltd., in which indemnification is sought.

We have undertaken to fulfill and honor in all respects the obligations of Protalix Ltd. pursuant to any indemnification agreements between Protalix Ltd. and its directors in effect prior to December 31, 2006 and to provide any substitute director and the officers of Protalix Ltd. with similar indemnification agreements. We further agreed that any provision of Protalix Ltd.'s charter documents that relate to exculpation and indemnification of officers and directors of Protalix Ltd. will not be amended, repealed or otherwise modified in any manner that would adversely affect the rights of the directors and officers, unless such modification is required by any applicable law.

Under Israeli law, an Israeli company may not exculpate an office holder from liability for a breach of the duty of loyalty of the office holder. An Israeli company may exculpate an office holder in advance from liability, in whole or in part, for damages caused due to a breach of duty of care owed to the company (other than in the event that such liability arises out of a breach of duty of care to the company upon distribution) but only if a provision authorizing such exculpation is inserted in its articles of association. Protalix Ltd.'s articles of association include such a provision.

An Israeli company may indemnify an office holder in respect of certain liabilities or expenses either in advance of an event or following an event provided a provision authorizing such indemnification is inserted in its articles of association. Protalix Ltd.'s articles of association contain such an authorization. An Israeli company may indemnify an office holder against the following liabilities or expenses incurred for acts performed as an office holder:

- (A) financial liability imposed on or incurred by him or her in favor of another person pursuant to a judgment, settlement or arbitrator's award approved by a court;
- (B) reasonable litigation expenses, including attorneys' fees, incurred by the office holder as a result of an investigation or proceeding instituted against him or her by an authority authorized to conduct such investigation or proceeding, provided that (i) no indictment was filed against such office holder as a result of such investigation or proceeding; and (ii) no financial liability, such as a criminal penalty, was imposed upon him or her as a substitute for the criminal proceeding as a result of such investigation or proceeding or, if such financial liability was imposed, it was imposed with respect to an offense that does not require proof of criminal intent or with regard to a monetary sanction;
- (C) reasonable litigation expenses, including attorneys' fees, incurred by the office holder or imposed by a court in proceedings instituted against him or her by the company, on its behalf or by a third party or in connection with criminal proceedings in which the office holder was acquitted or as a result of a conviction for a crime that does not require proof of criminal intent; and
- (D) a payment that the office holder is obligated to make to an injured party as set forth in Section 52(54)(a)(1)(a) of the Israeli Securities Law, 5278-1968, as amended, or the Israeli Securities Law, and reasonable litigation expenses, including attorneys' fees, that the office holder incurred in connection with a proceeding under Chapters H'3, H'4 or I'1 of the Israeli Securities Law.

An undertaking provided in advance by an Israeli company to indemnify an office holder with respect to (A), as abovementioned, must be limited to events that, in the opinion of the board of directors, can be foreseen based on the company's activities when the undertaking to indemnify is given, and to an amount or according to criteria determined by the board of directors as reasonable under the circumstances, and such undertaking shall detail the abovementioned events and amount or criteria. We are permitted to provide an office holder advance payments to cover expenses covered under (D) above.

An Israeli company may insure an office holder against the following liabilities incurred for acts performed as an office holder:

- a breach of duty of care to the company or to a third party;
- a breach of duty of loyalty to the company, to the extent that the office holder acted in good faith and had a reasonable basis to believe that the act would not be detrimental to the interests of the company;
- a financial liability imposed on the office holder in favor of a third party in respect of an act performed in his or her capacity as an office holder; and

- a payment that the office holder is obligated to make to an injured party as set forth in Section 52(54)(a)(1)(a) of the Israeli Securities Law and reasonable litigation expenses, including attorneys' fees, that the office holder incurred in connection with a proceeding under Chapters H'3, H'4 or I'1 of the Israeli Securities Law.

An Israeli company may not insure, indemnify or exculpate an office holder against any of the following:

- a breach of duty of loyalty, except to the extent that the office holder acted in good faith and had a reasonable basis to believe that the act would not be detrimental to the interests of the company;
- a grossly negligent or intentional violation of an office holder's duty of care;
- an act or omission committed with intent to derive illegal personal benefit; or
- a fine, civil fine, monetary sanction or ransom levied against the office holder.

Under the Israeli law, exculpation, indemnification and insurance of office holders must be approved by the board of directors of Protalix Ltd. and, in respect of directors of Protalix Ltd., also by the stockholders of Protalix Ltd. Such approvals were properly obtained.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors and officers or persons controlling us pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. With respect to insurance and indemnification for liabilities and expenses arising under the Israeli Securities Law, such insurance and indemnification is permissible only to the extent described in this Item 15.

#### **Item 16. Exhibits.**

The list of exhibits following the signature page of this registration statement is incorporated by reference herein.

#### **Item 17. Undertakings.**

(1) The undersigned registrant hereby undertakes:

a. To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

- To include any prospectus required by Section 10(a)(3) of the Securities Act;
- To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
- To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

*provided, however*, that the undertaking set forth in paragraphs (1)(a)(i), (1)(a)(ii) and (1)(a)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act, that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

b. That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof; and

c. To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

d. That, for the purpose of determining liability under the Securities Act to any purchaser:

i. Each prospectus filed by a registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

ii. Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which the prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however,* that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(2) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) The undersigned registrant hereby undertakes that:

a. For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance on Rule 430A and contained in a form of prospectus filed by the undersigned registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective; and

b. For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(4) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the undersigned registrant, pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the undersigned registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Tel Aviv, State of Israel, on April 17, 2020.

### PROTALIX BIOTHERAPEUTICS, INC.

By: /s/ Dror Bashan  
Dror Bashan  
Chief Executive Officer

## SIGNATURES AND POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Dror Bashan and Eyal Rubin, and each of them, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this registration statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the SEC granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons on April 17, 2020, in the capacities indicated.

| <u>Signature</u>  | <u>Title</u>   |
|---|--|
| <u>/s/ Dror Bashan</u><br>Dror Bashan                       | President, Chief Executive Officer<br>(Principal Executive Officer) and Director                 |
| <u>/s/ Eyal Rubin</u><br>Eyal Rubin                         | Chief Financial Officer, Treasurer and Secretary<br>(Principal Financial and Accounting Officer) |
| <u>/s/ Zeev Bronfeld</u><br>Zeev Bronfeld                   | Chairman of the Board  |
| <u>/s/ Amos Bar Shalev</u><br>Amos Bar Shalev               | Director   |
| <u>/s/ Pol F. Boudes, M.D.</u><br>Pol F. Boudes, M.D.       | Director   |
| <u>/s/ Davis Granot</u><br>Davis Granot                     | Director   |
| <u>/s/ Gwen A. Melincoff</u><br>Gwen A. Melincoff           | Director   |
| <u>/s/ Aharon Schwartz, Ph.D.</u><br>Aharon Schwartz, Ph.D. | Director   |

## EXHIBIT INDEX

| Exhibit<br>Number           | Description of Exhibit  |
|-----------------------------|---|
| <a href="#"><u>5.1</u></a>  | <a href="#"><u>Opinion of Mayer Brown LLP as to the validity of the securities registered hereunder.</u></a>  |
| <a href="#"><u>23.1</u></a> | <a href="#"><u>Consent of Kesselman &amp; Kesselman, Certified Public Accountants (Isr.), A member of PricewaterhouseCoopers International Limited, independent registered public accounting firm for the Registrant.</u></a> |
| <a href="#"><u>23.2</u></a> | <a href="#"><u>Consent of Mayer Brown LLP (included in Exhibit 5.1).</u></a>  |
| <a href="#"><u>24.1</u></a> | <a href="#"><u>Power of Attorney (included on the signature page hereto).</u></a>   |



Mayer Brown LLP  
1221 Avenue of the Americas  
New York, NY 10020-1001  
United States of America

T: +1 212 506 2500  
F: +1 212 262 1910

mayerbrown.com

April 17, 2020

Protalix BioTherapeutics, Inc.  
2 Snunit Street, Science Park  
P.O. Box 455  
Carmiel 2161401, Israel

Re: Protalix BioTherapeutics, Inc. – Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as counsel to Protalix BioTherapeutics, Inc., a Delaware corporation (the “**Company**”), in connection with the preparation and filing with the Securities and Exchange Commission (the “**Commission**”) under the Securities Act of 1933, as amended (the “**Securities Act**”), of a registration statement on Form S-3 (the “**Registration Statement**”) relating to the offer and sale by the selling stockholders identified in the Registration Statement (the “**Selling Stockholders**”) of an aggregate of 35,208,846 shares of the Company’s common stock, par value \$0.001 per share, (the “**Common Stock**”) consisting of (i) 17,604,423 shares of Common Stock (the “**Outstanding Shares**”) and (ii) 17,604,423 shares of Common Stock (the “**Warrant Shares**” and, together with the Outstanding Shares, the “**Shares**”) issuable upon exercise of warrants to initially purchase the Warrant Shares at an exercise price of \$2.36 per share (the “**Warrants**”) issued to the Selling Stockholders pursuant to the Securities Purchase Agreements (as defined below). The Shares being registered under the Registration Statement will be offered by the Selling Stockholders from time to time as permitted under the provisions of Rule 415 under the Securities Act.

The Company is registering the resale of the Shares pursuant to its obligations under the Securities Purchase Agreements, dated as of March 11, 2020 and March 12, 2020 (the “**Securities Purchase Agreements**”), between the Company and the Selling Stockholders. The Outstanding Shares and the Warrant were issued to the Selling Stockholders in a private placement pursuant to the Securities Purchase Agreements.

In connection with this opinion, we have examined such corporate records, documents, instruments, certificates of public officials and of the Company and such questions of law as we have deemed necessary for the purpose of rendering the opinions set forth herein. We also have examined the Registration Statement and the Securities Purchase Agreements.

Mayer Brown is a global services provider comprising an association of legal practices that are separate entities including Mayer Brown LLP (Illinois, USA), Mayer Brown International LLP (England), Mayer Brown (a Hong Kong partnership) and Taill & Chequer Advogados (a Brazilian partnership).

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In such examination, we have assumed the genuineness of all signatures and the authenticity of all items submitted to us as originals and the conformity with originals of all items submitted to copies. As to all parties other than the Company, we have assumed the due authorization, execution and delivery of all documents and the validity and enforceability thereof against all parties thereto in accordance with their respective terms.

Based on the foregoing, and subject to the further assumptions and qualifications set forth below, it is our opinion that:

1. The Outstanding Shares have been duly authorized and validly issued and are fully paid and non-assessable;
2. The Warrants have been duly authorized and validly issued and are fully paid and non-assessable; and
3. The Warrant Shares have been duly authorized and reserved for issuance upon exercise and, upon exercise of the Warrants, payment of the exercise price thereof and issuance and delivery in accordance with the terms of the Warrants, will be validly issued, fully paid and non-assessable.

This opinion letter has been prepared for use in connection with the Registration Statement. We are opining only as to the matters expressly set forth herein and that no opinion should be inferred as to any other matter. Our opinion herein is expressed solely with respect to the General Corporation Law of the State of Delaware. Our opinion is based on these laws as in effect on the date hereof and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein. We express no opinion to the extent that any other laws are applicable to the subject matter hereof and express no opinion and provide no assurance as to compliance with any federal or state securities law, rule or regulation.

We hereby consent to the filing of this opinion with the Commission as Exhibit 5.1 to the Registration Statement and to the reference to us under the caption "Legal Matters" in the prospectus included in the Registration Statement. In giving such consent, we do not hereby admit that we are acting within the category of persons whose consent is required under Section 7 of the Securities Act or the rules or regulations of the Commission thereunder.

Very truly yours,

/s/ Mayer Brown LLP

Mayer Brown LLP

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**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Protalix Biotherapeutics, Inc. of our report dated March 12, 2020 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in Protalix BioTherapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2019. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

Tel-Aviv, Israel  
April 17, 2020

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

*Kesselman & Kesselman, Trade Tower, 25 Hamered Street, Tel-Aviv 6812508, Israel,*  
P.O Box 50005 Tel-Aviv 6150001 Telephone: +972 -3- 7954555, Fax:+972 -3- 7954556, [www.pwc.com/il](http://www.pwc.com/il)

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