

Protalix BioTherapeutics, Inc.  
Form 10-K  
March 18, 2019

**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

**FORM 10-K**

**FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d)**

**OF THE SECURITIES EXCHANGE ACT OF 1934**

**(Mark One)**

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

**For the fiscal year ended December 31, 2018**

**OR**

..

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

**001-33357**

(Commission file number)

**PROTALIX BIOTHERAPEUTICS, INC.**

(Exact name of registrant as specified in its charter)

Delaware	<b><u>65-0643773</u></b>
State or other jurisdiction	(I.R.S. Employer
of incorporation or organization	Identification No.)

2 Snunit Street

Science Park

POB 455

**20100**

**Carmiel, Israel**

(Address of principal executive offices) (Zip Code)

**972-4-988-9488**

Registrant's telephone number, including area code

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

<b>Title of each class</b>	<b>Name of each exchange on which registered</b>
<b>Common stock, par value \$0.001 per share</b>	<b>NYSE AMERICAN</b>

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

**None**

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or 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.

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

Large accelerated filer  Accelerated filer  x  
Non-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 13(a) of the Exchange Act.

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

The aggregate market value of the voting common equity held by non-affiliates of the Registrant, as of June 30, 2018 was approximately \$62.2 million, based upon a per share price equal to \$0.43, the closing price for shares of the Registrant's common stock reported by the NYSE American for such date.

On March 1, 2019, approximately 148,382,299 shares of the Registrant's common stock, par value \$0.001 per share, were outstanding.

## FORM 10-K

## TABLE OF CONTENTS

	<b>Page</b>
<b><u>PART I</u></b>	
<u>Cautionary Statement Regarding Forward-Looking Statements</u>	<u>1</u>
<u>Item 1. Business</u>	<u>3</u>
<u>Item 1A. Risk Factors</u>	<u>32</u>
<u>Item 1B. Unresolved Staff Comments</u>	<u>57</u>
<u>Item 2. Properties</u>	<u>57</u>
<u>Item 3. Legal Proceedings</u>	<u>57</u>
<u>Item 4. Mine Safety Disclosures</u>	<u>57</u>
<b><u>PART II</u></b>	
<u>Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	<u>58</u>
<u>Item 6. Selected Financial Data</u>	<u>60</u>
<u>Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations</u>	<u>61</u>
<u>Item 7A. Quantitative and Qualitative Disclosures About Market Risk</u>	<u>70</u>
<u>Item 8. Financial Statements and Supplementary Data</u>	<u>70</u>
<u>Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	<u>71</u>
<u>Item 9A. Controls and Procedures</u>	<u>71</u>
<u>Item 9B. Other Information</u>	<u>73</u>
<b><u>PART III</u></b>	
<u>Item 10. Directors, Executive Officers and Corporate Governance</u>	<u>74</u>
<u>Item 11. Executive Compensation</u>	<u>77</u>
<u>Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	<u>86</u>
<u>Item 13. Certain Relationships and Related Transactions, and Director Independence</u>	<u>88</u>
<u>Item 14. Principal Accountant Fees and Services</u>	<u>90</u>
<b><u>PART IV</u></b>	
<u>Item 15. Exhibits and Financial Statement Schedules</u>	<u>91</u>
<u>Item 16. Form 10-K Summary</u>	<u>94</u>
<u>Signatures</u>	<u>95</u>

## PART I

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

### CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

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

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

the risk that the FDA or foreign regulatory authorities may not accept or approve a marketing application we file for any of our product candidates;

our ability to remediate the material weakness in internal control over financial reporting and to maintain effective internal control over financial reporting;

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

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

risks relating to 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;

risks related to our ability to maintain compliance with the continued listing standards of the NYSE American;

- our dependence on performance by third-party providers of services and supplies, including without limitation, clinical trial services;
- risks relating to our ability to finance our activities and research programs;
- delays in preparing and filing applications for regulatory approval of our product candidates in the United States, the European Union and elsewhere;
- the impact of development of competing therapies and/or technologies by other companies;
- the risk that products that are competitive to our product candidates may be granted orphan drug status in certain territories and, therefore, one or more of our product candidates may become be subject to potential marketing and commercialization restrictions;
- risks related to our supply of drug product to Pfizer Inc., or Pfizer, pursuant to our amended and restated exclusive license and supply agreement with Pfizer;
- risks related to the commercialization efforts for taliglucerase alfa in Brazil;
- risks related to our expectations with respect to the potential commercial value of our product and product candidates;
- the inherent risks and uncertainties in developing the types of drug platforms and products we are developing;
- potential product liability risks, and risks of securing adequate levels of product liability and clinical trial insurance coverage;
- the possibility of infringing a third-party's patents or other intellectual property rights;
- the uncertainty of obtaining patents covering our products and processes and in successfully enforcing our intellectual property rights against third-parties;
- risks relating to changes in healthcare laws, rules and regulations in the United States or elsewhere; and



the possible disruption of our operations due to terrorist activities and armed conflict, including as a result of the disruption of the operations of regulatory authorities, our subsidiaries, our manufacturing facilities and our customers, suppliers, distributors, collaborative partners, licensees and clinical trial sites.

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

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

## Item 1. Business

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

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

On October 19, 2017, Protalix Ltd., our wholly-owned subsidiary, and Chiesi entered into an Exclusive License and Supply Agreement, 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 pegunigalsidase alfa. Pegunigalsidase alfa, or PRX-102, is our chemically modified version of the recombinant protein alpha-Galactosidase-A protein that is currently being evaluated in phase III clinical trials for the treatment of Fabry disease. Under the terms and conditions of the Chiesi Ex-US Agreement, Protalix Ltd. retained the right to commercialize pegunigalsidase alfa in the United States. Under the Chiesi Ex-US Agreement, Chiesi made an upfront payment to Protalix Ltd. of \$25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to \$25.0 million in development costs, capped at \$10.0 million per year. Protalix Ltd. is also eligible to receive an additional up to \$320.0 million, in the aggregate, in regulatory and commercial milestone payments. Protalix Ltd. agreed to manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi is required to make tiered payments of 15% to 35% of its net sales under the Chiesi Ex-US Agreement, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa.

On July 23, 2018, Protalix Ltd. entered into an Exclusive License and Supply Agreement with Chiesi, or the Chiesi U.S. Agreement, with respect to the development and commercialization of pegunigalsidase alfa in the United States. Under the terms of the Chiesi U.S. Agreement, Protalix Ltd. granted to Chiesi exclusive licensing rights for the commercialization of PRX-102 in the United States. Protalix Ltd. is entitled to an upfront, non-refundable, non-creditable payment of \$25.0 million from Chiesi and additional 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. Protalix Ltd. is also eligible to receive an additional up to a maximum of \$760.0 million, in the aggregate, in regulatory and commercial milestone payments. Chiesi will also make tiered payments of 15% to 40% of its net sales under the Chiesi U.S. Agreement to Protalix Ltd., depending on the amount of annual sales, subject to certain terms and conditions, as consideration for product supply.

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

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

On May 1, 2012, the FDA approved for sale our first commercial product, taliglucerase alfa for injection, an enzyme replacement therapy, or ERT, for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease. Subsequently, taliglucerase alfa was approved for marketing by the regulatory authorities of other countries. Taliglucerase alfa is marketed under the name alfataliglicerase 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 Pfizer Agreement. In October 2015, we entered into the Amended Pfizer Agreement which amends and restates the Pfizer Agreement in its entirety. Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso in exchange for a cash payment equal to \$36.0 million. As part of the sale, we agreed to transfer our rights to Elelyso in Israel to Pfizer, while gaining full rights to Elelyso in

Brazil. We will continue to manufacture drug substance for Pfizer, subject to certain terms and conditions. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all revenues globally for Elelyso, excluding Brazil, where we are responsible for all expenses and retain all revenues.

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

On June 18, 2013, we entered into a Supply and Technology Transfer Agreement, or the Brazil Agreement, with Fiocruz, an arm of the Brazilian MoH, for taliglucerase alfa. Fiocruz's purchases of alfataliglycerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding our termination right, we are, at this time, continuing to supply alfataliglycerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglycerase 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.

## Our Strategy

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

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

**Oral Anti-TNF (OPRX-106) Anti Inflammatory.** Oral anti-TNF represents a novel mode of administering a recombinant anti-TNF protein. It is under development as an orally-delivered anti-inflammatory treatment using plant cells as a natural capsule for the expressed protein. Results from our phase II proof of concept efficacy study of OPRX-106 for the treatment of ulcerative colitis were announced in March 2018. We intend to identify and collaborate with a well-suited partner for further development. We are also exploring the option of conducting a controlled phase IIb study of OPRX-106 for the treatment of ulcerative colitis.

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

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

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

### **ProCellEx: Our Proprietary Protein Expression System**

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

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

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

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

Mammalian cell-based expression technology is based on the introduction of a human gene encoding for a specific therapeutic protein into the genome of a mammalian cell, and such systems have become the dominant system for the expression of recombinant proteins due to their capacity for sophisticated, proper protein folding (which is necessary for proteins to carry out their intended biological activity), assembly and post-expression modification, such as

glycosilation (the addition of sugar residues to a protein which is necessary to enable specific biological activity by the protein). Many of the biotechnology industry's largest and most successful therapeutic proteins, including Epogen<sup>®</sup>, Neupogen<sup>®</sup>, Cerezyme<sup>®</sup>, Rituxan<sup>®</sup>, Humira<sup>®</sup>, Enbrel<sup>®</sup>, Neulasta<sup>®</sup>, Remicade<sup>®</sup> and Herceptin<sup>®</sup> are produced through mammalian cell-based expression systems. Mammalian cell-based expression systems can produce proteins with superior quality and efficacy compared to proteins expressed in bacteria and yeast cell-based systems. As a result, the majority of currently approved therapeutic proteins, as well as those under development, are produced in mammalian cell-based systems.

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



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

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

### **Competitive Advantages of Our ProCellEx Protein Expression System**

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

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

***Ability to Penetrate Certain Patent-Protected Markets.*** ProCellEx has the potential to provide workaround manufacturing that does not infringe the method-based patents or other intellectual property rights of third parties. Certain biotherapeutic proteins available for commercial sale are not protected by patents that cover the compound and are available for use in the public domain. Rather, the process of expressing the protein product in mammalian or bacterial cell systems is protected by method-based patents. Using our plant cell-based protein expression technology, we are able to express an equivalent protein without infringing upon these method-based patents. Moreover, we expect to enjoy method-based patent protection for the proteins we develop using our ProCellEx system, although

there can be no assurance that any such patents will be granted. In some cases, we may be able to obtain patent protection for the compositions of the proteins themselves. We have filed for U.S. and international composition of matter patents for PRX-102 and certain of our other product candidates.

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

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

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

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

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

healthy volunteers.

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

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

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

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

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

## **Our Pipeline Drug Candidates**

### ***PRX-102 for the Treatment of Fabry Disease***

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

### ***Fabry Disease Background***

Fabry disease is a serious, life-threatening condition. It is a disease or condition associated with morbidity that has a substantial impact on survival, day-to-day function, and the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. Fabry disease is an X-linked multisystem lysosomal storage disorder caused by the absence or reduction of  $\alpha$ -galactosidase-A ( $\alpha$ -Gal-A) activity, which is a lysosomal enzyme that

catalyzes the hydrolysis of globotriaosylceramide (Gb3) from oligosaccharides, glycoproteins and glycolipids. The absence or reduction of this enzymatic activity leads to the progressive accumulation of glycolipids, especially Gb3, in capillary endothelial cells, podocytes, tubular cells, glomerular endothelial cells, mesangial cells, interstitial cells, cardiomyocytes, fibroblasts, and neurons. The accumulation of glycosphingolipids (e.g., Gb3) leads to chronic pain, skin lesions, cardiac deficiencies, and, in particular, renal involvement. End-stage renal failure and cardiomyopathy often lead to early death in Fabry patients. Fabry disease causes substantial reduction in life-expectancy, by an average of 15 years in female patients and 20 years in male patients, compared to the general population.

### ***Current Treatments of Fabry Disease***

Currently there are two enzyme replacement therapies drugs available on the market to treat Fabry disease. Fabrazyme, marketed by Genzyme Corporation (acquired by Sanofi), is approved for the treatment of Fabry disease in the United States and the European Union. Sanofi reported €755 million (approximately \$865 million) in worldwide sales of Fabrazyme in 2018. The other approved enzyme replacement therapy for the treatment of Fabry disease in the European Union is Replagal, which is marketed by Shire plc, or Shire (acquired by Takeda Pharmaceutical Company Limited, or Takeda, in 2019). Takeda reported \$490.3 million in sales of Replagal by Shire in 2018. In April 2016, Galafold™, a chaperone therapy manufactured by Amicus Therapeutics, Inc., or Amicus, was approved in the European Union as a monotherapy for Fabry disease in patients with amenable mutations. Galafold has also been accepted for marketing in a number of other countries. Amicus reported revenues of approximately \$91.2 million in sales of Galafold in 2018.

### ***PRX-102 Development Program***

Our phase III development program for PRX-102 for the treatment of Fabry disease includes three individual studies; the BALANCE, BRIDGE and BRIGHT studies.

#### ***The BALANCE Study***

In October 2016, the first patient was dosed in our global phase III clinical trial to study the efficacy and safety of PRX-102 for the treatment of Fabry disease. Over 40 sites are currently participating in this trial. The phase III clinical trial, which we refer to as the BALANCE Study, is a multi-center, randomized, double-blind, active control study of PRX-102 in Fabry patients with impaired renal function. The trial is designed to enroll up to 78 patients previously treated with Fabrazyme (agalsidase beta) with a stable dose for at least six months. Enrolled patients are randomized to continue treatment with 1 mg/kg of either Fabrazyme or PRX-102, at a 2:1 ratio of PRX-102 to Fabrazyme, respectively. Patients are treated via intravenous (IV) infusions every two weeks. The sites are recruiting adult symptomatic Fabry patients with plasma and/or leucocyte alpha galactosidase activity (by activity assay) less than 30% mean normal levels. All patients must have had treatment with a dose of 1 mg/kg agalsidase beta via infusion every two weeks for at least one year. In addition, to be included in the trial, patients need to have certain eGFR values and a meaningful decline in annualized eGFR slope. At the end of 2018, the BALANCE study was approximately 70% enrolled.

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

#### ***The BRIDGE Study***

The BRIDGE study, a supportive phase III clinical trial of PRX-102, is an open-label, single-arm, switchover study to assess the efficacy and safety of PRX-102 in Fabry patients currently treated with Replagal. The objective of the study is to generate safety and efficacy data of patients switched from Replagal to PRX-102 over a 12-month period. The endpoints of the study are safety, mean annualized change (slope) in eGFR, pain, plasma lyso GB3, immunogenicity and Quality of Life. Enrollment of the 22 patients required for the study was completed in December 2018.

Preliminary data from the first 16 patients enrolled in the BRIDGE study were announced in October 2018. The data demonstrates an improvement in kidney function, in both male and female Fabry patients, when switched from agalsidase alfa to pegunigalsidase alfa. Based on available historical serum creatinine and study 3-month screening period values for approximately two years while treated with agalsidase alfa before switching to pegunigalsidase alfa treatment, the annualized estimated glomerular filtration rate (eGFR) slope for patients on Replagal was (negative) –  $-6.8\text{ml}/\text{min}/1.73\text{m}^2$ . The mean eGFR slope for the same patients following six months of treatment with PRX-102 was changed to be (positive) –  $+3.7\text{ml}/\text{min}/1.73\text{m}^2$ . These results are statistically significant with a p-value of 0.015. Baseline characteristics of these patients were: mean estimated glomerular filtration rate (eGFR) 75.40 and 86.03  $\text{mL}/\text{min}/1.73\text{m}^2$  for males and females, with annualized eGFR slope of  $-8.0$  and  $-5.1 \text{ mL}/\text{min}/1.73\text{m}^2/\text{year}$ , respectively. This improvement in kidney function (e.g., eGFR) over time may potentially result in the delay or prevention of kidney failure in these populations.

In addition, in vitro analysis of PRX-102 in both human plasma and in lysosomal-like conditions shows significantly longer stability of enzyme activity compared to both commercially-available ERTs. In lysosomal-like conditions, approximately 84% of PRX-102's activity was shown to have been preserved after 10 days compared to approximately 1% remaining enzyme activity in each of the commercially available ERTs. These results were statistically significant with a p-value of 0.01.



The enzyme has been well tolerated in the study, with all adverse events being transient in nature without sequelae. Most of the patients who are eligible for home care therapy per country regulation are being treated under a home care arrangement in which certain of the scheduled infusions are performed at the patients' home. At the conclusion of the BRIDGE study, participating patients are offered the opportunity to enroll in a long-term extension study and continue treatment with PRX-102.

### ***The BRIGHT Study***

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

We plan to enroll up to 30 Fabry patients currently treated with an approved enzyme replacement therapy in the BRIGHT study. A safety and efficacy evaluation will occur at 12 months with additional long term follow-up. At the end of 2018, the BALANCE study was approximately 90% enrolled.

In February 2019, we announced preliminary pharmacokinetic (PK) data from the BRIGHT study. The results of the BRIGHT study demonstrate that PRX-102 was present and remained active in the plasma over the 4-week infusion intervals. The mean concentration of PRX-102 at day 28 was 138 ng/mL. In comparison, published data on Fabrazyme (1mg/kg every 2 weeks) shows a mean concentration of 20 ng/mL at 10 hours post infusion. In addition, the area under the curve (AUC) for PRX-102 was measured to be approximately 2,000,000 ng·hr/mL over 28 days. Based on published data, the AUC of Fabrazyme is approximately 10,000 ng·hr/mL. Pre-existing anti-drug antibodies (ADA) generated in patients prior to switching to PRX-102 had substantially little effect on the circulation of PRX-102 for the 4-week period evaluated, and PRX-102 concentration in circulation was higher than agalsidase beta, even in the presence of ADAs. A preliminary safety analysis of 19 patients enrolled in the BRIGHT study was also conducted, and indicated that PRX-102 is safe and well tolerated.

### ***Phase I/II Clinical Data***

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

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

### *Efficacy*

- Lyso Gb3 levels decreased approximately 90% from baseline (see Figure 1);
  
- Renal function remained stable with mean eGRF levels of 108.02 and 107.20 at baseline and 24 months, respectively with a modest annual eGFR slope of -2.1 (see Figure 2);
  
- An improvement across all the gastrointestinal symptoms evaluated, including severity and frequency of abdominal pain and frequency of diarrhea, were noted (see Figure 1);

· Cardiac parameters, including LVM, LVMI and EF, remained stable with no cardiac fibrosis development detected;

· In conclusion, an improvement of over 40% in disease severity was shown as measured by the Mainz Severity Score Index (MSSI), a score compiling the different elements of the disease severity including neurological, renal and cardiovascular parameters; and

· An improvement was noted in each of the individual parameters of the MSSI.

**Figure 1. Continuous reductions observed over 24 months**

**Figure 2. Continuous clinical stability observed over 24 months**

*Safety*

· The majority of adverse events were mild to moderate in severity, and transient in nature;

· During the first 12 months of treatment, only three of 16 patients (less than 19%) formed anti-drug antibodies (ADA), of which two of these patients (less than 13%) had neutralizing antibodies;

· Importantly, however, the ADAs turned negative for all three of these patients following 12 months of treatment; and

· The ADA positivity effect had no observed impact on the safety, efficacy or continuous biomarker reduction of PRX-102.



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

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

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

### ***OPRX-106 Development Program***

OPRX-102 for the treatment of ulcerative colitis was the subject of a phase IIa clinical trial, a randomized, open label, 2-arm study of OPRX-106 in patients with active mild to moderate ulcerative colitis. The trial evaluated key efficacy endpoints including clinical response and remission utilizing the Mayo score, as well as safety and pharmacokinetics.

Positive results from the trial were announced in March and June 2018. A total of 24 patients were enrolled in the study; 18 patients completed the study with six patients who did not complete the study. The dropout rate is consistent with other trials in similar patient populations, and none of the patients dropped out due to a side effect or serious adverse event. Patients were randomized to receive 2 mg or 8 mg of OPRX-106, administered orally, once daily, for 8 weeks. The average baseline Mayo score was 7.1 (from a scale of 0-12) and the average baseline mucosal endoscopy sub score was 2.1 (from a scale of 0-3). For the 18 patients who completed the study, 89% had a baseline Mayo score between 6 and 9, which meets the criteria of moderate disease activity, and 84% had a baseline mucosal endoscopy sub score of 2 and above indicating moderate to severe disease based on mucosal appearance.

The key efficacy endpoints of the study were met at week 8:

- 67% of patients experienced a clinical response in each of the 2mg dose and 8mg dose cohorts; and
- 44% of patients experienced a clinical remission in the 8mg dose and 11% in the 2mg dose for an overall average of 28%.

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

In addition to clinical response and remission, efficacy was also observed in mucosal healing, an important prognostic parameter in ulcerative colitis and other inflammatory bowel diseases, measured by endoscopy:

- 61% of patients experienced mucosal improvement; and
- 33% of patients experienced mucosal healing.

Mucosal improvement is defined as a decrease in endoscopy sub-score at week 8. Mucosal healing is defined as a reduction in, and achievement of, endoscopy sub-score  $\leq 1$  at week 8.

Other key efficacy endpoints were also achieved, as follows:

- 72% of patients showed an improvement in rectal bleeding scores;
- 72% of patients demonstrated an improvement in fecal calprotectin; and
  - 61% of patients showed improved Geboes score (a histopathological scoring for the assessment of disease activity in ulcerative colitis).

The positive trend in efficacy is consistent in substantially all patients. This trend is demonstrated by 89% of the patients having showed an improvement in Mayo score in both doses, with an average decrease in Mayo score of 46% at week 8 in the 8mg dose and 40% in the 2mg dose. In addition, all of the patients also showed an improvement in at least one of the other efficacy parameters.

No anti-drug antibodies were detected. In addition, no systemic absorption was observed. OPRX-106 was safe and well tolerated with only mild to moderate adverse events, which were transient in nature. Headaches were the most common adverse event reported.

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

#### ***alidornase alfa (PRX-110) for the Treatment of Cystic Fibrosis***

alidornase alfa is our proprietary plant cell recombinant form of human deoxyribonuclease I (DNase I) that we are developing for the treatment of CF, to be administered by inhalation. DNase I cleaves extracellular DNA and thins the thick mucus that accumulates in the lungs of CF patients. Currently, Pulmozyme® is the only DNase I commercially available, with annual sales of approximately CHF 739 million (approximately \$751 million) in sales for 2018 according to public reports by F. Hoffman-La Roche Ltd.

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

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



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

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

***alidornase alfa Development Program***

We completed a phase I clinical trial of alidornase alfa with 18 healthy volunteers in which alidornase alfa was found to be safe and tolerable. We have also completed a phase IIa clinical trial of alidornase alfa for the treatment of CF. Sixteen patients were enrolled in the study, all of whom completed the study. The phase II trial was a 28-day switchover study to evaluate the safety and efficacy of alidornase alfa in CF patients previously treated with Pulmozyme (currently the only commercially available DNase therapy). Participation in the trial was preceded by a two-week washout period from Pulmozyme before treatment with alidornase alfa via inhalation.

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

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

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

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

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

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

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

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

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

### **Commercialization Agreements with Chiesi Farmaceutici**

On October 19, 2017, Protalix Ltd. and Chiesi entered into the Chiesi Ex-US Agreement pursuant to which we granted to Chiesi an exclusive license for all markets outside of the United States to develop and commercialize pegunigalsidase alfa. Subsequently, on July 23, 2018, Protalix Ltd. and Chiesi entered into the Chiesi U.S. Agreement pursuant to which we granted to Chiesi an exclusive license for the United States to develop and commercialize pegunigalsidase alfa. Under the Chiesi Ex-US Agreement, Chiesi made an upfront payment to Protalix Ltd. of \$25.0 million in consideration for and as reimbursement of the costs sustained by Protalix Ltd. up to the effective date of the agreement, and Protalix Ltd. is entitled to additional payments of up to \$25.0 million in development costs, capped at \$10.0 million per year. Protalix Ltd. is also eligible to receive an additional up to \$320.0 million, in the aggregate, in regulatory and commercial milestone payments. Chiesi is required to make tiered payments of 15% to 35% of its net sales under the Chiesi Ex-US Agreement, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa.

Under the Chiesi U.S. Agreement, Chiesi made an upfront payment to Protalix Ltd. of \$25.0 million in consideration for and as reimbursement of the costs sustained by Protalix Ltd. up to the effective date of the agreement, and Protalix Ltd. is entitled to additional 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. Protalix Ltd. is also eligible to receive an additional up to a maximum

of \$760.0 million, in the aggregate, in regulatory and commercial milestone payments. Chiesi will also make tiered payments of 15% to 40% of its net sales to Protalix Ltd., depending on the amount of annual sales, subject to certain terms and conditions, as consideration for product supply.

Protalix Ltd. and Chiesi have agreed to a specific allocation of the responsibilities under the two agreements for the continued development efforts for pegunigalsidase alfa. Protalix Ltd. agreed to manufacture all of the PRX-102 needed for all purposes under the agreements, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix Ltd, subject to certain terms and conditions.

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

### **Technology Transfer Agreement with Fiocruz**

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

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

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

## **Intellectual Property**

We maintain a proactive intellectual property strategy which includes patent filings in multiple jurisdictions, including the United States and other commercially significant markets. As of December 31, 2018, we held, or had license rights to, 79 patents and 41 pending patent applications with respect to various compositions, methods of production and methods of use relating to our ProCellEx protein expression system and our proprietary product pipeline. Of the above, three are joint patents, five are joint patent applications and one is a licensed patent application.

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

We issued a series of 7.5% convertible notes in December 2016 and July 2017, which we refer to as the 2021 Notes, which are guaranteed by our subsidiaries and secured by perfected liens on all of our material assets, primarily consisting of our intellectual property assets, including a stock pledge of our foreign subsidiaries in favor of the holders of outstanding 2021 Notes.

As of December 31, 2018, our patent portfolio consisted of several patent families (consisting of patents and/or patent applications) covering our technology, protein expression methodologies and system and product candidates, as follows:

With respect to our ProCellEx protein expression system, we held 11 issued patents and five patent applications relating to the large scale production of proteins in cultured plant cells. The issued patents and any patents to issue in the future based on pending patent applications in this patent family, if at all, are expected to expire in 2028. One patent relating to a separate family, covering methods for culturing and harvesting plant cells and/or tissues in consecutive cycles is expected to expire in 2025.

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

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

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

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

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

We held a patent family containing 18 granted patents in Europe, United States, Australia, Japan, Russian Federation, China, Hong Kong, Singapore, New Zealand, Korea and South Africa, and six pending patent applications relating to multimeric protein structures of  $\alpha$ -galactosidase and to uses thereof in treating Fabry disease. The issued patents and any patents to issue in the future based on the patent applications in this patent family, if at all, are expected to expire in 2031.

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

We held a patent family containing 10 patent applications relating to chemically modified plant recombinant human DNase I and uses in therapy. The patents to issue in the future based on this patent application, if at all, are expected to expire in 2036.

We held three families containing three granted patents in Japan, Australia and United States, and seven patent applications relating to plant recombinant TNF alpha inhibitor polypeptides. The patents to issue in the future based on these patent applications, if at all, are expected to expire in 2034/2035.

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

We co-own and have an exclusive license to a patent family, containing three granted patents in Europe, United States and Australia, and five pending applications that cover use of plant cells expressing a TNF alpha polypeptide inhibitor in therapy. The patents to issue in the future based on these patent applications, if at all, are expected to

expire in 2034.

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

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

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



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

## Manufacturing

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

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

Our manufacturing facilities in Carmiel, Israel, have undergone successful audits by the FDA, the Irish Medicinal Board, ANVISA, the Israeli MOH, the TGA, Health Canada and the Turkish Ministry of Health.

Our current facility in Israel has been granted "Approved Enterprise" status, and we have elected to participate in the alternative benefits program. Our facility is located in a Zone A location, and, therefore, our income from the Approved Enterprise will be tax exempt in Israel for a 10-year period commencing with the year in which we first generate taxable income from the relevant Approved Enterprise and after we use our net operating loss carryforwards, or "NOLs." We expect to be entitled to similar tax benefits for a number of years thereafter. To remain eligible for these tax benefits, we must continue to meet certain conditions, and if we increase our activities outside of Israel, for

example, by future acquisitions, such increased activities generally may not be eligible for inclusion in Israeli tax benefit programs. In addition, our technology is subject to certain restrictions with respect to the transfer of technology and manufacturing rights. “See Risk Factors—The manufacture of our products is an exacting and complex process, and if we or one of our materials suppliers encounter problems manufacturing our products, it will have a material adverse effect on our business and results of operations.”

#### Raw Materials and Suppliers

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

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

## Competition

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

There are two approved ERTs for the treatment of Fabry disease; Fabrazyme which is marketed by Genzyme and Replagal, which is marketed by Shire. Fabrazyme is available in the United States and the European Union. Replagal is available in the European Union and certain other territories outside the United States. In addition, we are aware of other late clinical stage, early clinical stage and experimental drugs which are being developed for the treatment of Fabry disease by other companies. In addition, in May 2016, Galafold™ (migalastat), an oral small molecule pharmacological chaperone marketed by Amicus was approved in the European Union and other countries as a first line therapy for long-term treatment of adults and adolescents aged 16 years and older with a confirmed diagnosis of Fabry disease and who have an amenable mutation. In August 2018, the FDA granted accelerated approval of Galafold.

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

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

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

#### Scientific Advisory Board

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

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

2002 Hamilton-Fairley Award, European Society of Medical Oncology

2005 Wolf Prize for Medicine

2012 Nauta Award in Pharmacochimistry, The European Federation of Medicinal Chemistry (EFMC) (the highest award from the European Federation for Medicinal Chemistry)

Regent's Profession and Florence Ely Nelson Presidential Chair

Biodesign Institute, CIDV, Arizona State University

Member, National Academy of Sciences, USA

American Society of Plant Biology Leadership in Science Public Service Award (2004)

Charles J. Arntzen, Ph.D. Botanical Society of America Centennial Award (2006)

Fellow of American Society of Plant Biologists (2007)

Doctor of Science *honoris causa.*, Hebrew University of Jerusalem

Chair, Section O "Agriculture, Food, and Renewable Resources," American Association for the Advancement of Science (AAAS) (2011-2012)

## Government Regulation

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

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

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

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

After completion of clinical trials of a new drug product, FDA and foreign regulatory authority marketing approval must be obtained. Assuming that the clinical data support the product's safety and effectiveness for its intended use, a new drug application, or NDA, or a BLA is submitted to the FDA for review. Generally, it takes one to three years to

obtain approval. If questions arise during the FDA review process, approval may take a significantly longer period of time. The testing and approval processes require substantial time and effort and approval on a timely basis, if at all, or the approval that we receive may be for a narrower indication than we had originally sought, potentially undermining the commercial viability of the product. Even if regulatory approvals are obtained, approved products are subject to continual review and holders of an approved product are required, for example, to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain requirements concerning advertising and promotional labeling for the product. Also, quality control and manufacturing procedures relating to a product must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to comply with cGMP and other aspects of regulatory compliance. The later discovery of previously unknown problems or failure to comply with the applicable regulatory requirements with respect to any product may result in restrictions on the marketing of the product or withdrawal of the product from the market as well as possible civil or criminal sanctions. See also “—International Regulation.”

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



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

In 2012, the U.S. Congress passed the Food and Drug Administration Safety Innovations Act (FDASIA). Section 901 of the FDASIA amends the Federal Food, Drug, and Cosmetic Act (FDCA) to allow the FDA to base Accelerated Approval for drugs for serious conditions that fill an unmet medical need on whether the drug has an effect on a surrogate or an intermediate clinical endpoint. A surrogate endpoint used for Accelerated Approval is a marker, that is, a laboratory measurement, radiographic image, physical sign or other measure, that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a measure of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality. The FDA bases its decision on whether to accept the proposed surrogate or intermediate clinical endpoint on the scientific support for that endpoint. Studies that demonstrate a drug's effect on a surrogate or intermediate clinical endpoint must be "adequate and well controlled" as required by the FDCA.

The Accelerated Approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Under subpart H of the Accelerated Approval pathway, the FDA may grant marketing approval for a new drug product on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. The Accelerated Approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The United States federal government regulates healthcare through various agencies, including but not limited to the following: (i) the FDA, which administers the FDCA, as well as other relevant laws; (ii) the Center for Medicare & Medicaid Services (CMS), which administers the Medicare and Medicaid programs; (iii) the Office of Inspector

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

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

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

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

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

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

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

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

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

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

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

A licensure framework for follow-on biologic products; and

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

#### International Regulation

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

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

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

#### Israeli Government Programs

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

#### General Corporate Tax Structure in Israel

The income of Protalix Ltd., other than income from “Approved Enterprises,” is taxed in Israel at the regular rate (currently 23%).

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

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

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

### **Law for the Encouragement of Capital Investments, 1959**

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

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

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

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

A company that has an Approved Enterprise program is eligible for further tax benefits, as an alternative to exemption, if it qualifies as a foreign investors' company. A foreign investors' company eligible for benefits is essentially a company in which more than 25% of the share capital (in terms of shares, rights to profit, voting and appointment of directors) is owned (measured by both share capital and combined share and loan capital) by non-Israeli residents. A company that qualifies as a foreign investors' company and has an Approved Enterprise program is eligible for tax benefits for a 10-year benefit period and may enjoy a reduced corporate tax rate of 10% to 23%, depending on the amount of the company's shares held by non-Israeli shareholders.

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

Percent of Foreign Ownership	Rate of Reduced Tax
Over 25% but less than 49%	23%
49% or more but less than 74%	20%

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

74% or more but less than 90%	15%
90% or more	10%

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

A company that has elected to participate in the alternative benefits program and that subsequently pays a dividend out of the income derived from the portion of its facilities that have been granted Approved Enterprise status during the tax exemption period will be subject to corporate tax in respect of the amount of dividend distributed at the rate that would have been applicable had the company not elected the alternative benefits program (generally 10% to 23%, depending on the extent to which non-Israeli shareholders hold such company’s shares). If the dividend is distributed within 12 years after the commencement of the benefits period (or, in the case of a foreign investor’s company, without time limitation), the dividend recipient is taxed at the reduced withholding tax rate of 15% applicable to dividends from approved enterprises, or at the lower rate under an applicable tax treaty. After this period, the withholding tax rate is 25%, or at the lower rate under an applicable tax treaty. In the case of a company with a foreign investment level (as defined by the Investment Law) of 25% or more, the 12-year limitation on reduced withholding tax on dividends does not apply. The company must withhold this tax at its source, regardless of whether the dividend is converted into foreign currency.



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

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

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

The amended Investment Law specifies certain conditions for an Approved Enterprise to be entitled to benefits. These conditions include; inter alia, the following:

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

at least 25% of the Approved Enterprise's revenues during the benefits period must be derived from sales into a single country or a separate customs territory with a population of at least 14 million (starting from January 1, 2012, 1.4% must be added for each year).

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

In the future there may be changes in the law, subject to the preservation of benefits, which may affect the benefits available to companies under the Investment Law. The termination or substantial reduction of any of the benefits

available under the Investment Law could materially impact the cost of our future investments.

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

To date, Protalix Ltd. has received grants from the OCS under the Israeli Law for the Encouragement of Industrial Research, Development and Technology Innovation, 1984, and related regulations, or the Research Law. On January 1, 2016, the Israeli government established NATI which replaced many of the functions of the Office of the Chief Scientist of the Israeli Department of Labor, or the OCS. For purposes of clarity, references to NATI will include the OCS. NATI grants are made available to finance a portion of Protalix Ltd.'s research and development expenditures in Israel. As of December 31, 2018, NATI approved grants in respect of Protalix Ltd.'s continuing operations totaling approximately \$53.0 million, measured from inception. Protalix Ltd. is required to repay up to 100% of grants actually received (plus interest at the LIBOR rate applied to the grants received on or after January 1, 1999) to NATI through payments of royalties at a rate of 3% to 6% of the revenues generated from NATI-funded project, depending on the period in which revenues were generated. As of December 31, 2018, Protalix Ltd. either paid or accrued royalties payable of \$11.1 million and Protalix Ltd.'s contingent liability to NATI with respect to grants received was approximately \$41.9 million.

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

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

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

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

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

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

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

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

technology in the ordinary course of business.

Law for the Encouragement of Industry (Taxes), 1969

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

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

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

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

#### Tax Benefits for Research and Development

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

#### Employees

As of December 31, 2018, we had 184 employees, of whom 17 have a Ph.D. or an M.D. in their respective scientific fields. We believe that our relations with these employees are good. We believe that our success will greatly depend on our ability to identify, attract and retain capable employees. The Israeli Ministry of Labor and Welfare is authorized to make certain industry-wide collective bargaining agreements, or Expansion Orders, that apply to types of industries or employees including ours. These agreements affect matters such as cost of living adjustments to salaries, length of working hours and week, recuperation, travel expenses, and pension rights. Otherwise, our

employees are not represented by a labor union or represented under a collective bargaining agreement. See “Risk Factors—We depend upon key employees and consultants in a competitive market for skilled personnel. If we are unable to attract and retain key personnel, it could adversely affect our ability to develop and market our products.”

## Company Background

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

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

## Available Information

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

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

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

Protalix BioTherapeutics, Inc.

2 Snunit Street, Science Park

P.O. Box 455

Carmiel 20100, Israel

Attn: Mr. Yossi Maimon, Chief Financial Officer

## Item 1A. Risk Factors

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

### **Risks Related to Clinical Trials and Regulatory Matters**

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

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

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

Any failure or delay in commencement or completion of any clinical trials of pegunigalsidase alfa or our other product candidates will have a material adverse effect on our business, results of operations and financial condition. In addition, we or the FDA or other regulatory authorities may suspend any clinical trial at any time if it appears that we



are exposing participants in the trial to unacceptable safety or health risks or if the FDA or such other regulatory authorities, as applicable, find deficiencies in our IND submissions or the conduct of the trial. Any suspension of a clinical trial may have a material adverse effect on our business, results of operations and financial condition.

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

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

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

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

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

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

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

We depend upon independent investigators and collaborators, such as universities and medical institutions, to conduct our preclinical and clinical trials. These collaborators are not our employees, and we cannot control the amount or timing of resources that they devote to our clinical development programs. The investigators may not assign as great a

priority to our clinical development programs or pursue them as diligently as we would if we were undertaking such programs directly. If outside collaborators fail to devote sufficient time and resources to our clinical development programs, or if their performance is substandard, the approval of anticipated NDAs, BLAs and other marketing applications, and our introduction of new drugs, if any, may be delayed which could impair our clinical development programs and would have a material adverse effect on our business, results of operations and financial condition. The collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators also assist our competitors, our competitive position could be harmed.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

conventional products. As a result, we may experience a longer regulatory process in connection with obtaining regulatory approvals of any products that we develop, which may have a material adverse effect on our business, results of operations and financial condition.

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

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

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

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

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

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

## **Risks Related to Our Business**

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

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

candidates, which may delay the development of our drug candidates and materially and adversely impact our business, results of operations and financial condition.

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

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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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

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

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

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

Our NOLs, as of December 31, 2018, are equal to approximately \$211 million, of which approximately \$26 million may be restricted under Section 382 of the Internal Revenue Code (“IRC”). IRC Section 382 applies whenever a corporation with NOLs experiences an ownership change. As a result of IRC Section 382, the taxable income for any post-change year that may be offset by a pre-change NOL may not exceed the general IRC Section 382 limitation, which is the fair market value of the pre-change entity multiplied by the IRC long-term tax exempt rate. Significant judgment is required in determining any valuation allowance recorded against deferred tax assets. In assessing the need for a valuation allowance, we considered all available evidence, including past operating results, the most recent projections for taxable income and prudent and feasible tax planning strategies. We reassess our valuation allowance periodically and if future evidence allows for a partial or full release of the valuation allowance, a tax benefit will be recorded accordingly. Any ownership change (including as a result of conversion of our outstanding convertible notes into shares of our common stock), or any other limitation on our utilization of NOLs, could have a material adverse effect on our business, results of operations and financial condition.

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

Protalix Ltd. is our wholly-owned subsidiary and thus a controlled foreign corporation of our company for U.S. federal income tax purposes. This organizational structure may create inefficiencies, as certain types of income and investments of Protalix Ltd. that otherwise would not be currently taxable under general U.S. federal income tax

principles may become taxable. These inefficiencies may require us to use more of our NOLs than we otherwise might and may result in a tax liability without a corresponding distribution from our subsidiary which could have a material adverse effect on our business, results of operations and financial condition.

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

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

## **Risks Related to Our Financial Condition and Capital Requirements**

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

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

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

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

- make it more difficult for us to satisfy our financial obligations, including with respect to the convertible notes;

result in an event of default under our outstanding convertible notes if we fail to comply with the financial and other restrictive covenants contained in agreements governing any future indebtedness, which event of default could result in all of our debt becoming immediately due and payable;

· increase our vulnerability to general adverse economic, industry and competitive conditions;  
reduce the availability of our cash flow to fund working capital, capital expenditures, acquisitions and other general corporate purposes because we will be required to dedicate a substantial portion of our cash flow from operations to the payment of principal and interest on our indebtedness;

· limit our flexibility in planning for, or reacting to, and increasing our vulnerability to changes in our business, the industry in which we operate and the general economy;

· prevent us from raising funds necessary to purchase convertible notes surrendered to us by holders upon a fundamental change (as described in the indentures governing the two series of convertible notes), which failure would result in an event of default with respect to the convertible notes;

· place us at a competitive disadvantage compared to our competitors that have less indebtedness or are less highly leveraged and that, therefore, may be able to take advantage of opportunities that our debt levels or leverage prevent us from exploiting; and

· limit our ability to obtain additional financing.

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

**We are required to comply with a number of covenants under the indenture governing our outstanding 2021 Notes that could hinder our growth.**

The indenture governing our 2021 Notes contains a number of restrictive affirmative and negative covenants, which limit our ability to incur additional debt; exceed certain limits; pay dividends or distributions; or merge, consolidate or dispose of substantially all of our assets, including all of our intellectual property assets and other material assets securing such convertible notes. A breach of these covenants could result in default, and if such default is not cured or waived, the holders of the indebtedness could, among other things, elect to declare all amounts owed immediately due and payable, which could cause all or a large portion of our available cash flow to be used to pay such amounts and thereby reduce the amount of cash available to pursue our business plans or force us into bankruptcy or liquidation, or, result in the foreclosure on the assets that secure the debt, including all of our intellectual property assets, which would force us to relinquish rights to such assets that we may believe are critical to our business. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Any default on our debt will have a material adverse effect on our business, results of operations and financial condition.

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

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

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



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

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

The stock market in general, and the market for life sciences companies in particular, have experienced extreme price and volume fluctuations that may have been unrelated or disproportionate to the operating performance of the listed companies. There have been dramatic fluctuations in the market prices of securities of biotechnology companies. These price fluctuations may be rapid and severe and may leave investors little time to react. Broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. The trading price of our common stock has been volatile and has been subject to wide price fluctuations in response to various factors, many of which are beyond our control. The volatility of our stock price has from time to time in recent periods affected our market capitalization. Stock price fluctuations that adversely affect our market capitalization may result in our failure to meet the continued market capitalization-based listing requirement for The NYSE American, which would require us to take steps to gain compliance with alternate listing standards or take remedial steps to bring us into compliance. A failure to maintain or regain compliance with applicable listing standards could adversely affect the liquidity of our common stock and could result in an event of default under the indenture governing our 2021 notes which would have a material adverse effect on our business, results of operations and financial condition.

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

To date, we have not generated significant revenues from product sales and only minimal revenues from research and development services and other fees, other than the milestone and other payments we have received in connection with our agreements with Pfizer and Chiesi. For the years ended December 31, 2018, 2017 and 2016, we had net losses from continuing operations of \$26.5 million, \$83.4 million and \$29.2 million, respectively, primarily as a result of expenses incurred through a combination of research and development activities and expenses supporting those activities, which includes share-based compensation expense. Drug development and commercialization is very capital intensive. We fund all of our operations and capital expenditures from the revenues we generate from licensing fees and grants, the net proceeds of equity and debt offerings and other sources. Based on our current plans, expectations and capital resources, we believe that our cash and cash equivalents will be sufficient to enable us to meet our planned operating needs for at least 12 months. However, changes may occur that could consume our existing capital at a faster rate than projected, including, among others, the cost and timing of regulatory approvals, changes in the progress of our research and development efforts and the costs of protecting our intellectual property rights.

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

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

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

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

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

### **Risks Related to Investing in our Common Stock**

#### **The market price of our common stock may fluctuate significantly.**

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

- the progress and results of our ongoing studies regarding pegunigalsidase alfa and our other product candidates;
- announcements regarding partnerships or collaborations by us or our competitors;
- restatements of historical financial results and changes in financial forecasts;
- purchases of alfataliglicerase in Brazil;
- developments concerning intellectual property rights and regulatory approvals;

- the announcement of new products or product enhancements by us or our competitors;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts;
- developments in the biotechnology industry; and
- general market conditions and other factors, including factors unrelated to our operating performance.

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

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

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

A substantial majority of our outstanding shares of our common stock are freely tradable without restriction or further registration under the federal securities laws, unless owned by our affiliates. In addition, we may sell additional shares of our common stock in the future to raise capital and a substantial number of shares of our common stock are reserved for issuance upon the exercise of stock options and upon conversion of our outstanding convertible notes. We cannot predict the size of future issuances, if any. At December 31, 2018, there were outstanding options to purchase common stock issued covering approximately 10.2 million shares of our common stock with a weighted average exercise price of \$1.57 per share. Also at December 31, 2018, there were approximately 7.3 million shares of common stock available for future for issuance in connection with future grants of incentives under our amended 2006 stock incentive plan and approximately 76.7 million shares of common stock reserved for issuance upon conversion of our outstanding convertible notes. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities.

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

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

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

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

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

Our directors and executive officers, principal stockholders and affiliated entities beneficially own, in the aggregate, approximately 4.3% of our common stock, as of March 1, 2019, giving effect to stock options that are held by such persons that are exercisable within such 60 days from such date. As a result, if some or all of them acted together, they would have the ability to exert substantial influence over the election of our Board of Directors and the outcome of issues requiring approval by our stockholders. This concentration of ownership may have the effect of delaying or preventing a change in control of our company that may be favored by other stockholders. This could prevent the consummation of transactions favorable to other stockholders, such as a transaction in which stockholders might otherwise receive a premium for their shares over current market prices.

**We have identified a material weakness in our internal control over financial reporting and subsequently restated certain of our financial statements as a result of factors related to that weakness. This may adversely affect the accuracy and reliability of our financial statements and impact our reputation, business and the price of our common stock, as well as lead to a loss of investor confidence in us.**

We identified a material weakness in our internal control over financial reporting existed in that we did not maintain effective internal controls related to accounting for complex revenue contracts. Specifically, we did not properly assess the performance obligations we had with regard to certain of our out-licensing arrangements which became material to our company in 2018. Our management previously concluded that this material weakness exists in our internal control over financial reporting as of March 31, 2018 and in subsequent periods. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis.

On March 14, 2019, we concluded that we would restate our previously issued consolidated financial statements as of and for the fiscal quarters ended March 31, 2018, June 30, 2018 and September 30, 2018 to correct for errors in our revenue recognition procedures.

While we have developed and are in the process of implementing a plan to remediate this material weakness, the material weakness will not be considered remediated until management designs and implements effective controls that operate for a sufficient period of time and management concludes, through testing, that these controls are effective. We will monitor the effectiveness of our remediation plan and will refine its remediation plan, as needed, and we may identify additional material weaknesses in our internal control over financial reporting in the future. We can give no assurance that the measures we take will remediate the material weakness or that additional material weaknesses will not arise in the future. If we are unable to remediate this material weakness or we identify additional material

weaknesses in our internal control over financial reporting in the future, our ability to analyze, record and report financial information accurately, to prepare our financial statements within the time periods specified by the rules and forms of the Commission and to otherwise comply with our reporting obligations under the federal securities laws, and in relation to covenants under the indenture governing our outstanding convertible note, will likely be adversely affected.

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

Effective internal controls are necessary for us to provide reliable financial reports and effectively prevent fraud. If we cannot provide reliable financial reports or prevent fraud, our results of operation could be harmed. As disclosed, we have identified a material weakness in our internal control over financial reporting relating to complex accounting for complex revenue contracts.

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

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

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

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

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

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



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

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

## **Risks Related to the Commercialization of Drug Products**

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

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

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

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

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

We currently have very limited sales, marketing or distribution capabilities and no experience in building a sales force and distribution capabilities. Under our arrangements with Pfizer and Chiesi, we have outlicensed the marketing rights to Elelyso and pegunigalsidase alfa except that we retained the marketing rights to alfataliglicerase in Brazil. We have not licensed the marketing or commercialization rights to any of our other product candidates to any party. The

commercialization of a drug product requires that we commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and with supporting distribution capabilities. Factors that may inhibit our efforts to commercialize our products directly and without strategic partners include:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

### **Risks Related to Intellectual Property Matters**

**The intellectual property and assets owned by our subsidiaries are subject to security agreements that secure our payment and other obligations under our 2021 Notes, and our subsidiaries have guaranteed all of those obligations.**

In connection with the issuance of our 2021 Notes, we entered into security agreements pursuant to which our subsidiaries provided first priority security interests in all of their assets, which consist of all of our intellectual property and other material assets. The security agreements secure certain payment, indemnification and other obligations under the 2021 Notes. If we were to default on certain of our obligations, or in certain other circumstances generally related to a bankruptcy or insolvency, holders of our outstanding 2021 Notes could seek to foreclose on the collateral under the security agreements to obtain satisfaction our obligations, and our business could be materially and adversely impacted, which would in turn have a material adverse effect on our results of operations and financial



condition.

Furthermore, in connection with the issuance of the 2021 Notes, our subsidiaries guaranteed all of our obligations under the indenture governing such convertible notes. If we were to default on our obligations under the indenture, the holders could require our subsidiaries to satisfy all of those obligations under the guarantees.

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

As of December 31, 2018, we had 41 pending patent applications of which five are joint pending patent applications with a third party and one is an-in licensed application. However, the filing of a patent application does not mean that we will be issued a patent, or that any patent eventually issued will be as broad as requested in the patent application or sufficient to protect our technology. Any modification required to a current patent application may delay the approval of such patent application which would have a material adverse effect on our business, results of operations and financial condition. In addition, there are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications to not be granted, including known or unknown prior art, deficiencies in the patent application or the lack of originality of the technology. Our competitive position and future revenues will depend in part on our ability and the ability of our licensors and collaborators to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing the proprietary rights of third parties. We have filed U.S. and international patent applications for process patents, as well as composition of matter patents, for taliglucerase alfa and other product candidates. However, we cannot predict:

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

As of December 31, 2018, we held, or had license rights to, 79 patents. If patent rights covering our products or technologies are not sufficiently broad, they may not provide us with sufficient proprietary protection or competitive advantages against competitors with similar products and technologies. Furthermore, if the U.S. Patent and Trademark Office or foreign patent offices issue patents to us or our licensors, others may challenge the patents or circumvent the patents, or the patent office or the courts may invalidate the patents. Thus, any patents we own or license from or to third parties may not provide any protection against our competitors and those who infringe upon our patents.

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

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

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

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

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

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

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

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

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

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

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

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

## **Risks Relating to Our Operations in Israel**

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

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

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

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

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

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

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

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

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

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

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

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

These restrictions may impair our ability to sell our technology assets or to outsource manufacturing outside of Israel. The restrictions will continue to apply for a certain period of time even after we have repaid the full amount of royalties payable for the grants. For the years ended December 31, 2016, 2017 and 2018, we recorded grants totaling \$5.8 million, \$3.3 million and \$2.2 million from NATI, respectively. The grants represent 19.1%, 10.4% and 6%, respectively, of our gross research and development expenditures for the years ended December 31, 2016, 2017 and 2018. If we fail to satisfy the conditions of the Research Law, we may be required to refund certain grants previously received together with interest and penalties, and may become subject to criminal charges, any of which could have a material adverse effect on our business, results of operations and financial condition.

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

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



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

the judgment was rendered by a court which was, according to the laws of the state of the court, competent to render the judgment;

the judgment may no longer be appealed;

the obligation imposed by the judgment is enforceable according to the rules relating to the enforceability of judgments in Israel and the substance of the judgment is not contrary to public policy; and

the judgment is executory in the state in which it was given.

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

the judgment was obtained by fraud;  
there is a finding of lack of due process;

the judgment was rendered by a court not competent to render it according to the laws of private international law in Israel;

the judgment is at variance with another judgment that was given in the same matter between the same parties and that is still valid; or

at the time the action was brought in the foreign court, a suit in the same matter and between the same parties was pending before a court or tribunal in Israel.

#### Item 1B. Unresolved Staff Comments

None.

#### Item 2.

#### Properties

Our manufacturing facility and executive offices are located in Carmiel, Israel. The facilities currently contain approximately 20,000 sq/ft of manufacturing space and additional 48,000 sq/ft of laboratory, warehouse and office space and are leased at a rate of approximately \$63,000 per month. In addition, we are entitled to use an additional 13,000 sq/ft in the same facility, which we intend to utilize in connection with an anticipated expansion of our manufacturing facilities. Our facilities are equipped with the requisite laboratory services required to conduct our business, and we believe that the existing facilities are adequate to meet our needs for the foreseeable future. Our original lease for the facility was in effect until 2016, at which time we extended the term until 2021. We retain two addition options to extend the term for a five-year period, for an aggregate of 10 additional years. Upon the exercise of each remaining option to extend the term of the lease, if any, the then current base rent shall be increased by 10%.

#### Item 3.

#### Legal Proceedings

We are not involved in any material legal proceedings.

#### Item 4.

#### Mine Safety Disclosures

Not applicable.

57

## PART II

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

Our common stock is traded on the NYSE American under the symbol "PLX."

As of March 1, 2019, there were approximately 80 holders of record of our common stock. A substantially greater number of holders of our common stock are "street name" or beneficial holders, whose shares are held of record by banks, brokers and other financial institutions.

### STOCK PERFORMANCE GRAPH

The following graph compares the cumulative total shareholder return data for our common stock from December 31, 2013 through December 31, 2018 to the cumulative return over such time period of (i) The NYSE American Index and (ii) The Nasdaq Biotechnology Index. The graph assumes an investment of \$100 on December 31, 2013 in each of our common stock, the stocks comprising the NYSE American Index and the stocks comprising the Nasdaq Biotechnology Index, including dividend reinvestment, if any.

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



## Item 6.

## Selected Financial Data

The selected consolidated financial data below should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. The selected consolidated statements of operations data for the years ended December 31, 2018, 2017 and 2016 and the selected consolidated balance sheet data as of December 31, 2018 and 2017, are derived from the audited consolidated financial statements included elsewhere in this Annual Report. The statement of operations data for the years ended December 31, 2015 and 2014 and the balance sheet data as of December 31, 2016, 2015 and 2014 are derived from audited financial statements not included in this Annual Report. We adopted, retrospectively, ASU 2014-08 during 2015 regarding discontinued operations which resulted in the reclassification of prior year amounts. The historical results presented below are not necessarily indicative of future results..

	Year Ended December 31,				
	2014	2015	2016	2017	2018
	(in thousands, except share and per share amounts)				
<b>Consolidated Statement of Operations Data:</b>					
Revenues from selling goods	\$3,523	\$4,364	\$9,199	\$19,242	\$8,978
Revenues from license and R&D services				1,836	25,262
Cost of goods sold	630	730	8,398	15,231	9,302
Research and development expenses, net	22,224	20,025	24,608	28,834	33,330
Selling, general and administrative expenses	9,228	7,279	9,356	11,530	10,916
Financial income (expenses), net	(4,739 )	(3,612 )	3,987	(48,923 )	(7,149 )
Loss from continuing operations	\$33,298	\$27,282	\$29,176	\$83,440	\$26,457
(Loss) income from discontinued operations	3,355	85,319	(189 )		
Net (loss) income for the year	(29,943 )	58,037	(29,365 )	(83,440 )	(26,457 )
<b>Net (loss) income per share of common stock, basic and diluted:</b>					
Loss from continuing operations	\$(0.36 )	\$(0.29 )	\$(0.29 )	\$(0.64 )	\$(0.18 )
(Loss) income from discontinued operations	0.04	0.90	(0.00 )		
Net (loss) income per share of common stock	(0.32 )	0.61	(0.29 )	(0.64 )	(0.18 )
Weighted average number of shares of common stock used in computing net loss per share of common stock	92,891,846	94,922,390	101,387,704	131,085,958	147,135,182
<b>Consolidated Balance Sheet Data:</b>					
Cash and cash equivalents	\$54,767	\$76,374	\$63,281	\$51,163	\$37,808
All other assets	23,590	20,879	18,966	21,051	23,323

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

Total assets	78,357	97,253	82,247	72,214	61,131
Current liabilities	64,354	11,235	66,212	22,752	25,353
Long term convertible notes	67,351	67,796	19,343	46,267	47,966
Total liabilities	133,958	86,380	92,204	101,671	114,012
Total stockholders' equity (capital deficiency)	(55,601 )	10,873	(9,957 )	(29,457 )	(52,881 )

## **Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations**

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

### **Overview**

We are a biopharmaceutical company focused on the development and commercialization of recombinant therapeutic proteins based on our proprietary ProCellEx<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 recombinant therapeutic proteins that primarily target large, established pharmaceutical markets and that in most cases rely upon known biological mechanisms of action. With our experience to date, we believe ProCellEx will enable us to develop additional proprietary recombinant proteins that are therapeutically superior to existing recombinant proteins currently marketed for the same indications, including applying the unique properties of our ProCellEx system for the oral delivery of therapeutic proteins.

On October 19, 2017, Protalix Ltd., our wholly-owned subsidiary, and Chiesi entered into the Chiesi Ex-US Agreement pursuant to which Chiesi was granted an exclusive license for all markets outside of the United States to commercialize pegunigalsidase alfa. Pegunigalsidase alfa is our chemically modified version of the recombinant protein alpha-Galactosidase-A protein that is currently being evaluated in phase III clinical trials for the treatment of Fabry disease. Under the terms and conditions of the Chiesi Ex-US Agreement, Protalix Ltd. retained the right to commercialize pegunigalsidase alfa in the United States. Under the Chiesi Ex-US Agreement, Chiesi made an upfront payment to Protalix Ltd. of \$25.0 million in connection with the execution of the agreement and Protalix Ltd. is entitled to additional payments of up to \$25.0 million in development costs, capped at \$10.0 million per year. Protalix Ltd. is also eligible to receive an additional up to \$320.0 million, in the aggregate, in regulatory and commercial milestone payments. Protalix Ltd. agreed to manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Chiesi is required to make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of pegunigalsidase alfa.

On July 23, 2018, Protalix Ltd. entered into the Chiesi U.S. Agreement with respect to the development and commercialization of pegunigalsidase alfa in the United States. Under the terms of the Chiesi U.S. Agreement, Protalix Ltd. granted to Chiesi exclusive licensing rights for the commercialization of PRX-102 in the United States.



Protalix Ltd. is entitled to an upfront, non-refundable, non-creditable payment of \$25.0 million from Chiesi and additional 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. Protalix Ltd. is also eligible to receive an additional up to a maximum of \$760.0 million, in the aggregate, in regulatory and commercial milestone payments. Chiesi will also make tiered payments of 15% to 40% of its net sales under the Chiesi U.S. Agreement to Protalix Ltd., depending on the amount of annual sales, subject to certain terms and conditions, as consideration for product supply.

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

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

On May 1, 2012, the FDA approved for sale our first commercial product, taliglucerase alfa for injection, an ERT for the long-term treatment of adult patients with a confirmed diagnosis of type 1 Gaucher disease. Subsequently, taliglucerase alfa was approved for marketing by the regulatory authorities of other countries. Taliglucerase alfa is marketed under the name alfataliglicerase 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 Pfizer Agreement. In October 2015, we entered into the Amended Pfizer Agreement which amends and restates the Pfizer Agreement in its entirety. Pursuant to the Amended Pfizer Agreement, we sold to Pfizer our share in the collaboration created under the initial Pfizer Agreement for the commercialization of Elelyso in exchange for a cash payment equal to \$36.0 million. As part of the sale, we agreed to transfer our rights to Elelyso in Israel to Pfizer, while gaining full rights to Elelyso in Brazil. We will continue to manufacture drug substance for Pfizer, subject to certain terms and conditions. Under the Amended Pfizer Agreement, Pfizer is responsible for 100% of expenses, and entitled to all revenues globally for Elelyso, excluding Brazil, where we are responsible for all expenses and retain all revenues.

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

On June 18, 2013, we entered into the Brazil Agreement with Fiocruz, an arm of the Brazilian MoH, for taliglucerase alfa. Fiocruz's purchases of alfataliglicerase to date have been significantly below certain agreed upon purchase milestones and, accordingly, we have the right to terminate the Brazil Agreement. Notwithstanding our termination right, we are, at this time, continuing to supply alfataliglicerase to Fiocruz under the Brazil Agreement, and patients continue to be treated with alfataliglicerase in Brazil. We are discussing with Fiocruz potential actions that Fiocruz may take to comply with its purchase obligations and, based on such discussions, we will determine what we believe to be the course of action that is in 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 an ongoing phase III clinical trial.

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

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

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.

### **Critical Accounting Policies**

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

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

### ***Functional Currency***

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

### ***Revenues***

Our primary sources of revenues include our sales of taliglucerase alfa in Brazil and of drug substance to Pfizer under our Amended Pfizer Agreement. We recognize revenue from the Amended Pfizer at a point in time when control over the product is transferred to customers (upon delivery).

We also generate revenues from the Chiesi agreements. According to Accounting Standard Codification Topic 606, Revenue from contracts with customers, or ASC 606, a performance obligation is a promise to provide a distinct good or service or a series of distinct goods or services. Goods and services that are not distinct are bundled with other goods or services in the contract until a bundle of goods or services that is distinct is created. A good or service promised to a customer is distinct if the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract.

We have identified two performance obligations in each of the Chiesi agreements as follows: (1) the license and research and development services and (2) a contingent performance obligation regarding future manufacturing.

We determined that the licenses granted to Chiesi together with the research and development services should be combined into a single performance obligation under each agreement since Chiesi cannot benefit from a license without the research and development services. The research and development services are highly specialized and are dependent on the supply of the drug.

The future manufacturing is contingent on regulatory approvals of the drug and we deem these services to be separately identifiable from other performance obligations in the contract. Manufacturing services post-regulatory approval are not interdependent or interrelated with the license and research and development services.

The transaction price was comprised of fixed consideration and variable consideration (capped research and development reimbursements). Under ASC 606, the consideration to which we would be entitled upon the achievement of contractual milestones, which are contingent upon the occurrence of future events, are a form of variable consideration. We estimate variable consideration using the most likely method. Amounts included in the transaction price are recognized only when it is probable that a significant reversal of cumulative revenues will not occur, usually upon achievement of a specific milestone. We used significant judgment when it determined variable consideration.

Since the customer benefits from the research and development services as the entity performs, revenue from granting the license and the research and development services is recognized over time using the cost-to-cost method. We used significant judgment when it determined the costs expected to be incurred upon satisfying the identified performance obligation.

Revenue from additional research and development services ordered by Chiesi is recognized over time using the cost-to-cost method.

We accounted for the Chiesi U.S. agreement as a modification of the Chiesi Ex-U.S. Agreement. As such, we recorded revenue through a cumulative catch-up adjustment in the amount in the third quarter of 2018 of \$6.2 million.

Our revenue recognition accounting policy prior to January 1, 2018, was materially the same

**Research and Development Expense**

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

- internal costs associated with research and development activities;
- payments made to third party contract research organizations, investigative/clinical sites and consultants; manufacturing development costs;
- personnel-related expenses, including salaries, benefits, travel, and related costs for the personnel involved in research and development;
- activities relating to the advancement of product candidates through preclinical studies and clinical trials; and facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, as well as laboratory and other supplies.

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

<b>Project</b>	<b>Status</b>	<b>Expected Near Term Milestones</b>
PRX-102 – pegunigalsidase alfa	Phase III clinical trial, ongoing	Finalize enrollment in the remaining two clinical trials
OPRX-106 – Oral antiTNF	Phase IIa completed	Evaluate potential partnership or proceed with phase IIb clinical trial
PRX-110 – alidornase alfa	Phase IIa completed	Evaluate potential partnership

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

The costs and expenses of our projects are partially funded by grants we have received from NATI. Each grant is deducted from the related research and development expenses as the costs are incurred. For additional information regarding the grant process, see “Business—Israeli Government Programs—Encouragement of Industrial Research, Development and Technology Innovation, 1984” in Item 1 of this Annual Report. There can be no assurance that we will continue to receive grants from NATI in amounts sufficient for our operations, if at all. In addition, under the two Chiesi Agreements, Protalix Ltd. is entitled to payments of up to \$45.0 million in the aggregate to cover development costs for pegunigalsidase alfa, capped at \$17.5 million per year.

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



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

### ***Share-Based Compensation***

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

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

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

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

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

volatility, including the implied volatility of traded options, historical volatility and the period that the shares of the company are being publicly traded.

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

### **Convertible Notes**

All outstanding convertible notes are accounted for using the guidance set forth in the Financial Accounting Standards Board, or FASB, Accounting Standards Codification (ASC) 815 requiring that we determine whether the embedded conversion option must be separated and accounted for separately. ASC 470-20 regarding debt with conversion and other options requires the issuer of a convertible debt instrument that may be settled in cash upon conversion to separately account for the liability (debt) and equity (conversion option) components of the instrument in a manner that reflects the issuer's nonconvertible debt borrowing rate. We accounted for the 4.5% convertible notes, which we refer to as the 2018 Notes, as liability, on an aggregated basis, in their entirety.

Our 2021 Notes were accounted for partially as liability and equity components of the instrument and partially as a debt host contract with an embedded derivative resulting from the conversion feature. During the year ended December 31, 2017, the embedded derivative was reclassified to additional paid in capital.

Issuance costs regarding the issuance of the 2021 Notes are amortized using the effective interest rate.

During the year ended December 31, 2018, note holders converted \$1.15 million aggregate principal amount of the 2021 Notes into a total of 1,537,415 shares of common stock, and cash payments of approximately \$15,887, in the aggregate. In addition, in June 2018, we exchanged \$3.42 million aggregate principal amount of our outstanding 4.50% convertible promissory notes due 2018, which we refer to as the 2018 Notes, for 2,613,636 shares of common stock and approximately \$2.23 million in cash and delivered the necessary funds under the indenture governing the 2018 Notes, which was \$2.53 million. On September 15, 2018, the 2018 Notes matured and have been paid in full.

As of December 31, 2018, a total of \$57.9 million aggregate principal amount of the 2021 Notes were outstanding. In addition, as of December 31, 2018, none of the 2018 Notes were outstanding.

### ***Year ended December 31, 2018 Compared to the Year Ended December 31, 2017***

#### *Revenues from Selling Goods*

We recorded revenues of \$9 million for the year ended December 31, 2018, a decrease of approximately \$10.2 million, or 53%, compared to revenues of \$19.2 million for the year ended December 31, 2017. Revenues include \$3.7 million of products sold in Brazil and \$5.3 million of drug substance sold to Pfizer. The decrease resulted from a decrease of \$6.9 million in sales of drug substance to Pfizer and \$3.4 million in sales of drug product to Brazil.

#### *Revenues from License and R&D Services*

We recorded revenues of \$25.3 million for the year ended December 31, 2018 an increase of \$23.5 million compared to revenues of \$1.8 million for the year ended December 31, 2017. Revenues from the license agreements represent the revenues we recognized in connection with the Chiesi agreement including a cumulative catch-up adjustment in the third quarter in the amount of \$6.2 million.

#### *Cost of Goods Sold*

Cost of goods sold was \$9.3 million for the year ended December 31, 2018, a decrease of \$5.9 million or 39%, compared to the cost of revenues of \$15.2 million for the year ended December 31, 2017.

*Research and Development Expenses*

Research and development expenses were \$35.5 million for the year ended December 31, 2018, an increase of \$3.3 million, or 10% from \$32.2 million for the year ended December 31, 2017. The increase resulted primarily from an increase in clinical trial activity during 2018.

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

*Selling, General and Administrative Expenses*

Selling, general and administrative expenses were \$10.9 million for the year ended December 31, 2018, a decrease of \$0.6 million, or 5%, from \$11.5 million for the year ended December 31, 2017. The decrease resulted primarily from a decrease in sales expenses.

*Financial Expenses and Income*

Financial expense was \$7.1 million for the year ended December 31, 2018, compared to financial expenses of \$48.9 million for the year ended December 31, 2017. Financial expenses for the year ended December 31, 2017 included a charge of \$38.1 million as a result of the re-measurement of the fair value of the 2021 Notes embedded derivative. In addition, financial expenses are comprised primarily from interest expense on our outstanding convertible notes.

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

*Revenues from Selling Goods*

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

resulted from an increase in the amount of \$3.1 million of product sold to Brazil and \$7.0 million of drug substance sold to Pfizer.

*Revenues from License and R&D Services*

We recorded revenues of \$1.8 million for the year ended December 31, 2017. Revenues from the license agreement represent the revenues we recognized in connection with the Chiesi Ex-US Agreement.

*Cost of Goods Sold*

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

*Research and Development Expenses*

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

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

*Selling, General and Administrative Expenses*

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

*Financial Expenses and Income*

Financial expense was \$48.9 million for the year ended December 31, 2017, compared to financial income of \$4.0 million for the year ended December 31, 2016. Financial expenses included a charge of \$38.1 million as a result of the re-measurement of the fair value of the 2021 Notes embedded derivative. In addition, financial expenses is comprised primarily from interest expense on convertible notes.

**Liquidity and Capital Resources***Sources of Liquidity*

As a result of our significant research and development expenditures and the lack of significant revenue from sales of taliglucerase alfa, we have generated operating losses from our continuing operations since our inception. To date, we have funded our operations primarily with proceeds equal to \$31.3 million from the sale of shares of convertible preferred and ordinary shares of Protalix Ltd., and an additional \$14.1 million in connection with the exercise of warrants issued in connection with the sale of such shares, through December 31, 2008. In addition, on October 25, 2007, we generated gross proceeds of \$50.0 million in connection with an underwritten public offering of our common stock and on each of March 23, 2011 and February 22, 2012, we generated gross proceeds of \$22.0 million and \$27.2 million, respectively, in connection with underwritten public offerings of our common stock. We believe that the funds currently available to us as are sufficient to satisfy our capital needs for at least 12 months.

The following table summarizes our public funding sources since 2007:

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

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

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

In the fourth quarter of 2017, Chiesi made a payment to Protalix Ltd. of \$25.0 million in connection with the execution of the Chiesi Ex-US Agreement and in third quarter of 2018, Chiesi made a payment to Protalix Ltd. of \$25.0 million in connection with the execution of the Chiesi U.S. Agreement.

### *Cash Flows*

Net cash used in operations was \$7.7 million for the year ended December 31, 2018. The net loss from continuing operations for the year ended December 31, 2018 was \$26.5 million. Net cash used in investing activities for the year ended December 31, 2018 was \$0.6 million and consisted primarily of purchase of property and equipment. Net cash used in financing activities was \$4.8 million which consisted of cash settlement for certain conversions of our convertible notes.

Net cash used in operations was \$10.0 million for the year ended December 31, 2017. The net loss from continuing operations for the year ended December 31, 2017 of \$83.4 million was partially offset by a change of \$38.1 million in the fair value of convertible notes embedded derivative and an increase of \$24.2 million in contract liability. Net cash used in investing activities for the year ended December 31, 2017 was \$1.1 million and consisted primarily of purchase of property and equipment. Net cash used in financing activities was \$1.4 million which consisted of cash settlement of \$11.0 million for certain conversions of our convertible notes which was partially offset by \$9.5 million of net proceeds from the issuance of our 2021 Notes.

### *Future Funding Requirements*



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

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

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

### **Effects of Inflation and Currency Fluctuations**

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the years ended December 31, 2016, 2017 or 2018.

Currency fluctuations could affect us by increased or decreased costs mainly for goods and services acquired outside of Israel. We do not believe currency fluctuations have had a material effect on our results of operations during the years ended December 31, 2016, 2017 or 2018.

### **Off-Balance Sheet Arrangements**

We have no off-balance sheet arrangements as of December 31, 2017 and 2018.

### **Recently Issued Accounting Pronouncements**

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

**Contractual Obligations**

The following table summarizes our significant contractual obligations at December 31, 2018:

(U.S. dollars in thousands)	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Convertible notes - interest	\$13,032	\$ 4,344	\$ 8,688		
Convertible notes - principal amount	\$57,918		\$ 57,918		
Operating lease obligations	\$3,028	\$ 1,233	\$ 1,795		
Purchase obligations (1)	\$3,157	\$ 3,157			
Certain clinical contract	\$18,809	\$ 11,115	\$ 7,579	\$ 115	
Liability for employee rights upon retirement	\$2,374				\$ 2,374
Total	\$98,318	\$ 19,849	\$ 75,980	\$ 115	\$ 2,374

(1) Represents open purchase orders issued to certain suppliers and other vendors mainly in connection with our research and development activities that were outstanding as of December 31, 2018.

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

**Selected Quarterly Financial Data (unaudited)**

	Three Months Ended				2018			
	2017				2018			
	(U.S. dollars in thousands, except per share data)							
	March 31	June 30	Sept. 30	Dec. 31	March 31	June 30	Sept. 30	Dec. 31
					(as restated)	(as restated)	(as restated)	
Revenues from selling goods	\$2,889	\$6,358	\$7,526	\$2,469	\$4,553	\$ 2,006	\$ 663	\$1,756
Revenues from license agreements				1,836	2,161	2,832	11,672	8,597
Operating loss	6,365	10,805	7,765	9,582	5,151	6,744	3,741	3,672
Net (loss) profit for the period	\$(59,148)	\$450	\$(11,437)	\$(13,305)	\$(7,239)	\$( 8,462 )	\$( 5,322 )	\$(5,434)
Earnings (loss) per share of common stock, basic and diluted:								
Net basic income (loss) per share of common stock	\$(0.48 )	\$0.00	\$(0.09 )	\$(0.10 )	\$(0.05 )	\$( 0.06 )	\$( 0.04 )	\$(0.04 )
Net diluted income (loss) per share of common stock	\$(0.48 )	\$(0.06 )	\$(0.09 )	\$(0.10 )	\$(0.05 )	\$( 0.06 )	\$( 0.04 )	\$(0.04 )

**Item 7A. Quantitative and Qualitative Disclosures about Market Risk****Currency Exchange Risk**

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

Approximately 35% of our costs, including salaries, expenses and office expenses, are incurred in NIS. Inflation in Israel may have the effect of increasing the U.S. dollar cost of our operations in Israel. If the U.S. dollar declines in value in relation to the NIS, it will become more expensive for us to fund our operations in Israel. A revaluation of 1%

of the NIS will affect our loss before tax by less than 1%. The exchange rate of the U.S. dollar to the NIS, based on exchange rates published by the Bank of Israel, was as follows:

	Year Ended December		
	31,		
	2016	2017	2018
Average rate for period	3.841	3.600	3.595
Rate at year-end	3.845	3.467	3.748

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

### **Interest Rate Risk**

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

## **Item 8. Financial Statements and Supplementary Data**

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

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

None.

## **Item 9A. Controls and Procedures**

### **Evaluation of Disclosure Controls and Procedures**

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

The evaluation of our disclosure controls and procedures included a review of the controls' objectives and design, our implementation of the controls and their effect on the information generated for use in this Annual Report on Form 10-K. This type of evaluation will be performed on a quarterly basis so that the conclusions of management, including the Chief Executive Officer and Chief Financial Officer, concerning the effectiveness of the disclosure controls and procedures can be reported in our periodic reports on Form 10-Q and Form 10-K. The overall goals of these various evaluation activities are to monitor our disclosure controls and procedures, and to modify them as necessary. Our intent is to maintain the disclosure controls and procedures as dynamic systems that change as conditions warrant.

Based on the controls evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the end of the period covered by this Form 10-K, our disclosure controls and procedures were not effective as of December 31, 2018 due to the material weakness in internal control over financial reporting described below.

Our Chief Executive Officer and Chief Financial Officer have concluded that notwithstanding the existence of the material weakness, the consolidated financial statements included in this Annual Report on Form 10-K present fairly, in all material respects, our financial position, results of operations and cash flows for the periods presented in conformity with U.S. generally accepted accounting principles. Additional corrective actions continue to address the internal control material weakness as described below under the section "Remediation Plan."

## Management's Report on Internal Control over Financial Reporting

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

Management assessed our internal control over financial reporting as of December 31, 2018, the end of our fiscal year. Management based its assessment on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Management's assessment included evaluation of elements such as the design and operating effectiveness of key financial reporting controls, process documentation, accounting policies and our overall control environment.

Based on our assessment, management has concluded that our internal control over financial reporting was not effective as of the end of the fiscal year to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles. We determined that a material weakness in our internal control over financial reporting existed as of December 31, 2018 in that we did not maintain effective internal controls related to accounting for complex revenue contracts. Specifically, we did not properly assess the performance obligations we had with regard to certain out-licensing arrangements which became material to our company during 2018. We reviewed the results of management's assessment with the Audit Committee of our Board of Directors.

The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by Kesselman & Kesselman, an independent registered public accounting firm, as stated in their report included herein.

### **Remediation Plan**

In response to the identified material weakness, our management, with the oversight of the Audit Committee of the Board of Directors, has updated our revenue recognition processes and controls with respect to out-licensing arrangements, and intends to continue to update our revenue recognition processes and controls and to implement additional control procedures, including retaining a globally recognized business and accounting advisory firm to assist us in improving our internal processes in connection with revenue recognition. While certain remedial actions have been completed in the first quarter of 2019, we intend to continue to update our revenue recognition processes and controls and to implement additional control procedures as the need to do so is identified by our management. The remediation efforts are intended both to address the identified material weakness and to enhance our overall financial control environment.

The material weakness will not be considered remediated until our management designs and implements effective controls that operate for a sufficient period of time and management has concluded, through testing, that these controls are effective. We will monitor the effectiveness of our remediation plan and will refine its remediation plan as appropriated.

### **Inherent Limitations on Effectiveness of Controls**

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent or detect all error and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. The design of a control system must reflect the fact that



there are resource constraints, and the benefits of controls must be considered relative to their costs. Further, because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, within a company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Controls can also be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Projections of any evaluation of controls effectiveness to future periods are subject to risks. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures.

#### Changes in internal controls

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15f and 15d-15f under the Exchange Act) that occurred during the year ended December 31, 2018 that have materially affected, or that are reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. Other Information**

None.

73

## PART III

**Item 10. Directors, Executive Officers and Corporate Governance**

Our directors and executive officers, their ages and positions as of March 1, 2019 are as follows:

<b>Name</b>	<b>Age</b>	<b>Position</b>
<b>Directors</b>		
Shlomo Yanai	66	Chairman of the Board
Moshe Manor	62	President and Chief Executive Officer, Director
Amos Bar Shalev	66	Director
Zeev Bronfeld	67	Director
David Granot	72	Director
Aharon Schwartz, Ph.D.	76	Director
<b>Executive Officers</b>		
Yoseph Shaaltiel, Ph.D.	65	Executive VP, Research and Development
Einat Brill Almon, Ph.D.	59	Senior Vice President, Product Development
Yossi Maimon, CPA	48	Vice President, Chief Financial Officer, Treasurer and Secretary
Yaron Naos	55	Senior Vice President, Operations

**Shlomo Yanai.** Shlomo Yanai has served as the Chairman of our Board of Directors since July 2014. Mr. Yanai is currently the Chairman of the Board of Cambrex Corporation (NYSE:CBM) and has served on its board of directors since November 2012. He also serves as a director of PDL BioPharma, Inc. (NASDAQ:PDLI), since June 2018, as a non-employee member of the board of managers of Q Holdco LLC, and as a senior advisor to Moelis & Company. Mr. Yanai served as a director of Lumenis Ltd. from 2012 through 2015; of Sagent Pharmaceuticals, Inc. from April 2015 through August 2016; of Perrigo Co. plc (NASDAQ:PRGO) from November 2015 through January 2017; and of Quinpario Acquisition Corp. 2 (NASDAQ:QPACU) from November 2014 through July 2017. Mr. Yanai served as President and Chief Executive Officer of Teva Pharmaceutical Industries Ltd., or Teva (NASDAQ:TEVA, TASE:TEVA), from March 2007 until May 2012 and, prior to joining Teva, Mr. Yanai was President and Chief Executive Officer of Makhteshim-Agan Industries Ltd. from 2003 until 2006. Before that, he was a Major General in the Israel Defense Forces, where he served for 32 years in various positions, the last two positions being Commanding Officer of the Southern Command and Head of the Division of Strategic Planning. Mr. Yanai was the head of the Israeli security delegation to the peace talks at Camp David, Shepherdstown and Wye River. He currently serves as a member of the Board of Governors of the Technion — Israel Institute of Technology of Haifa, Israel, and of the Board of Trustees of Bar-Ilan University — Israel, as well as an honorary member of the Board of the Institute for Policy and Strategy of the Interdisciplinary Center (IDC), Herzliya, Israel. Mr. Yanai holds a bachelor's degree in political science and economics from Tel Aviv University, a master's degree in national resources management from George Washington University, and is a graduate of the Advanced Management Program of Harvard Business School and U.S. National War College (NDU). Mr. Yanai was the recipient of the Max Perlman Award for Excellence in Global Business Management from Tel Aviv University, Israel in 2005 and was awarded an honorary doctorate by Bar-Ilan University, Israel in 2012. We believe Mr. Yanai's qualifications to serve as Chairman of our Board of Directors

include his vast global operating experience in the life-science and pharmaceutical and agro-chemicals industry. He also brings a global perspective to the Board, incorporating his industry and Board leadership experience and his distinguished military service.

**Moshe Manor.** Mr. Manor has served as our President and Chief Executive Officer and as a director of our Company since November 2014. Mr. Manor served in a number of senior executive positions at Teva (NASDAQ:TEVA, TASE:TEVA) from 1984 through 2012. Most recently, he served as President, Teva Asia & Pacific where he led the strategy and development of a high growth region for Teva. Prior to that, he was Group Vice President, Global Branded Products, leading the Innovative Commercial and Research & Development franchises. From 2006 through 2008, Mr. Manor was Senior Vice President, Global Innovative Resources, and was responsible for generating over \$3 billion in sales with Copaxone® and Azilect®. Previously, he served as director of Teva Israel. Most recently, Mr. Manor serves on the Board of Directors of Coronis Partners, and as Chairman of the Board of Directors of a startup company, MEway Pharma. He holds a BA in Economics from the Hebrew University in Jerusalem, and an MBA from the Tel-Aviv University. We believe Mr. Manor's qualifications to serve on our Board of Directors include his extensive experience in the life-science and pharmaceutical industry on a global scale.

**Amos Bar Shalev.** Mr. Bar Shalev has served as our director since July 2008. Previously, Mr. Bar Shalev served as a director of Protalix Ltd. from 2005 through January 2008, and as our director from 2006 through 2008. Mr. Bar Shalev brings to us extensive experience in managing technology companies. Currently, Mr. Bar Shalev serves on the boards of directors of Aposense Ltd. (TASE: APOS), an Israeli publicly-traded company listed on the TASE, since 2011, as well as Twine Solutions Ltd., a privately-held technology company, since 2015, and of Steam CC Ltd., since 2017, both privately-held Israeli companies. From 2004 through 2012, Mr. Bar Shalev served as a director of Technorov Holdings (1993) Ltd. and managed its portfolio. In addition, he served on the board of directors of Highcon Systems Ltd., a privately-held Israeli company, from 2010 through 2012. From 1997 through 2004, he was a Managing Director of TDA Capital Partners, a management company of the TGF (Templeton Tadiran) Fund. From 2004 through 2007, he was the President of Win Buyer Ltd. He has served on the board of directors of a number of Israeli publicly traded and privately-held Israeli companies including, among others, Velox Ltd., NESS Ltd. (acquired by BioNess Inc.), Idanit (acquired by Scitex Corporation Ltd.), Objet Geometrix (merged with Stratasys, Inc. (NASDAQ:SSYS)), Verisity, Scitex Vision (acquired by Hewlett Packard), Golden Wings Investment Company Ltd., the venture capital fund of the Israeli Air Force Veterans Business Club, Win Buyer Ltd. and Sun Light Ltd. He received his B.Sc. in Electrical Engineering from the Technion, Israel in 1978 and M.B.A. from the Tel Aviv University in 1981. He holds the highest award from the Israeli Air Force for technological achievements. We believe Mr. Bar Shalev's qualifications to serve on our Board of Directors include his years of experience in the management of Israeli businesses.

**Zeev Bronfeld.** Mr. Bronfeld has served as a director of Protalix Ltd. since 1996 and as our director since December 2006. Mr. Bronfeld brings to us vast experience in management and value building of biotechnology companies. He is an experienced businessman who is involved in a number of biotechnology companies. He was a co-founder of Bio-cell Ltd., a former Israeli publicly-traded holding company that specialized in biotechnology companies and served as its Chief Executive Officer from 1986 through 2015. Mr. Bronfeld currently serves as a director of Entera Bio Ltd. (NASDAQ: ENTX), as well as The Trendlines Group (SGX:42T), D.N.A. Biomedical Solutions Ltd. (TASE:DNA) and Electreon Wireless Ltd. (TASE:ELWS) (formerly, Biomedix Incubator Ltd.), all of which are public companies. Mr. Bronfeld is also a director of a number of privately-held companies, most of which are involved in the life sciences, such as Contipi Medical Ltd and TransBiodiesel Ltd. From 2008 through January 2017, Mr. Bronfeld served as a director of Macrocare Ltd., a Nasdaq-listed company that merged into Leap Therapeutics, Inc. (NASDAQ:LPTX). Mr. Bronfeld received a B.A. in Economics from the Hebrew University in 1975. We believe Mr. Bronfeld's qualifications to serve on our Board of Directors include his years of experience in the management of private and public Israeli companies, including life science companies.

**David Granot.** Mr. Granot has served as our director since August 2018. Mr. Granot currently serves on the Board of Directors of Ormat Technologies, Inc. (NYSE:ORA, TASE:ORA), and of Bezeq Israeli Telecommunication, Co. Ltd. (TASE:BEZQ) since May 22, 2012, where he served as temporary Acting Chairman, July 2017 through May 2018. He also serves on the Board of Directors of Alrov Properties & Lodgings Ltd. (TASE:ALRPR); and Jerusalem Economy Ltd. (TASE:ECJM), each of which is an Israeli public company. He also serves on the board of directors of Tempo Beverages Ltd. and Geregu Power PLC, each of which is a privately-held company. From 2009 through 2017, he was a director of Harel Insurance Investments and Financial Ltd. and Chairman of the Nostro investment committee of Harel Insurance. In addition, from 2001 through 2007, he served as the Chief Executive Officer of the First International Bank of Israel Ltd, from 1998 through 2000 he served as the Chief Executive Officer of the Israel Discount Bank and from 1995 through 1998 he served as the Chief Executive Officer of the Israel Union Bank. He

holds a B.A. in Economics and an MBA, both from the Hebrew University of Jerusalem. We believe Mr. Granot's qualifications to serve on our Board of Directors include his extensive financial and banking knowledge, as well as vast management and business experience.

**Aharon Schwartz, Ph.D.** Dr. Schwartz has served as our director since November 2014. He retired from Teva in 2011 where he served in a number of positions from 1975 through 2011, the most recent being Vice President, Head of Teva Innovative Ventures from 2008. Dr. Schwartz is currently chairman of the board of directors of BiolineRx Ltd. (NASDAQ:BLRX, TASE:BLRX) and a member of the board of directors of Barcode Ltd and Foamix Pharmaceuticals Ltd. (NASDAQ:FOMX). He also works as an independent consultant. From January 2013 through November 2017, he served as a member of the board of directors of Alcobra Ltd. (NASDAQ:ADHD), which is now called Arcturus Therapeutics Ltd. Dr. Schwartz received his Ph.D. in organic chemistry in 1978 from the Weizmann Institute of Science, his M.Sc. in organic chemistry from the Technion and a B.Sc. in chemistry and physics from the Hebrew University of Jerusalem. Dr. Schwartz received a second Ph.D. in 2014 from the Hebrew University of Jerusalem in the history and philosophy of science. We believe Dr. Schwartz's qualifications to serve on our Board of Directors include his years of experience in life science companies.

**Yoseph Shaaltiel, Ph.D.** Dr. Shaaltiel founded Protalix Ltd. in 1993 and has served as our Executive Vice President, Research and Development since December 2006. From 2006 through 2014, he served on our Board of Directors. Prior to establishing Protalix Ltd., from 1988 to 1993, Dr. Shaaltiel was a Research Associate at the MIGAL Technological Center. He also served as Deputy Head of the Biology Department of the Biological and Chemical Center of the Israeli Defense Forces and as a Biochemist at Makor Chemicals Ltd. Dr. Shaaltiel was a Postdoctoral Fellow at the University of California at Berkeley and at Rutgers University in New Jersey. He has co-authored over 40 articles and abstracts on plant biochemistry and holds several patents. Dr. Shaaltiel received his Ph.D. in Plant Biochemistry from the Weizmann Institute of Science, an M.Sc. in Biochemistry from the Hebrew University and a B.Sc. in Biology from the Ben Gurion University.

**Einat Brill Almon, Ph.D.** Dr. Almon joined Protalix Ltd. in December 2004, originally as a Senior Director and later as a Vice President and became our Senior Vice President, Product Development in 2006. Dr. Almon has many years of experience in the management of life science projects and companies, including biotechnology and agrobiotech, with direct experience in clinical, device and scientific software development, as well as a strong background and work experience in intellectual property. Prior to joining Protalix Ltd., from 2001 to 2004, she served as Director of R&D and IP of Medgenics Medical (Israel) Ltd. (formerly, Biogenics Ltd.), a company that developed an autologous platform for tissue-based protein drug delivery. Medgenics Medical, based in Israel, is a wholly-owned subsidiary of Aevi Genomic Medicine, Inc. (NASDAQ:GNMX) (formerly, Medgenics Inc.). Dr. Almon has trained as a biotechnology patent agent at leading IP firms in Israel. Dr. Almon holds a Ph.D. and an M.Sc. in molecular biology of cancer research from the Weizmann Institute of Science, a B.Sc. from the Hebrew University and has carried out Post-Doctoral research at the Hebrew University in the area of plant molecular biology.

**Yossi Maimon, CPA.** Mr. Maimon joined Protalix Ltd. in October 2006 as its Chief Financial Officer and became our Vice President and Chief Financial Officer in 2006. Prior to joining Protalix, from 2002 to 2006, he served as the Chief Financial Officer of Colbar LifeScience Ltd., or Colbar, a biomaterial company focusing on aesthetics, where he led all of the corporate finance activities, fund raisings and legal aspects of Colbar including the sale of Colbar to Johnson and Johnson (NYSE:JNJ). In March 2019, Mr. Maimon assumed a similar position in a privately held biotech startup company on a temporary basis. Mr. Maimon has a B.A. in accounting from the City University of New York and an MBA from Tel Aviv University, and he is a Certified Public Accountant in the United States (New York State) and Israel.

**Yaron Naos.** Mr. Yaron Naos joined Protalix in 2004, originally as a Senior Director for Operations and later as Vice President for Production, and became our Senior Vice President, Operations in 2018. Mr. Naos has a wealth of hands-on experience and knowledge in the field of pharmaceutical development. Prior to joining Protalix, he served for a decade as R&D Product Manager at Dexion Pharmaceutical Co., one of Israel's largest pharmaceutical companies, where he was responsible for technology transfer from R&D to production, and in charge of R&D activities that led to the commercialization of many products. Later, Mr. Naos was plant manager of Medibrands Pharmaceutical Company, as well as logistics manager of Mediline for period of four years, where he was responsible for all operational activities, from procurement to distribution. Mr. Naos holds a B.Sc. in Food Engineering and Biotechnology from the Technion-Israel Technology Institute and an MBA from Haifa University.

### **Section 16(a) Beneficial Ownership Reporting Compliance**

Section 16(a) of the Exchange Act requires our directors, executive officers and holders of more than 10% of our common stock to file with the Commission reports regarding their ownership and changes in ownership of our equity securities. We believe that all Section 16 filings requirements were met by our officers and directors during 2018. In making this statement, we have relied solely upon examination of the copies of Forms 3, 4 and 5, Schedule 13s and written representations of our former and current directors, officers and 10% stockholders.

### **Audit Committee**

The Audit Committee is currently comprised of Mr. Bar Shalev, Mr. Bronfeld, Dr. Schwartz and Mr. Granot. We require that all Audit Committee members possess the required level of financial literacy and at least one member of the Audit Committee meet the current standard of requisite financial management expertise as required by the NYSE American and applicable rules and regulations of the Commission.



Our Audit Committee operates under a formal charter that governs its duties and conduct. A current copy of the Audit Committee Charter is available on our website at <http://www.protalix.com>.

All members of the Audit Committee are independent from our executive officers and management.

Our independent registered public accounting firm reports directly to the Audit Committee.

Our Audit Committee meets with management and representatives of our registered public accounting firm prior to the filing of officers' certifications with the Commission to receive information concerning, among other things, effectiveness of the design or operation of our internal controls over financial reporting, as required by Section 404 of SOX.

Our Audit Committee has adopted a Policy for Reporting Questionable Accounting and Auditing Practices and Policy Prohibiting Retaliation against Reporting employees to enable confidential and anonymous reporting of improper activities to the Audit Committee.

Mr. Bar Shalev, Mr. Bronfeld, Dr. Schwartz and Mr. Granot each qualify as "audit committee financial experts" under the applicable rules of the Commission. In making the determination as to these individuals' status as audit committee financial experts, our Board of Directors determined they have accounting and related financial management expertise within the meaning of the aforementioned rules, as well as the listing standards of the NYSE American.

### **Code of Business Conduct and Ethics**

We have adopted a Code of Business Conduct and Ethics that includes provisions ranging from restrictions on gifts to conflicts of interest. All of our employees and directors are bound by this Code of Business Conduct and Ethics. Violations of our Code of Business Conduct and Ethics may be reported to the Audit Committee.

The Code of Business Conduct and Ethics includes provisions applicable to all of our employees, including senior financial officers and members of our Board of Directors and is posted on our website ([www.protalix.com](http://www.protalix.com)). We intend to post amendments to or waivers from any such Code of Business Conduct and Ethics.

## Item 11. Executive Compensation

### Compensation Discussion and Analysis

The primary goals of the Compensation Committee of our Board of Directors with respect to executive compensation are to attract and retain the most talented and dedicated executives possible, to tie annual and long-term cash and stock incentives to achievement of specified performance objectives, and to align executives' incentives with stockholder value creation. To achieve these goals, the Compensation Committee implements and maintains compensation plans that tie a portion of executives' overall compensation to key strategic goals such as developments in our clinical path, the establishment of key strategic collaborations, the build-up of our pipeline and the strengthening of our financial position. The Compensation Committee evaluates individual executive performance with a goal of setting compensation at levels the committee believes are comparable with executives in other companies of similar size and stage of development operating in the biotechnology industry while taking into account our relative performance and our own strategic goals.

### Elements of Compensation

Executive compensation consists of following elements:

**Base Salary.** Base salaries for our executives are established based on the scope of their responsibilities taking into account competitive market compensation paid by other companies for similar positions. Generally, we believe that executive base salaries should be targeted near the median of the range of salaries for executives in similar positions with similar responsibilities at comparable companies. The Compensation Committee convenes, from time to time to evaluate present and future executive compensation, which evaluation generally includes an evaluation of the peer group considered in analyzing executive compensation. The Compensation Committee intends to continue reviewing and revising the peer group periodically to ensure that it continues to reflect companies similar to our Company in size and development stage. The Compensation Committee also reviews executive compensation reports and an analysis of publicly-traded biotechnology companies prepared by third party experts from a well-known consulting firm for additional data and other information regarding executive compensation for comparative purposes.

Base salaries are usually reviewed annually, and adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience. The base salaries of each of our President and Chief Executive Officer, our Executive Vice President, Research and Development, our Senior Vice President, Product Development, our Vice President and Chief Financial Officer and our Senior Vice President, Operations, who we refer to collectively as the “Named Executive Officers,” are discussed herein. In March 2016, our Board of Directors adopted certain recommendations of the Compensation Committee regarding the compensation of our Named Executive Officers at that time with no change in the base salary component, as discussed below.

**Annual Bonus.** The Compensation Committee has the authority to award discretionary annual bonuses to our executive officers. The discretionary annual bonus awards were intended to compensate officers for achieving financial, clinical, regulatory and operational goals and for achieving individual annual performance objectives. For any given year, the compensation objectives vary, but relate generally to strategic factors such as developments in our clinical path, the execution of a license agreement for the commercialization of product candidates, the establishment of key strategic collaborations, the build-up of our pipeline and financial factors such as capital raising. Bonuses are awarded generally based on corporate performance, with adjustments made within a range for individual performance, at the discretion of the Compensation Committee. The Compensation Committee determines, on a discretionary basis, the size of the entire bonus pool and the amount of the actual award to each Named Executive Officer.

The Compensation Committee selects, in its discretion, the executive officers of our Company or our subsidiary who are eligible to receive bonuses for any given year. Any bonus granted by the Compensation Committee will generally be paid upon the achievement of a specific milestone, subject to certain terms and conditions. The Compensation Committee has not fixed a minimum or maximum award for any executive officer’s annual discretionary bonus. Each of our executive officers is eligible for a discretionary annual bonus under his or her employment agreement.

**Performance Bonus.** In March 2016, the Compensation Committee adopted a new performance-based bonus plan for the Named Executive Officers and other members of our management. The new bonus plan is designed to provide cash bonuses over a three-year period based on our Company’s achievement of what we consider to be major milestones. The amounts payable to each person for each milestone were determined after consideration of both personal and Company objectives and are based on a multiple of the person’s monthly salary. Such multiples range from a maximum of 12 months to a minimum of one-half a month. Each bonus is payable upon the achievement of the applicable milestone, subject to certain terms and conditions. The bonus plan is summarized as follows:

Milestone	Chief Executive Officer	Exec. VP, R&D	Sr. VP, Product Development	VP and Chief Financial Officer	Chief Operating Officer
Clinical Development Milestone for Certain Product Candidate	\$ 108,000	\$ 42,000	\$ 72,000 to \$108,000	\$ 36,000	\$ 34,000
	\$	\$	\$	\$	\$

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

Regulatory Development Milestone for Same Product Candidate	108,000 to \$216,000	84,000 to \$168,000	108,000 to \$216,000	36,000 to \$54,000	34,000 to \$68,000
Clinical Development Milestone for Certain Product Candidate	\$ 54,000	\$ 10,500	\$ 27,000 to \$54,000	\$ 9,000	\$ 8,500
Clinical Development Milestone for Certain other Product Candidate	\$ 54,000	\$ 10,500	\$ 27,000 to \$54,000	\$ 9,000	\$ 8,500
General Regulatory Milestone	\$ 102,000	\$ 42,000	\$ 36,000	\$ 18,000	\$ 102,000
Substantial Transaction involving a Certain Product Candidate	\$ 128,000	\$ 21,000	\$ 18,000	\$ 115,000 to \$141,000	\$ 17,000
Substantial Transaction involving other Product Candidate	\$ 112,000	\$ 10,500	\$ 9,000	\$ 49,000 to \$60,000	\$ 8,500
Corporate Finance Milestones	\$ 216,000			\$ 197,000 to \$242,000	
Early-Stage Clinical Milestones	\$ 72,000	\$ 252,000	\$ 72,000	\$ 36,000	\$ 68,000

***Options and Share-Based Compensation.*** Our amended 2006 Stock Incentive Plan authorizes us to grant options to purchase shares of common stock, restricted stock and other securities to our employees, directors and consultants. Our Compensation Committee is the administrator of the stock incentive plan. Stock option or other grants are generally made at the commencement of employment and following a significant change in job responsibilities or to meet other special retention or performance objectives. The Compensation Committee reviews and approves stock option and other awards to executive officers based upon a review of competitive compensation data, its assessment of individual performance, a review of each executive's existing long-term incentives, and retention considerations. The exercise price of stock options granted under our amended 2006 Stock Incentive Plan must be equal to at least 100% of the fair market value of our common stock on the date of grant; however, in certain circumstances, grants may be made at a lower price to Israeli grantees who are residents of the State of Israel.

***Severance and Change in Control Benefits.*** The Compensation Committee granted the following payments that would be payable in connection with a change of control: \$1 million to the President and Chief Executive Officer and \$400,000 to each of the other executive Vice Presidents. Such payments are subject to certain terms and conditions. In addition to the foregoing, pursuant to the employment agreements entered into with each of our executive officers, the executive officer is entitled to be insured by Protalix Ltd. under a Manager's Policy in lieu of severance. The intention of such Manager's Policies is to provide the Israel-based officers with severance protection of one month's salary for each year of employment. In addition, the stock options and restricted stock granted to each of our Named Executive Officers provide that all of such instruments are subject to accelerated vesting immediately upon a change in control of our Company.

***Other Compensation.*** Consistent with our compensation philosophy, we intend to continue to maintain our current benefits for our executive officers; however, the Compensation Committee in its discretion may revise, amend, or add to the officer's executive benefits if it deems it advisable. As an additional benefit to all of our Israel-based Named Executive Officers and for most of our employees, we generally contribute to certain funds amounts equaling a total of approximately 15% of their gross salaries for certain pension and other savings plans for the benefit of the Named Executive Officers. In addition, in accordance with customary practice in Israel, our Israel-based executives' agreements require us to contribute towards their vocational studies, and to provide annual recreational allowances, a Company car and a Company phone. We believe these benefits are currently equivalent with median competitive levels for comparable companies.

***Executive Compensation.*** We refer to the "Summary Compensation Table" set forth below for information regarding the compensation earned during the fiscal year ended December 31, 2018 by our President and Chief Executive Officer, our Executive Vice President, Research and Development, our Senior Vice President, Product Development, our Vice President and Chief Financial Officer and our Senior Vice President, Operations.

## **Compensation Committee Report**

*The above report of the Compensation Committee does not constitute soliciting material and shall not be deemed filed or incorporated by reference into any other filing by us under the Securities Act of 1933 or the Exchange Act.*

The Compensation Committee has reviewed and discussed the Compensation Discussion and Analysis set forth below with our management. Based on this review and discussion, the Compensation Committee has recommended to our Board of Directors that the Compensation Discussion and Analysis be included in our Annual Report on Form 10-K and our annual proxy statement on Schedule 14A.

Respectfully submitted on March 14, 2019, by the members of the Compensation Committee of the Board of Directors.

*Amos Bar Shalev*

*Zeev Bronfeld*

*Aharon Schwartz, Ph.D.*

*David Granot*

**Summary Compensation Table**

The following table sets forth a summary for the fiscal years ended December 31, 2018, 2017 and 2016, respectively, of the cash and non-cash compensation awarded, paid or accrued by us or Protalix Ltd. to our President and Chief Executive Officer, our Executive Vice President, Research and Development, our Senior Vice President, Product Development, our Vice President and Chief Financial Officer and our Senior Vice President, Operations, who we refer to collectively as the “Named Executive Officers.” There were no restricted stock awards, long-term incentive plan payouts or other compensation paid during fiscal years 2018, 2017 and 2016 by us or Protalix Ltd. to the Named Executive Officers, except as set forth below. All of the Named Executive Officers are employees of our subsidiary, Protalix Ltd. All currency amounts are expressed in U.S. dollars.

Name and Principal Position	Year	Salary(\$)	Bonus (\$)	Stock Award(s) (\$)	Option Award(s) (\$)	All Other Compensation (\$)(1)	Total (\$)
Moshe Manor President and Chief Executive Officer	2018	356,551	150,000		106,820	104,283	717,654
	2017	355,290	374,000	-	103,354	105,056	937,700
Yoseph Shaaltiel, Ph.D. Executive Vice President, Research and Development	2016	333,058	-	-	250,299	98,925	682,282
	2018	288,719			60,575	84,148	433,442
	2017	288,326	62,176		41,454	80,786	472,742
Einat Brill Almon, Ph.D. Senior Vice President, Product Development	2016	270,248	-	18,211	103,279	73,325	465,063
	2018	249,583	120,000		59,089	75,369	504,041
	2017	249,243	157,508		37,686	74,798	519,235
Yossi Maimon, CPA Vice President, Chief Financial Officer	2016	233,486	-	16,043	93,890	66,822	410,241
	2018	282,649	140,000		59,089	75,813	557,551
	2017	282,197	363,647		37,686	75,448	758,978
Yaron Naos (2) Senior Vice President, Operations	2016	264,696	-	16,043	93,890	70,153	444,782
	2018	218,058			40,878	80,338	339,274

(1)Includes employer contributions to pension and/or insurance plans and other miscellaneous payments.

(2)Mr. Naos was promoted to Senior Vice President, Operations in May 2018.

**Grants of Plan-Based Awards**

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

The following table summarizes the grant of awards made to the Named Executive Officers during 2018 as of December 31, 2018.

Name	Grant date	All other		Grant date
		option awards:	Exercise or	
		Number of securities underlying options (#)	base price of option awards (\$/Sh)	fair value of stock and option awards (\$)
(a)	(b)	(j)	(k)	(l)
Moshe Manor	August 13, 2018	1,300,000	0.56	388,688
Yoseph Shaaltiel	August 13, 2018	700,000	0.56	209,294
Einat Brill Almon	August 13, 2018	700,000	0.56	209,294
Yossi Maimon	August 13, 2018	700,000	0.56	209,294
Yaron Naos	August 13, 2018	600,000	0.56	179,395



**Outstanding Equity Awards at Fiscal Year-End**

The following table sets forth information with respect to the Named Executive Officers concerning equity awards as of December 31, 2018.

Name	Option Awards		Option Exercise Price (\$)	Option Expiration Date
	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)		
Moshe Manor	900,000	-	2.37	9/29/2024
	81,250	1,218,750	0.56	9/13/2028
Yoseph Shaaltiel	50,000	-	2.65	2/25/2019
	145,000	-	6.90	2/25/2020
Einat Brill Almon	257,812	17,188	1.72	3/23/2025
	43,750	656,250	0.56	9/13/2028
	130,000	-	6.90	2/25/2020
	234,375	15,625	1.72	3/23/2025
Yossi Maimon	43,750	656,250	0.56	9/13/2028
	130,000	-	6.90	2/25/2020
	234,375	15,625	1.72	3/23/2025
Yaron Naos	43,750	656,250	0.56	9/13/2028
	50,000	-	2.65	2/25/2019
	115,000	-	6.90	2/25/2020
	46,875	3,125	1.72	3/23/2025
	37,500	562,500	0.56	9/13/2028

**Potential Payments upon Termination or Change-in-Control/Corporate Transaction**

Each of our Named Executive Officers (while they remain employed by our Company) is entitled to be insured by Protalix Ltd. under a Manager's Policy in lieu of severance upon termination. The intention of such Manager's Policies is to provide our officers with severance protection of one month's salary for each year of employment. The following payments would be payable in connection with a change of control of our Company: \$1 million to the President and Chief Executive Officer and \$400,000 to each of the other executive Vice Presidents, subject to certain terms and conditions. In addition to the foregoing, the vesting periods of outstanding options and restricted stock held by our Named Executive Officers are accelerated upon a change of control. Had we experienced a change in control/corporate transaction on December 31, 2018, the value of the acceleration of the vesting period of our Named Executive Officers were above the market value of our common stock and, accordingly, the value of the acceleration

of the stock options held by each of them as of such date would be zero. In addition, all of the restricted stock held by the Named Executive Officers had vested by their terms prior to said date.

## **Employment Arrangements**

**Moshe Manor.** Pursuant to Mr. Manor's employment agreement, his current monthly base salary is NIS 95,000 and Mr. Manor is entitled to an annual discretionary bonus subject to the sole discretion of our Board of Directors. The Board of Directors shall determine the bonus on the basis of agreed-upon annual objectives which shall include both measurable and strategic parameters. The monthly salary is subject to cost of living adjustments from time to time as may be required by law. The Board of Directors also granted to Mr. Manor options to purchase 900,000 shares of our common stock at an exercise price equal to \$2.37 per share, the closing sales price of the common stock on the NYSE American for the last trading day immediately preceding the effective date of the grant. The options vest over four years on a quarterly basis in 16 equal increments, subject to certain conditions. Vesting of the options will be accelerated in full upon a Corporate Transaction or a Change in Control, as those terms are defined in our 2006 Stock Incentive Plan, as amended. Mr. Manor's employment agreement is terminable by our Company on 90 days written notice for any reason during the first year of the agreement's term and on 180 days written notice thereafter. Mr. Manor may terminate the agreement on 90 days written notice for any reason during its term. We may terminate the Agreement for cause without notice. Mr. Manor is entitled to be insured by the Company under a Manager's Policy in lieu of severance, Company contributions towards vocational studies, annual recreational allowances, a Company car, a Company laptop and a Company phone. Mr. Manor is entitled to 25 working days of vacation.

**Yoseph Shaaltiel, Ph.D.** Pursuant to Dr. Shaaltiel's employment agreement, his current monthly base salary is NIS 80,750 per month. The employment agreement is terminable by our Company on 90 days' written notice for any reason and we may terminate the agreement for cause without notice. In addition, vesting of all of Dr. Shaaltiel's options and restricted shares will be accelerated in full upon a Corporate Transaction or a Change in Control, as those terms are defined in our 2006 Stock Incentive Plan, as amended. Dr. Shaaltiel is entitled to be insured by Protalix Ltd. under a Manager's Policy in lieu of severance, Company contributions towards vocational studies, annual recreational allowances, a Company car, a Company laptop and a Company phone. Dr. Shaaltiel is entitled to 29 working days of vacation.

**Einat Brill Almon, Ph.D.** Pursuant to Dr. Almon's employment agreement, her current monthly base salary is NIS 69,825 per month. She is also entitled to certain specified bonuses in the event that Protalix achieves certain specified clinical development milestones within specified timelines. In addition, vesting of all of Dr. Brill Almon's options and restricted shares will be accelerated in full upon a Corporate Transaction or a Change in Control, as those terms are defined in our 2006 Stock Incentive Plan, as amended. The employment agreement is terminable by either party on 60 days' written notice for any reason and we may terminate the agreement for cause without notice. Dr. Brill Almon is entitled to be insured by Protalix Ltd. under a Manager's Policy in lieu of severance, Company contributions towards vocational studies, annual recreational allowances, a Company car, a Company laptop and a Company phone at up to NIS 1,000 per month. Dr. Brill Almon is entitled to 29 working days of vacation.

**Yossi Maimon, CPA.** Pursuant to Mr. Maimon's employment agreement, his current monthly base salary is NIS 69,825 and Mr. Maimon is entitled to an annual discretionary bonus and additional discretionary bonuses in the event Protalix achieves significant financial milestones, subject to the Board's sole discretion. The monthly salary is subject to cost of living adjustments from time to time. In addition, vesting of all of Mr. Maimon's options and restricted shares will be accelerated in full upon a Corporate Transaction or a Change in Control, as those terms are defined in our 2006 Stock Incentive Plan, as amended. The employment agreement is terminable by either party on 60 days' written notice for any reason and we may terminate the agreement for cause without notice. Mr. Maimon is entitled to be insured by Protalix Ltd. under a Manager's Policy in lieu of severance, Company contributions towards vocational studies, annual recreational allowances, a Company car, a Company laptop and a Company phone. Mr. Maimon is entitled to 29 working days of vacation.

**Yaron Naos.** Mr. Naos' current monthly base salary is NIS 65,550 and he is entitled to an annual discretionary bonus for performance subject to the sole discretion of our compensation committee. The monthly salary is subject to cost of living adjustments from time to time as may be required by law. In addition, vesting of all of Mr. Naos' options and restricted shares will be accelerated in full upon a Corporate Transaction or a Change in Control, as those terms are defined in our 2006 Stock Incentive Plan, as amended. Mr. Naos' employment is terminable by either party on 60 days' written notice for any reason and we may terminate the agreement for cause without notice. Mr. Naos is entitled to be insured by Protalix Ltd. under a Manager's Policy in lieu of severance, Company contributions towards vocational studies, annual recreational allowances, a Company car, a Company phone, and a Company laptop. Mr. Naos is entitled to 29 working days of vacation.

## **Pay Ratio Disclosure**

In August 2015 pursuant to a mandate of The Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, or the Dodd-Frank Act, the Commission adopted a rule requiring annual disclosure of the ratio of the median employee's annual total compensation to the total annual compensation of the principal executive officer, or PEO. Mr. Manor is our PEO. The purpose of the new required disclosure is to provide a measure of the equitability of pay within our Company. We believe our compensation philosophy and process yield an equitable result and is presenting such information in advance of the required disclosure date as follows:

Median Employee total annual compensation	\$48,507
PEO total annual compensation	\$717,654
Ratio of PEO to Median Employee Compensation	14.79

In determining the median employee for fiscal year 2017, we prepared a list of all our employees as of December 31, 2017. Employees on leave of absence were excluded from the list and wages and salaries were annualized for those employees that were not employed for the full year ended December 31, 2017. The median amount was selected from the annualized list. At December 31, 2018, the median employee for fiscal year 2017 was no longer our employee. Accordingly, for purposes of the foregoing calculations, we chose a new median employee whose compensation for the year ended December 31, 2017 was substantially similar to the median employee identified for fiscal year 2017. As of December 31, 2018, we employed 184 persons.

### **Amended 2006 Stock Incentive Plan**

Our Board of Directors and our stockholders approved our 2006 Stock Incentive Plan on December 14, 2006. Our stockholders have approved amendments to the plan on June 17, 2012, November 10, 2014 and May 13, 2018. Of the 23,841,655 shares reserved for issuance under the plan, as amended, as of December 31, 2018, there are outstanding options to purchase 10,150,675 shares of our common stock in the aggregate, subject to adjustment for a stock split or any future stock dividend or other similar change in our common stock or our capital structure. As of December 31, 2018, options to acquire 7,303,119 shares of common stock remain available for grant under the amended 2006 Stock Incentive Plan.

Our amended 2006 Stock Incentive Plan provides for the grant of stock options, restricted stock, restricted stock units, stock appreciation rights and dividend equivalent rights, collectively referred to as “awards.” Stock options granted under the amended 2006 Stock Incentive Plan may be either incentive stock options under the provisions of Section 422 of the IRC, or non-qualified stock options. Incentive stock options may be granted only to employees. Awards other than incentive stock options may be granted to employees, directors and consultants. Shares issued in connection with awards other than options or stock appreciation rights shall count as one and one-half (1.5) shares for each share issued for purposes of the number of shares authorized for issuance under the plan.

The amended 2006 Stock Incentive Plan is also designed to comply with the provisions of the Israeli Income Tax Ordinance New Version, 1961 (including as amended pursuant to Amendment 132 thereto), or the Tax Ordinance, and is intended to enable us to grant awards to grantees who are Israeli residents as follows: (i) awards to employees pursuant to Section 102 of the Tax Ordinance; and (ii) awards to non-employees pursuant to Section 3(I) of the Tax Ordinance. For this purpose, “employee” refers only to employees, office holders and directors of our Company or a related entity excluding those who are considered “Controlling Stockholders” pursuant to, or otherwise excluded by, the Tax Ordinance. In accordance with the terms and conditions imposed by the Tax Ordinance, grantees who receive awards under the amended 2006 Stock Incentive Plan may be afforded certain tax benefits in Israel as described below.

Our Board of Directors or the Compensation Committee, referred to as the “plan administrator,” will administer our amended 2006 Stock Incentive Plan, including selecting the grantees, determining the number of shares to be subject to each award, determining the exercise or purchase price of each award, and determining the vesting and exercise periods of each award.

The exercise price of stock options granted under the 2006 Stock Incentive Plan must be equal to at least 100% of the fair market value of our common stock on the date of grant; however, in certain circumstances, grants may be made at a lower price to Israeli grantees who are residents of the State of Israel. If, however, incentive stock options are granted to an employee who owns stock possessing more than 10% of the voting power of all classes of our stock or the stock of any parent or subsidiary of our Company, the exercise price of any incentive stock option granted must equal at least 110% of the fair market value on the grant date and the maximum term of these incentive stock options must not exceed five years. The maximum term of all other awards must not exceed 10 years (or five years in the case of an incentive stock option granted to any participant who owns stock representing more than 10% of the voting power of all classes of our stock or the stock of any parent or subsidiary of our Company). The plan administrator will determine the exercise or purchase price (if any) of all other awards granted under the amended 2006 Stock Incentive Plan.

Under the amended 2006 Stock Incentive Plan, incentive stock options and options to Israeli grantees may not be sold, pledged, assigned, hypothecated, transferred or disposed of in any manner other than by will or by the laws of descent or distribution and may be exercised during the lifetime of the participant only by the participant. Other awards shall be transferable by will or by the laws of descent or distribution and to the extent and in the manner authorized by the

plan administrator by gift or pursuant to a domestic relations order to members of the participant's immediate family. The amended 2006 Stock Incentive Plan permits the designation of beneficiaries by holders of awards, including incentive stock options.

If the service of a participant in the amended 2006 Stock Incentive Plan is terminated for any reason other than cause, the participant may exercise awards that were vested as of the termination date for a period ending upon the earlier of 12 months from the date of termination (or such shorter or longer period set forth in the award agreement) or the expiration date of the awards unless otherwise determined by the plan administrator. If the service of a participant in the amended 2006 Stock Incentive Plan is terminated for cause, the participant may exercise awards that were vested as of the termination date for a period ending upon the earlier of 14 days from the date of termination (or such shorter or longer period set forth in the award agreement) or the expiration date of the awards unless otherwise determined by the plan administrator.

In the event of a corporate transaction, all awards will terminate unless assumed by the successor corporation. Unless otherwise provided in a participant's award agreement, in the event of a corporate transaction and with respect to the portion of each award that is assumed or replaced, then such portion will automatically become fully vested and exercisable immediately upon termination of a participant's service if the participant is terminated by the successor company or us without cause within 12 months after the corporate transaction. With respect to the portion of each award that is not assumed or replaced, such portion will automatically become fully vested and exercisable immediately prior to the effective date of the corporate transaction so long as the participant's service has not been terminated prior to such date.

In the event of a change in control, except as otherwise provided in a participant's award agreement, following a change in control (other than a change in control that also is a corporate transaction) and upon the termination of a participant's service without cause within 12 months after a change in control, each award of such participant that is outstanding at such time will automatically become fully vested and exercisable immediately upon the participant's termination. In addition, the stock options and shares of restricted stock issued to each of our Named Executive Officers are subject to accelerated vesting immediately upon a corporate transaction or a change in control of our Company, as defined in our amended 2006 Stock Incentive Plan.

Under our amended 2006 Stock Incentive Plan, a corporate transaction is generally defined as:

a merger or consolidation in which we are not the surviving entity, except for the principal purpose of changing our Company's state of incorporation;

the sale, transfer or other disposition of all or substantially all of our assets;

the complete liquidation or dissolution of our Company;

any reverse merger in which we are the surviving entity but our shares of common stock outstanding immediately prior to such merger are converted or exchanged by virtue of the merger into other property, whether in the form of securities, cash or otherwise, or in which securities possessing more than forty percent (40%) of the total combined voting power of our outstanding securities are transferred to a person or persons different from those who held such securities immediately prior to such merger; or

acquisition in a single or series of related transactions by any person or related group of persons of beneficial ownership of securities possessing more than fifty percent (50%) of the total combined voting power of our outstanding securities but excluding any such transaction or series of related transactions that the plan administrator determines not to be a corporate transaction (provided however that the plan administrator shall have no discretion in connection with a corporate transaction for the purchase of all or substantially all of our shares unless the principal

purpose of such transaction is changing our Company's state of incorporation).

Under our amended 2006 Stock Incentive Plan, a change of control is defined as:

the direct or indirect acquisition by any person or related group of persons of beneficial ownership of securities possessing more than fifty percent (50%) of the total combined voting power of our outstanding securities pursuant to a tender or exchange offer made directly to our stockholders and which a majority of the members of our board (who have generally been on our board for at least 12 months) who are not affiliates or associates of the offeror do not recommend stockholders accept the offer; or

a change in the composition of our board over a period of 12 months or less, such that a majority of our board members ceases, by reason of one or more contested elections for board membership, to be comprised of individuals who were previously directors of our Company.

Unless terminated sooner, the amended 2006 Stock Incentive Plan will automatically terminate on December 31, 2028. Our Board of Directors has the authority to amend, suspend or terminate our amended 2006 Stock Incentive Plan. No amendment, suspension or termination of the amended 2006 Stock Incentive Plan shall adversely affect any rights under awards already granted to a participant. To the extent necessary to comply with applicable provisions of federal securities laws, state corporate and securities laws, the IRC, the rules of any applicable stock exchange or national market system, and the rules of any non-U.S. jurisdiction applicable to awards granted to residents therein (including the Tax Ordinance), we shall obtain stockholder approval of any such amendment to the 2006 Stock Incentive Plan in such a manner and to such a degree as required.



### ***Impact of Israeli Tax Law***

The awards granted to employees pursuant to Section 102 of the Tax Ordinance under the amended 2006 Stock Incentive Plan may be designated by us as approved options under the capital gains alternative, or as approved options under the ordinary income tax alternative.

To qualify for these benefits, certain requirements must be met, including registration of the options in the name of a trustee. Each option, and any shares of common stock acquired upon the exercise of the option, must be held by the trustee for a period commencing on the date of grant and deposit into trust with the trustee and ending 24 months thereafter.

Under the terms of the capital gains alternative, we may not deduct expenses pertaining to the options for tax purposes.

Under the amended 2006 Stock Incentive Plan, we may also grant to employees options pursuant to Section 102(c) of the Tax Ordinance that are not required to be held in trust by a trustee. This alternative, while facilitating immediate exercise of vested options and sale of the underlying shares, will subject the optionee to the marginal income tax rate of up to 50% as well as payments to the National Insurance Institute and health tax on the date of the sale of the shares or options. Under the 2006 Stock Incentive Plan, we may also grant to non-employees options pursuant to Section 3(I) of the Tax Ordinance. Under that section, the income tax on the benefit arising to the optionee upon the exercise of options and the issuance of common stock is generally due at the time of exercise of the options.

These options shall be further subject to the terms of the tax ruling that has been obtained by Protalix Ltd. from the Israeli tax authorities in connection with the merger. Under the tax ruling, the options issued by us in connection with the assumption of Section 102 options previously issued by Protalix Ltd. under the capital gains alternative shall be issued to a trustee, shall be designated under the capital gains alternative and the issuance date of the original options shall be deemed the issuance date for the assumed options for the calculation of the respective holding period.

### **Compensation of Directors**

The following table sets forth information with respect to compensation of our non-employee directors during fiscal year 2018. The fees to our current directors were paid by Protalix Ltd.

<b>Name</b>	<b>Fees Earned or Paid in Cash (\$)</b>	<b>Option Award(s) (\$)</b>	<b>Total (\$)</b>
Shlomo Yanai	200,000	-	200,000
Zeev Bronfeld	80,000		80,000
Amos Bar Shalev	80,000		80,000
Aharon Schwartz, Ph.D.	65,556		65,556
David Granot (1)	19,758		19,758
Yodfat Harel Buchris (2)	20,000		20,000

(1) Mr. Granot joined the Board of Directors on August 9, 2018.

(2) Ms. Harel Buchris' tenure on the Board ended on May 13, 2018.

Directors' fees paid to each of Zeev Bronfeld and Yodfat Harel Buchris are paid to the applicable director's employer in accordance with arrangements between the director and the employer.

## Compensation Committee Interlocks and Insider Participation

Our Compensation Committee currently consists of Amos Bar Shalev, Zeev Bronfeld, Aharon Schwartz, Ph.D. and David Granot. No member of our Compensation Committee or any executive officer of our Company or of Protalix Ltd. has a relationship that would constitute an interlocking relationship with executive officers or directors of another entity. No Compensation Committee member is or was an officer or employee of ours or of Protalix Ltd. Further, none of our executive officers serves on the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our Board of Directors or Compensation Committee.

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

The following table sets forth information, as of March 1, 2019, regarding beneficial ownership of our common stock:

· each person who is known by us to own beneficially more than 5% of our common stock;

· each director;

· each of our Chief Executive Officer, our Executive Vice President, Research and Development, our Senior Vice President, Product Development, our Vice President and Chief Financial Officer and our Senior Vice President, Operations; and

· all of our directors and executive officers collectively.

Unless otherwise noted, we believe that all persons named in the table have sole voting and investment power with respect to all shares of our common stock beneficially owned by each of them. For purposes of this table, a person is deemed to be the beneficial owner of securities that can be acquired by such person within 60 days from March 1, 2019 upon exercise of options, warrants and convertible securities. Each beneficial owner's percentage ownership is determined by assuming that options, warrants and convertible securities that are held by such person (but not those held by any other person) and that are exercisable within such 60 days from such date have been exercised. The information set forth below is based upon information obtained from the beneficial owners, upon information in our possession regarding their respective holdings and upon information filed by the holders with the Commission. The percentages of beneficial ownership are based on 148,382,299 shares of our common stock outstanding as of March 1, 2019.

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

The address for all directors and officers is c/o Protalix BioTherapeutics, Inc., 2 Snunit Street, Science Park, P.O. Box 455, Carmiel, Israel, 20100.

Name and Address of Beneficial Owner	Amount and Nature of Beneficial Ownership	Percentage of Class (%)
Board of Directors and Executive Officers		
Shlomo Yanai (1)	150,000	*
Moshe Manor (2)	1,112,500	*
Amos Bar Shalev	1,680	*
Zeev Bronfeld (3)	2,162,481	1.5
David Granot	—	—
Aharon Schwartz, Ph.D.	—	—
Einat Brill Almon, Ph.D. (4)	652,500	*
Yossi Maimon (5)	662,500	*
Yaron Naos (6)	439,563	*
Yoseph Shaaltiel, Ph.D. (7)	1,303,416	*
All executive officers and directors as a group (10 persons) (8)	6,484,640	4.3
5% Holders		
Citigroup Global Markets Inc. (9)	9,214,117	5.8
Highbridge Capital Management LLC (10)	16,468,605	9.99
UBS O'Connor LLC (11)	9,411,764	6.0

\* less than 1%.

(1) Consists of 150,000 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2019.

(2) Consists of 50,000 outstanding shares of our common stock and 1,062,500 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2019. Does not include 1,137,500 shares of our common stock underlying options that will not vest within 60 days of March 1, 2019.

(3) Consists of shares of our common stock held by EBC Holdings Ltd., an investment company wholly-owned by Mr. Bronfeld.

(4) Consists of 185,000 outstanding shares of our common stock and 467,500 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2019. Does not include 612,500 shares of our common stock underlying options that will not vest within 60 days of March 1, 2019.

(5) Consists of 195,000 outstanding shares of our common stock and 467,500 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2019. Does not include 612,500 shares of our common stock underlying options that will not vest within 60 days of March 1, 2019.

(6) Consists of 199,563 outstanding shares of our common stock held and 240,000 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2019. Does not include 525,000 shares of our common stock underlying options that will not vest within 60 days of March 1, 2019.

(7) Consists of 795,916 outstanding shares of our common stock and 507,500 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2019. Does not include 612,500 shares of our common stock underlying options that will not vest within 60 days of March 1, 2019.

(8) Consists of 3,589,640 outstanding shares of our common stock and 2,895,000 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2019. Does not include 3,500,000 shares of our common stock underlying options that will not vest within 60 days of March 1, 2019.

(9) Based solely on a Schedule 13G/A on February 8, 2019 for December 31, 2018 by Citigroup Global Markets Inc., Citigroup Financial Products Inc., Citigroup Global Markets Holdings Inc. and Citigroup Inc., or collectively, Citigroup, and on a Schedule 13F-HR filed by Citigroup Inc. on February 12, 2019 for December 31, 2018. Consists of 9,214,177 shares of our common stock issuable upon conversion of a convertible note. The address for Citigroup is 388 Greenwich Street, New York, NY 10013.

(10) The principal business office of Highbridge Capital Management LLC, or Highbridge is 40 West 57th Street, 32nd Floor, New York, New York 10019. Holdings are based on a Form 13F-HR filed by Highbridge on

February 14, 2019 for December 31, 2018. Consists of 16,468,605 shares of common stock issuable upon conversion of convertible notes held by funds managed by Highbridge. Each such note is subject to a blocker provision of such notes pursuant to which the holder of each such note does not have the right to convert the note to the extent that such conversion would result in beneficial ownership by the holder thereof, together with any persons whose beneficial ownership of the common stock would be aggregated with such holder's for purposes of Section 13(d) or Section 16 of the Exchange Act, for more than 9.99% of the common stock, and, accordingly, the disclosed amounts do not include shares that exceed the blocker provision.

The address of UBS O'Connor LLC, or UBS O'Connor, is One North Wacker Drive, ~~32~~<sup>31</sup> Floor, Chicago, Illinois 60606. Based solely on a Schedule 13G/A filed on February 12, 2019 for December 31, 2018 by UBS O'Connor, Kevin Russell, or Mr. Russell, and Andrew Martin, or Mr. Martin and on a Schedule 13F-HR filed by UBS O'Connor on February 15, 2019 for December 31, 2018. UBS O'Connor serves as the investment manager to Nineteen77 Global Multi-Strategy Alpha Master Limited, or GLEA. In such capacity, UBS O'Connor exercises (11) voting and investment power over the shares of common stock held for the account of GLEA. Mr. Russell is the Chief Investment Officer of UBS O'Connor and Mr. Martin is a Portfolio Manager for O'Connor, and each also exercises voting and investment power over the shares of common stock held for the account of GLEA. As a result, each of UBS O'Connor, Mr. Russell and Mr. Martin may be deemed to have beneficial ownership of the shares of common stock held for the account of GLEA. Includes 9,411,764 shares of common stock issuable upon conversion of a convertible note held by GLEA.

### Equity Compensation Plan Information

The following table provides information as of December 31, 2018 with respect to the shares of our common stock that may be issued under our existing equity compensation plan.

Plan Category	A Number of Securities to be Issued Upon Exercise of Outstanding Options	B Weighted Average Exercise Price of Outstanding Options	C Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column A)
Equity Compensation Plans Approved by Stockholders	10,150,675	1.57	7,303,119
Equity Compensation Plans Not Approved by Stockholders	-	-	-
Total	10,150,675	1.57	7,303,119

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

#### Certain Relationships and Related Transactions

All related party transactions are reviewed and approved by the Audit Committee, as required by the Audit Committee Charter.

#### Family Relationships

There are no family relationships among directors or executive officers of our Company.

#### Corporate Governance and Independent Directors

In compliance with the listing requirements of the NYSE American, we have a comprehensive plan of corporate governance for the purpose of defining responsibilities, setting high standards of professional and personal conduct and assuring compliance with such responsibilities and standards. We currently regularly monitor developments in the area of corporate governance to ensure we are in compliance with the standards and regulations required by the NYSE American. A summary of our corporate governance measures follows.

### **Independent Directors**

We believe a majority of the members of our Board of Directors are independent from management. When making determinations from time to time regarding independence, the Board of Directors will reference the listing standards adopted by the NYSE American as well as the independence standards set forth in the Sarbanes-Oxley Act of 2002, or the SOX, and the rules and regulations promulgated by the Commission under that Act. We anticipate our Board of Directors will analyze whether a director is independent by evaluating, among other factors, the following:

Whether the member of the Board of Directors has any material relationship with us, either directly, or as a partner, stockholder or officer of an organization that has a relationship with us;

Whether the member of the Board of Directors is a current employee of our Company or any of our subsidiaries, or was an employee of our Company or any of our subsidiaries within three years preceding the date of determination;

Whether the member of the Board of Directors is, or in the three years preceding the date of determination has been, affiliated with or employed by (i) a present internal or external auditor of our Company or any affiliate of such auditor or (ii) any former internal or external auditor of our Company or any affiliate of such auditor, which performed services for us within three years preceding the date of determination;



Whether the member of the Board of Directors is, or in the three years preceding the date of determination has been, part of an interlocking directorate, in which any of our executive officers serve on the Compensation Committee of another company that concurrently employs the member as an executive officer;

Whether the member of the Board of Directors receives any compensation from us, other than fees or compensation for service as a member of the Board of Directors and any committee of the Board of Directors and reimbursement for reasonable expenses incurred in connection with such service and for reasonable educational expenses associated with Board of Directors or committee membership matters;

Whether an immediate family member of the member of the Board of Directors is a current executive officer of our Company or was an executive officer of our Company within three years preceding the date of determination;

Whether an immediate family member of the member of the Board of Directors is, or in the three years preceding the date of determination has been, affiliated with or employed in a professional capacity by (i) a present internal or external auditor of ours or any of our affiliates or (ii) any former internal or external auditor of our Company or any affiliate of ours which performed services for us within three years preceding the date of determination; and

Whether an immediate family member of the member of the Board of Directors is, or in the three years preceding the date of determination has been, part of an interlocking directorate, in which any of our executive officers serve on the Compensation Committee of another company that concurrently employs the immediate family member of the member of the Board of Directors as an executive officer.

The above list is not exhaustive and we anticipate that the Audit Committee will consider all other factors which could assist it in its determination that a director will have no material relationship with us that could compromise that director's independence.

Under these standards, our Board of Directors has determined that Mr. Bar Shalev, Mr. Bronfeld, Dr. Schwartz and Mr. Granot are considered "independent" pursuant to the rules of the NYSE American and Section 10A(m)(3) of the Exchange Act. In addition, our Board of Directors has determined that these directors are able to read and understand fundamental financial statements and have substantial business experience that results in their financial sophistication, qualifying them for membership on our audit committee. Our Board of Directors has also determined that Mr. Yanai, Mr. Bar Shalev, Mr. Bronfeld, Mr. Granot and Dr. Schwartz are "independent" pursuant to the rules of the NYSE American.

The position of chairman of the board is not held by our chief executive officer at this time. The Board of Directors does not have a policy mandating the separation of these functions. We believe it is in our best interest that Mr. Yanai serve as the chairman of our board. This decision was based on Mr. Yanai's vast global operating experience in the life-science and pharmaceutical and agro-chemicals industry as well as the global perspective he brings to our Board

of Directors, incorporating his industry and board leadership experience and his distinguished military service. Our non-management directors hold formal meetings, separate from management, at least twice per year.

## The Board's Role in Risk Oversight

Our Board of Directors oversees an enterprise-wide approach to risk management, designed to support the achievement of business objectives, including organizational and strategic objectives, to improve long-term organizational performance and enhance stockholder value. The involvement of our Board of Directors in setting our business strategy is a key part of its assessment of management's plans for risk management and its determination of what constitutes an appropriate level of risk for the Company. The participation of our Board of Directors in our risk oversight process includes receiving regular reports from members of senior management on areas of material risk to our Company, including operational, financial, legal and regulatory, and strategic and reputational risks. While the full board has the ultimate oversight responsibility for the risk management process, various committees of the board also have responsibility for risk management. For example, financial risks, including internal controls, are overseen by the audit committee and risks that may be implicated by our executive compensation programs are overseen by the compensation committee. Upon identification of a risk, the assigned board committee or our full Board of Directors discuss or review risk management and risk mitigation strategies. Additional review or reporting on enterprise risks is conducted as needed or as requested by our Board of Directors or a committee thereof.

## Item 14. Principal Accountant Fees and Services

The following table sets forth fees billed to us by our independent registered public accounting firm during the fiscal years ended December 31, 2018 and 2017 for: (i) services rendered for the audit of our annual financial statements and the review of our quarterly financial statements; (ii) services by our independent registered public accounting firm that are reasonably related to the performance of the audit or review of our financial statements and that are not reported as Audit Fees; (iii) services rendered in connection with tax compliance, tax advice and tax planning; and (iv) all other fees for services rendered.

	Year Ended December 31,	
	2018	2017
Audit Fees	\$207,343	\$231,000
Audit Related Fees	\$	\$25,300
Tax Fees	\$37,463	\$33,179
All Other Fees	\$-	\$-

## Policy on Audit Committee Pre-Approval of Audit and Permissible Non-Audit Services of Independent Auditors

Our Audit Committee has the sole authority to approve the scope of the audit and any audit-related services, as well as all audit fees and terms. The Audit Committee must pre-approve any audit and non-audit services provided by our independent registered public accounting firm. The Audit Committee will not approve the engagement of the independent registered public accounting firm to perform any services that the independent registered public accounting firm would be prohibited from providing under applicable laws, rules and regulations, including those of self-regulating organizations. The Audit Committee will approve permitted non-audit services by our independent registered public accounting firm only if it determines that using a different firm to perform such services will be more effective or economical. The Audit Committee annually reviews and pre-approves the statutory audit fees that can be provided by the independent registered public accounting firm.

**PART IV****Item 15. Exhibits and Financial Statement Schedules**

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

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

	<b>Page</b>
<u>Report of Independent Registered Public Accounting Firm</u>	<u>F-2</u>
<u>Consolidated Balance Sheets as of December 31, 2017 and 2018</u>	<u>F-4</u>
<u>Consolidated Statements of Operations for the years ended December 31, 2016, 2017 and 2018</u>	<u>F-5</u>
<u>Consolidated Statements of Changes in Capital Deficiency for the years ended December 31, 2016, 2017 and 2018</u>	<u>F-6</u>
<u>Consolidated Statements of Cash Flows for the years ended December 31, 2016, 2017 and 2018</u>	<u>F-7</u>
<u>Notes to Consolidated Financial Statements</u>	<u>F-9</u>

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

3. *Exhibits.*

<b>Exhibit Number</b>	<b>Exhibit Description</b>	<b>Incorporated by Reference</b>				<b>Filed Herewith</b>
		<b>Form</b>	<b>File Number</b>	<b>Exhibit</b>	<b>Date</b>	
<u>3.1</u>	<u>Certificate of Incorporation of the Company</u>	<u>8-K</u>	<u>333-48677</u>	<u>3.1</u>	<u>April 1, 2016</u>	
<u>3.2</u>	<u>Amendment to Certificate of Incorporation of the Company</u>	<u>Def 14A</u>	<u>001-33357</u>	<u>Appen. A</u>	<u>July 1, 2016</u>	
<u>3.3</u>	<u>Second Amendment to Certificate of Incorporation of the Company</u>	<u>Def 14A</u>	<u>001-33357</u>	<u>Appen. A</u>	<u>October 17, 2018</u>	
<u>3.4</u>	<u>Bylaws of the Company</u>	<u>8-K</u>	<u>001-33357</u>	<u>3.2</u>		

					<u>April 1, 2016</u>
<u>4.1</u>	<u>Form of Restricted Stock Agreement/Notice</u>	<u>8-K</u>	<u>001-33357</u>	<u>4.1</u>	<u>July 18, 2012</u> -
<u>4.2</u>	<u>Indenture, dated as of December 7, 2016, between Protalix BioTherapeutics, Inc. the guarantors party thereto, The Bank of New York Mellon Trust Company, N.A., as trustee and Wilmington Savings Fund Society, FSB, as collateral agent</u>	<u>8-K</u>	<u>001-33357</u>	<u>4.1</u>	<u>December 7, 2016</u>
<u>4.3</u>	<u>Form of 7.50% Convertible Note due 2018 (Issued in Financing)</u>	<u>8-K</u>	<u>001-33357</u>	<u>4.2</u>	<u>December 7, 2016</u>
<u>4.4</u>	<u>Form of 7.50% Convertible Note due 2018 (Issued in Exchange)</u>	<u>8-K</u>	<u>001-33357</u>	<u>4.3</u>	<u>December 7, 2016</u>

<u>4.5</u>	<u>First Supplemental to Indenture, dated as of July 24, 2017, by and among Protalix BioTherapeutics, Inc., the guarantors party thereto, The Bank of New York Mellon Trust Company, N.A., as trustee, and Wilmington Savings Fund Society, FSB, as collateral agent</u>	<u>8-K</u>	<u>001-33357</u>	<u>4.2</u>	<u>July 25, 2017</u>
<u>4.6</u>	<u>Second Supplemental Indenture, dated as of November 27, 2017, by and among Protalix BioTherapeutics, Inc., the guarantors party hereto and The Bank of New York Mellon Trust Company, N.A., as trustee, registrar, paying agent and conversion agent</u>	<u>8-K</u>	<u>001-33357</u>	<u>4.1</u>	<u>December 1, 2017</u>
<u>10.1</u>	<u>2006 Stock Incentive Plan, as amended</u>	<u>Def 14A</u>	<u>001-33357</u>	<u>Appen. B</u>	<u>March 6, 2018</u>
<u>10.2</u>	<u>Employment Agreement between Protalix Ltd. and Yoseph Shaaltiel, dated as of September 1, 2004</u>	<u>8-K</u>	<u>001-33357</u>	<u>10.2</u>	<u>January 8, 2007</u>
<u>10.3</u>	<u>Employment Agreement between Protalix Ltd. and Einat Almon, dated as of December 19, 2004</u>	<u>8-K</u>	<u>001-33357</u>	<u>10.3</u>	<u>January 8, 2007</u>
<u>10.4</u>	<u>Employment Agreement between Protalix Ltd. and Yossi Maimon, dated as of October 15, 2006</u>	<u>8-K</u>	<u>001-33357</u>	<u>10.5</u>	<u>January 8, 2007</u>
<u>10.5</u>	<u>Lease Agreement between Protalix Ltd. and Angel Science Park (99) Ltd., dated as of October 28, 2003 as amended on April 18, 2005</u>	<u>8-K</u>	<u>001-33357</u>	<u>10.9</u>	<u>January 8, 2007</u>
<u>10.6</u>	<u>Unprotected Lease Agreement</u>	<u>10-K</u>	<u>001-33357</u>	<u>10.21</u>	<u>March 17, 2008</u>
<u>10.7†</u>	<u>Amended and Restated Agreement between Protalix Ltd. and Comercio e Serviços Ltda, dated June 17, 2013</u>	<u>10-Q</u>	<u>001-33357</u>	<u>10.1</u>	<u>May 8, 2014</u>
<u>10.8†</u>	<u>Technology Transfer and Supply Agreement made as of June 18, 2013 by and between Protalix Ltd. and Fundação Oswaldo Cruz</u>	<u>10-Q</u>	<u>001-33357</u>	<u>10.3</u>	<u>May 8, 2014</u>
<u>10.9</u>	<u>Employment Agreement with Moshe Manor dated September 28, 2014</u>	<u>8-K</u>	<u>001-33357</u>	<u>10.1</u>	<u>September 29, 2014</u>
<u>10.10†</u>	<u>Amended and Restated Exclusive License and Supply Agreement by and between Pfizer Inc. and Protalix Ltd., dated October 12, 2015</u>	<u>10-Q/A</u>	<u>001-33357</u>	<u>10.1</u>	<u>December 11, 2015</u>

<u>10.11</u>	<u>Form of Note Purchase Agreement, dated of December 1, 2016 among Protalix BioTherapeutics, Inc. and the Purchasers</u>	8-K	<u>001-33357</u>	<u>10.1</u>	<u>December 7, 2016</u>	
<u>10.12</u>	<u>Form of Exchange Agreement, dated of December 1, 2016 among Protalix BioTherapeutics, Inc. and the Existing Holders</u>	8-K	<u>001-33357</u>	<u>10.2</u>	<u>December 7, 2016</u>	
<u>10.13</u>	<u>Form of U.S. Security Agreement, dated of December 7, 2016 among Protalix BioTherapeutics, Inc., the guarantors party thereto and Wilmington Savings Fund Society, FSB, as collateral agent</u>	8-K	<u>001-33357</u>	<u>10.3</u>	<u>December 7, 2016</u>	
<u>10.14</u>	<u>Form of Security Agreement/Debenture, dated of December 7, 2016 between Protalix BioTherapeutics, Inc. and Altshuler Shaham Trusts Ltd., as security trustee</u>	8-K	<u>001-33357</u>	<u>10.4</u>	<u>December 7, 2016</u>	
<u>10.15</u> †	<u>Exclusive License and Supply Agreement dated as of October 17, 2017, made by and between Protalix Ltd. and Chiesi Farmaceutici S.p.A.</u>	10-K	<u>001-33357</u>	<u>10.16</u>	<u>March 6, 2018</u>	
<u>10.16</u> †	<u>Exclusive U.S. License and Supply Agreement dated as of July 23, 2018, made by and between Protalix Ltd. and Chiesi Farmaceutici S.p.A.</u>	10-Q	<u>001-33357</u>	<u>10.1</u>	<u>November 7, 2018</u>	
<u>21.1</u>	<u>Subsidiaries</u>	10-K	<u>001-33357</u>	<u>21.1</u>	<u>February 26, 2010</u>	
<u>23.1</u>	<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>					X
<u>31.1</u>	<u>Certification of Chief Executive Officer pursuant to Rule 13a-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</u>					X
<u>31.2</u>	<u>Certification of Chief Financial Officer pursuant to Rule 13a-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</u>					X
<u>32.1</u>	<u>18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Certification of Chief Executive Officer</u>					X
<u>32.2</u>	<u>18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Certification of Chief Financial Officer</u>					X



101.INS	XBRL INSTANCE FILE	X
101.SCH	XBRL SCHEMA FILE	X
101.CAL	XBRL CALCULATION FILE	X
101.DEF	XBRL DEFINITION FILE	X
101.LAB	XBRL LABEL FILE	X
101.PRE	XBRL PRESENTATION FILE	X

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

**Item 16. Form 10-K Summary**

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, as of March 18, 2019.

PROTALIX  
BIOTHERAPEUTICS,  
INC.

By: /s/ Moshe Manor  
Moshe Manor

POWER OF ATTORNEY

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

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

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ Moshe Manor Moshe Manor	President, Chief Executive Officer (Principal Executive Officer) and Director	March 18, 2019
/s/ Yossi Maimon Yossi Maimon	Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer)	March 18, 2019

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

/s/ Shlomo Yanai Shlomo Yanai	Chairman of the Board	March 18, 2019
/s/ Amos Bar Shalev Amos Bar Shalev	Director	March 18, 2019
/s/ Zeev Bronfeld Zeev Bronfeld	Director	March 18, 2019
/s/ David Granot David Granot	Director	March 18, 2019
/s/ Aharon Schwartz Aharon Schwartz, Ph.D.	Director	March 18, 2019

**PROTALIX BIOTHERAPEUTICS, INC.**

**CONSOLIDATED FINANCIAL STATEMENTS**

TABLE OF CONTENTS

	<b>Page</b>
<b><u>REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM</u></b>	<b><u>F-2</u></b>
<b><u>CONSOLIDATED FINANCIAL STATEMENTS</u></b>	
<u>Consolidated Balance Sheets as of December 31, 2017 and 2018</u>	<u>F-4</u>
<u>Consolidated Statements of Operations for the years ended December 31, 2016, 2017 and 2018</u>	<u>F-5</u>
<u>Consolidated Statements of Changes in Capital Deficiency for the years ended December 31, 2016, 2017 and 2018</u>	<u>F-6</u>
<u>Consolidated Statements of Cash Flows for the years ended December 31, 2016, 2017 and 2018</u>	<u>F-7</u>
<u>Notes to Consolidated Financial Statements</u>	<u>F-9</u>

## **REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the board of directors and stockholders of

**Protalix Biotherapeutics, Inc.**

### *Opinions on the Financial Statements and Internal Control over Financial Reporting*

We have audited the accompanying consolidated balance sheets of Protalix BioTherapeutics, Inc. and its subsidiaries (the “Company”) as of December 31, 2018 and 2017, and the related consolidated statements of operations, changes in capital deficiency and cash flows for each of the three years in the period ended December 31, 2018 including the related notes (collectively referred to as the “consolidated financial statements”). We also have audited the Company’s internal control over financial reporting as of December 31, 2018 based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017 and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company did not maintain, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO because a material weakness in internal control over financial reporting existed as of that date related to accounting for revenue recognition in complex agreements.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis. The material weakness referred to above is described in the accompanying Management’s Annual Report on Internal Control over Financial Reporting appearing under Item 9A. We considered this material weakness in determining the nature, timing, and extent of audit tests applied in our audit of the 2018 consolidated financial statements, and our opinion regarding the effectiveness of the Company’s internal control over financial reporting does not affect our opinion on those consolidated financial statements.

***Basis for Opinions***

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

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

Kesselman & Kesselman, Trade Tower, 25 Hamered Street, Tel-Aviv 6812508, Israel, P.O Box 5005 Tel-Aviv 6150001 Telephone: +972 -3- 7954555, Fax:+972 -3- 7954556, [www.pwc.co.il](http://www.pwc.co.il)

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

***Definition and Limitations of Internal Control over Financial Reporting***

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

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

**/S/ Kesselman & Kesselman**  
**Certified Public Accountants (Isr.)**

**A member of PricewaterhouseCoopers International Limited**

Tel Aviv, Israel

March 14, 2019

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

Kesselman & Kesselman, Trade Tower, 25 Hamered Street, Tel-Aviv 6812508, Israel, P.O Box 5005 Tel-Aviv 6150001 Telephone: +972 -3- 7954555, Fax:+972 -3- 7954556, [www.pwc.co.il](http://www.pwc.co.il)

F-3



**PROTALIX BIOTHERAPEUTICS, INC.**  
**CONSOLIDATED BALANCE SHEETS**

(U.S. dollars in thousands, except share and per share amounts)

	December 31,	
	2017	2018
<b>ASSETS</b>		
<b>CURRENT ASSETS:</b>		
Cash and cash equivalents	\$51,163	\$37,808
Accounts receivable – Trade	1,721	4,729
Other assets	1,934	1,877
Inventories	7,833	8,569
Total current assets	62,651	52,983
<b>NON-CURRENT ASSETS:</b>		
Funds in respect of employee right upon retirement	1,887	1,758
Property and equipment, net	7,676	6,390
Total assets	\$72,214	\$61,131
<b>LIABILITIES NET OF CAPITAL DEFICIENCY</b>		
<b>CURRENT LIABILITIES:</b>		
Accounts payable and accruals:		
Trade	\$7,521	\$5,211
Other	9,310	10,274
Contracts liability		9,868
Convertible notes	5,921	
Total current liabilities	22,752	25,353
<b>LONG TERM LIABILITIES:</b>		
Convertible notes	46,267	47,966
Contracts liability	25,015	33,027
Liability for employee rights upon retirement	2,586	2,374
Other long term liabilities	5,051	5,292
Total long term liabilities	78,919	88,659
Total liabilities	101,671	114,012
<b>COMMITMENTS (Note 6)</b>		
<b>CAPITAL DEFICIENCY:</b>		
Common Stock, \$0.001 par value: Authorized - as of December 31, 2017 and 2018, 250,000,000 shares; issued and outstanding, respectively - as of December 31, 2017 and 2018, 143,728,797 shares and 148,382,299 shares, respectively	144	148
Additional paid-in capital	266,495	269,524

Accumulated deficit	(296,096)	(322,553)
Total capital deficiency	(29,457 )	(52,881 )
Total liabilities net of capital deficiency	\$72,214	\$61,131

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

F-4

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

	Year ended December 31,		
	2016	2017	2018
REVENUES FROM SELLING GOODS	\$9,199	\$19,242	\$8,978
REVENUES FROM LICENSE AND R&D SERVICES		1,836	25,262
COST OF GOODS SOLD	(8,398)	(15,231)	(9,302)
RESEARCH AND DEVELOPMENT EXPENSES	(30,412)	(32,170)	(35,534)
Less – grants	5,804	3,336	2,204
RESEARCH AND DEVELOPMENT EXPENSES, NET	(24,608)	(28,834)	(33,330)
<b>SELLING, GENERAL AND ADMINISTRATIVE EXPENSES</b>	(9,356)	(11,530)	(10,916)
OPERATING LOSS	(33,163)	(34,517)	(19,308)
FINANCIAL EXPENSES	(4,192)	(9,725)	(7,685)
FINANCIAL INCOME	589	188	536
LOSS FROM CHANGE IN FAIR VALUE OF CONVERTIBLE NOTES EMBEDDED DERIVATIVE	(6,473)	(38,061)	
(LOSS) GAIN ON EXTINGUISHMENT OF CONVERTIBLE NOTES	14,063	(1,325)	
FINANCIAL (EXPENSES) INCOME – NET	3,987	(48,923)	(7,149)
LOSS FROM CONTINUING OPERATIONS	(29,176)	(83,440)	(26,457)
LOSS FROM DISCONTINUED OPERATIONS	(189)		
NET LOSS FOR THE YEAR	\$(29,365)	\$(83,440)	\$(26,457)
Net loss per share of common stock – basic and diluted			
Loss from continuing operations	\$(0.29)	\$(0.64)	\$(0.18)
Loss from discontinued operations	(0.00)		
Net loss per share of common stock	\$(0.29)	\$(0.64)	\$(0.18)
Weighted average number of shares of common stock used in computing loss per share of common stock, basic and diluted	101,387,704	131,085,958	147,135,182

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

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

	Common Stock Number of shares	Common Stock Amount	Additional paid-in Stock Capital	Accumulated deficit	Total
Balance at January 1, 2016	99,800,397	100	194,064	(183,291 )	10,873
Changes during 2016:					
Issuance of common stock, net of issuance cost	23,846,735	24	6,824		6,848
Equity component of convertible notes			685		685
Share-based compensation related to stock options			920		920
Share-based compensation related to restricted stock award	7,843	*	68		68
Exercise of options granted to employee (including net exercise)	479,110	*	14		14
Net loss from continuing operations				(29,176 )	(29,176)
Net loss from discontinued operations				(189 )	(189 )
Balance at December 31, 2016	124,134,085	124	202,575	(212,656 )	(9,957 )
Changes during 2017:					
Share-based compensation related to stock options			337		337
Reclassification of embedded derivative			43,634		43,634
Convertible note conversions	19,594,712	20	18,634		18,654
Equity component of convertible notes			1,315		1,315
Net loss				(83,440 )	(83,440)
Balance at December 31, 2017	143,728,797	144	266,495	(296,096 )	(29,457)
Changes during 2018:					
Share-based compensation related to stock options			498		498
Share-based compensation related to restricted stock award	29,898	*	16		16
Convertible notes conversions	2,009,968	2	1,367		1,369
Convertible notes payment	2,613,636	2	1,148		1,150
Net loss				(26,457 )	(26,457)
Balance at December 31, 2018	148,382,299	148	269,524	(322,553 )	(52,881)

\* Represents an amount of less than \$1 thousand.

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

F-6

**PROTALIX BIOTHERAPEUTICS, INC.****CONSOLIDATED STATEMENTS OF CASH FLOWS**

(U.S. dollars in thousands)

	Year ended December 31,		
	2016	2017	2018
<b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>			
Net loss	\$(29,365)	\$(83,440)	\$(26,457)
Loss from discontinued operations	(189 )		
Loss from continuing operations	(29,176)	(83,440)	(26,457)
Adjustments required to reconcile net loss to net cash used in operating activities:			
Share based compensation	988	337	514
Depreciation	1,983	1,920	1,671
Financial expenses (income), net (mainly exchange differences)	13	(40 )	20
Changes in accrued liability for employee rights upon retirement	10	(18 )	(18 )
(Gain) loss on amounts funded in respect of employee rights upon retirement	7	(21 )	(46 )
Loss (gain) on sale of fixed assets	(7 )	6	
Loss (gain) on extinguishment of convertible notes	(14,063)	1,325	
Net loss (income) in connection with convertible notes		(116 )	213
Change in fair value of convertible notes embedded derivative	6,473	38,061	
Amortization of debt issuance costs and debt discount	568	2,334	2,602
Issuance of shares for interest payment in connection with conversions of convertible notes		2,391	234
Changes in operating assets and liabilities:			
Increase (decrease) in contract liability (including non-current portion)	(411 )	24,178	17,880
(Increase) decrease in accounts receivable and other assets	(1,133 )	25	(3,099 )
Decrease (increase) in inventories	522	(2,588 )	(736 )
Increase (decrease) in accounts payable and accruals	2,139	4,902	(761 )
Increase in other long term liabilities		750	241
Net cash used in continuing operations	(32,087)	(9,994 )	(7,742 )
Net cash used in discontinued operations	(11 )		
Net cash used in operating activities	\$(32,098)	\$(9,994 )	\$(7,742 )
<b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>			
Purchase of property and equipment	\$(849 )	\$(971 )	\$(686 )
Proceeds from sale of property and equipment	20	3	
(Increase) decrease in restricted deposit	(106 )	(146 )	62
Amounts funded in respect of employee rights upon retirement, net	(32 )	(5 )	33
Net cash used in investing activities	\$(967 )	\$(1,119 )	\$(591 )
<b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>			
Net payment for convertible notes		(10,961)	(4,752 )
Net proceeds from issuance of convertible notes	19,681	9,542	

Edgar Filing: Protalix BioTherapeutics, Inc. - Form 10-K

Exercise of options	14		
Net cash (used in) provided by financing activities	\$19,695	\$(1,419 )	\$(4,752 )
EFFECT OF EXCHANGE RATE CHANGES ON CASH AND CASH EQUIVALENTS	277	414	(270 )
NET DECREASE IN CASH AND CASH EQUIVALENTS	(13,093)	(12,118)	(13,355)
BALANCE OF CASH AND CASH EQUIVALENTS AT BEGINNING OF YEAR	76,374	63,281	51,163
BALANCE OF CASH AND CASH EQUIVALENTS AT END OF YEAR	\$63,281	\$51,163	\$37,808

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

F-7

**PROTALIX BIOTHERAPEUTICS, INC.**

**CONSOLIDATED STATEMENTS OF CASH FLOWS**

(U.S. dollars in thousands)

(CONTINUED)

	Year ended December 31,		
	2016	2017	2018
<b>SUPPLEMENTARY INFORMATION ON INVESTING AND FINANCING ACTIVITIES NOT INVOLVING CASH FLOWS:</b>			
Purchase of property and equipment	\$595	\$526	\$225
Issuance of common stock, net of issuance cost	\$6,848		
Convertible note conversions		\$16,263	\$2,285
As to extinguishment of convertible notes, see note 8.			
<b>SUPPLEMENTARY DISCLOSURE ON CASH FLOWS</b>			
Interest paid	\$3,659	\$4,854	\$4,585

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



**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**NOTE 1 - SIGNIFICANT ACCOUNTING POLICIES**

**a. General**

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

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

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

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

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

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

On October 19, 2017, Protalix Ltd. and Chiesi Farmaceutici S.p.A. (“Chiesi”) entered into an Exclusive License and Supply Agreement (the “Chiesi Ex-U.S. Agreement”) pursuant to which Chiesi was granted an exclusive license for all markets outside of the United States to commercialize pegunigalsidase alfa. On July 23, 2018, Protalix Ltd. entered into an Exclusive License and Supply Agreement with Chiesi (the “Chiesi U.S. Agreement”), with respect to the commercialization of pegunigalsidase alfa in the United States.

Under each of the Chiesi Ex-U.S. Agreement and the Chiesi U.S. Agreement, Chiesi made an upfront payment to Protalix Ltd. of \$25.0 million in connection with the execution of the agreement. In addition, under the Chiesi Ex-U.S. Agreement, Protalix Ltd. is entitled to additional payments of up to \$25.0 million in pegunigalsidase alfa development costs, capped at \$10.0 million per year and to receive additional payments of up to \$320.0 million, in the aggregate, in regulatory and commercial milestone payments. Under the Chiesi U.S. Agreement, Protalix Ltd. is entitled to payments of up to a maximum of \$20.0 million to cover development costs for pegunigalsidase alfa, subject to a maximum of \$7.5 million per year, and to receive an additional up to a maximum of \$760.0 million, in the aggregate, in regulatory and commercial milestone payments.

Under the terms of both of the Chiesi agreements, Protalix Ltd. will manufacture all of the pegunigalsidase alfa needed under the agreements, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Under the Chiesi Ex-U.S. Agreement, Chiesi is required to make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales outside of the United States, as consideration for product supply. Under the Chiesi U.S. Agreement, Chiesi is required to make tiered payments of 15% to 40% of its net sales, depending on the amount of annual sales in the United States, as consideration for product supply.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

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

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

In 2017, the Company received a purchase order from the Brazilian MoH for the purchase of alfataliglicerase for the treatment of Gaucher patients in Brazil for consideration of approximately \$24.3 million. Shipments started in June 2017. The Company recorded revenues of \$7.1 million and \$3.7 million for sales of alfataliglicerase to Fiocruz in 2017 and 2018, respectively.

Based on its current cash resources and commitments, the Company believes it will be able to maintain its current planned development activities and the corresponding level of expenditures for at least 12 months from the date of approval of the financial statements as of December 31, 2018, although no assurance can be given that it will not need additional funds prior to such time. If there are unexpected increases in general and administrative expenses or research and development expenses, the Company may need to seek additional financing.

*Revision of Prior Year Financial Information*

The Company has identified an error in the recognized revenue for the last quarter of 2017 and accordingly has revised certain items in its consolidated financial statements for December 31, 2017 presented herein. The impact of the revision on the balance sheet as of December 31, 2017 was a decrease in Contracts Liability and in Accumulated Losses by \$1.8 million and the impact on the statements of operations for the year then ended was an increase in Revenues and a correspondent decrease in the Loss for the year by the same amount. Loss per share was reduced by \$0.01 as a result of the revision. The Company evaluated the materiality of the error from quantitative and qualitative perspectives, and concluded that the error was immaterial to the Company's prior annual consolidated financial statements. Since the revision was not material to any prior interim period or annual consolidated financial statements, no amendments to previously filed interim or annual periodic reports was required. Consequently, the Company revised the historical consolidated financial information presented herein.

**b. Basis of presentation**

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

**c. Use of estimates in the preparation of financial statements**

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

**d. Functional currency**

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

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

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

**e. Cash equivalents**

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

**f. Inventories**

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

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

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

**g. Property and equipment**

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

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

	<b>Years</b>
Laboratory equipment	5
Furniture	10-15
Computer equipment	3

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

**h. Impairment in value of long-lived assets**

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

**i. Income taxes**

1. Deferred income taxes

Deferred taxes are determined utilizing the assets and liabilities method based on the estimated future tax effects of the differences between the financial accounting and tax bases of assets and liabilities under the applicable tax laws. Deferred tax balances are computed using the tax rates expected to be in effect when those differences reverse. A valuation allowance in respect of deferred tax assets is provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has provided a full valuation allowance with respect to its deferred tax assets. The Company used tax rates of 27%, 23% and 21%. See note 10.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

2. Uncertainty in income taxes

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

**j. Revenue Recognition**

On January 1, 2018, the Company adopted the new accounting standard, ASC 606, Revenue from Contracts with Customers ("ASC 606"), and all the related amendments, using the modified retrospective method. The implementation of this Accounting Standards Update (ASU) did not have a material impact on the Company's consolidated financial statement.

*The Company's revenue recognition accounting policy from January 1, 2018, following the adoption of the new revenue standard*

A contract with a customer exists only when: the parties to the contract have approved it and are committed to perform their respective obligations, the Company can identify each party's rights regarding the distinct goods or services to be transferred ("performance obligations"), the Company can determine the transaction price for the goods or services to be transferred, the contract has commercial substance and it is probable that the Company will collect the consideration to which it will be entitled in exchange for the goods or services that will be transferred to the customer.

Revenues are recorded in the amount of consideration to which the Company expects to be entitled in exchange for performance obligations upon transfer of control to the customer.

1. Revenues from selling products

The Company recognizes revenues from selling goods at a point in time when control over the product is transferred to customers (upon delivery).

## 2. Revenues from Chiesi Agreements

According to ASC 606, a performance obligation is a promise to provide a distinct good or service or a series of distinct goods or services. Goods and services that are not distinct are bundled with other goods or services in the contract until a bundle of goods or services that is distinct is created. A good or service promised to a customer is distinct if the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract.

The Company has identified two performance obligations in each of the Chiesi agreements as follows: (1) the license and research and development services and (2) a contingent performance obligation regarding future manufacturing.

The Company determined that the licenses granted to Chiesi together with the research and development services should be combined into a single performance obligation under each agreement since Chiesi cannot benefit from a license without the research and development services. The research and development services are highly specialized and are dependent on the supply of the drug.

The future manufacturing is contingent on regulatory approvals of the drug and the Company deems these services to be separately identifiable from other performance obligations in the contract. Manufacturing services post-regulatory approval are not interdependent or interrelated with the license and research and development services.

The transaction price was comprised of fixed consideration and variable consideration (capped research and development reimbursements). Under ASC 606, the consideration to which the Company would be entitled upon the achievement of contractual milestones, which are contingent upon the occurrence of future events, are a form of variable consideration. The Company estimates variable consideration using the most likely method. Amounts included in the transaction price are recognized only when it is probable that a significant reversal of cumulative revenues will not occur, usually upon achievement of a specific milestone. The Company used significant judgment when it determined variable consideration.

Since the customer benefits from the research and development services as the entity performs, revenue from granting the license and the research and development services is recognized over time using the cost-to-cost method. The Company used significant judgment when it determined the costs expected to be incurred upon satisfying the identified performance obligation.



Revenue from additional research and development services ordered by Chiesi is recognized over time using the cost-to-cost method.

We accounted for the Chiesi U.S. agreement as a modification of the Chiesi Ex-U.S. Agreement. As such, the Company recorded revenue through a cumulative catch-up adjustment in the third quarter of 2018 in the amount of \$6.2 million.

Our revenue recognition accounting policy prior to January 1, 2018, was materially the same.

#### **k. Research and development costs**

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

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

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

**l. Concentration of credit risks and trade receivable**

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

**m. Share-based compensation**

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

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

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

The Company elects to account for forfeitures as they occur.

**n. Net (loss) earnings per share**

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

Diluted LPS is calculated in continuing operations. The calculation of diluted LPS does not include 23,532,492, 76,848,199 and 74,583,792 shares of Common Stock underlying outstanding options, restricted shares of Common Stock and shares issuable upon conversion of the convertible notes for the fiscal years ended December 31, 2016, 2017 and 2018, respectively, because the effect would be anti-dilutive.

**o. Convertible notes**

All outstanding convertible notes are accounted for using the guidance set forth in the Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (ASC) 815 requiring that the Company determine whether the embedded conversion option must be separated and accounted for separately. ASC 470-20 regarding debt with conversion and other options requires the issuer of a convertible debt instrument that may be settled in cash upon conversion to separately account for the liability (debt) and equity (conversion option) components of the instrument in a manner that reflects the issuer’s nonconvertible debt borrowing rate. The Company accounted for the 2018 Notes (as defined in note 8a) as a liability, on an aggregated basis, in their entirety.

The 2021 Notes were accounted for partially as liability and equity components of the instrument and partially as a debt host contract with an embedded derivative resulting from the conversion feature. During the year ended December 31, 2017, the embedded derivative was reclassified to additional paid in capital, see note 8.

Issuance costs regarding the issuance of the 2021 Notes are amortized using the effective interest rate. The debt discount and debt issuance costs regarding the issuance of the 2018 Notes are deferred and amortized over the 2018 Notes period (5 years).

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

As of December 31, 2018, a total of \$57.9 million aggregate principal amount of the 2021 Notes were outstanding. In addition, as of December 31, 2018, none of the 2018 Notes were outstanding.

**p. Recently adopted standards**

In May 2014, the FASB issued guidance on revenues from contracts with customers that superseded most current revenue recognition guidance, including industry-specific guidance. The underlying principle is to recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which an entity expects to be entitled to in exchange for those goods or services. The guidance provides a five-step analysis of transactions to determine when and how revenue is recognized. Other major provisions require capitalization of certain contracts costs, consideration of the time value of money in the transaction price, and allowing estimates of variable consideration to be recognized before contingencies are resolved in certain circumstances. The guidance also requires enhanced disclosures regarding the nature, amount timing and uncertainty of revenues and cash flows arising from an entity's contracts with customers. On January 1, 2018, the Company adopted the new accounting standard, ASC 606, and all the related amendments, using the modified retrospective method. The implementation of this Accounting Standards Update (ASU) did not have a material impact on the Company's consolidated financial statements.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash (a Consensus of the FASB Emerging Issues Task Force) ("ASU 2016-18"), which requires entities to include amounts generally described as restricted cash and restricted cash equivalents in cash and cash equivalents when reconciling beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for annual reporting periods (including interim periods within those annual reporting periods) beginning after December 15, 2017. This standard, adopted as of January 1, 2018, had no material impact on the Company's financial statements.

In January 2016, the FASB issued ASU No. 2016-01, Financial Instruments—Overall (Subtopic 825-10), which addresses certain aspects of recognition, measurement, presentation, and disclosure of financial instruments. The amended guidance requires changes in the fair value of equity investments to be recognized through net income, rather than other comprehensive income. This standard was adopted on January 1, 2018 and its adoption had no material impact on the Company's financial statements.

**q. Recently issued accounting pronouncements**

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842), which supersedes the existing guidance for lease accounting, Leases (Topic 840). The new standard requires lessees to record assets and liabilities on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the income statement. The Company plans to adopt the standard as of January 1, 2019 on a modified retrospective basis and will not restate comparative periods. The Company will elect the package of practical expedients permitted under the transition guidance within the new standard, which among other things, allows the Company to carryforward the historical lease classification. The Company will make an accounting policy election to keep leases with an initial term of 12 months or less off of the balance sheet. The Company will recognize those lease payments in the Statements of Operations on a straight-line basis over the lease period. The Company expects that adoption of the standard will result in recognition of approximately \$5.9 million of lease assets and lease liabilities as of January 1, 2019 on the Company's balance Sheets.

In June 2018, the FASB issued ASU 2018-07, "Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-based Payment Accounting" that expands the scope of ASC Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of ASC Topic 718 to nonemployee awards except for certain exemptions specified in the amendment. The guidance is effective for fiscal years beginning after December 15, 2018, including interim reporting periods within that fiscal year. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. The Company does not expect to have a material impact on its financial statements.

**NOTE 2 - COMMERCIALIZATION AGREEMENTS**

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

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

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

Protalix also agreed to provide Pfizer with:

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

F-14

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

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

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

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

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

Revenues from the Pfizer Agreements as well as revenues from sales of Elelyso in Israel were presented as discontinued operations. The impact of the discontinued operations in the results of 2016 is immaterial.

In October 2017, Protalix Ltd. entered into the Chiesi Ex-U.S. Agreement with respect to the commercialization of pegunigalsidase alfa (hereafter – the drug) for treatment of Fabry disease. Under the terms of the Chiesi Agreement, 2. Protalix Ltd. granted to Chiesi exclusive licensing rights for the commercialization of the drug for all markets outside of the United States. At the effective date, Protalix Ltd. had maintained the exclusive commercialization rights to the drug in the United States, which rights were subsequently granted to Chiesi in July 2018.

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

The consideration consists of the following:

- a. Upfront, non-refundable payment of \$25.0 million.
- b. Additional payments of up to \$25.0 million in development costs, capped at \$10.0 million per year.
- c. Milestone payments of up to \$320.0 million with respect to certain regulatory and commercial events as defined in the Chiesi Agreement.
- d. Additional payments as consideration for the supply of the drug. The payment will vary from 15% to 35% of Chiesi's average selling price of the drug, depending on the amount of annual sales.
- e. Protalix will be the sole manufacturer of the drug.

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

In July 2018, Protalix Ltd. entered into the Chiesi U.S. Agreement with respect to the commercialization of the drug 3. for treatment of Fabry disease. Under the terms of the Chiesi U.S. Agreement, Protalix Ltd. granted to Chiesi exclusive licensing rights for the commercialization of the drug for all markets in the United States.

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



**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

The consideration consists of the following:

- a. Upfront, non-refundable payment of \$25.0 million.
- b. Additional payments of up to \$20.0 million in development costs, capped at \$7.5 million per year.
- c. Milestone payments of up to \$760.0 million with respect to certain regulatory and commercial events as defined in the Chiesi Agreement.
- d. Additional payments as consideration for the supply of the drug. The payment will vary from 15% to 40% of Chiesi's average selling price of the drug, depending on the amount of annual sales.
- e. Protalix will be the sole manufacturer of the drug.

Chiesi does not have sublicensing rights.

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

**NOTE 3 - PROPERTY AND EQUIPMENT**

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

<i>(U.S. dollars in thousands)</i>	December 31,	
	2017	2018
Laboratory equipment	\$16,561	\$16,732
Furniture and computer equipment	2,438	2,565
Leasehold improvements	16,123	16,191
Equipment under construction	19	18
	\$35,141	\$35,506
Less – accumulated depreciation and amortization	(27,465)	(29,116)
	\$7,676	\$6,390

- b. Depreciation in respect of property and equipment totaled approximately \$2.0 million, \$1.9 million and \$1.7 million for the years ended December 31, 2016, 2017 and 2018, respectively.

**NOTE 4 - INVENTORIES**

a. Inventories at December 31, 2017 and 2018 consisted of the following:

<i>(U.S. dollars in thousands)</i>	December 31,	
	2017	2018
Raw materials	\$3,838	\$3,792
Work in progress	485	
Finished goods	3,510	4,777
Total inventory	\$7,833	\$8,569

- b. During the years ended December 31, 2017 and 2018, the Company recorded approximately \$0.5 million and \$1.1 million, respectively, for write-down of inventory under cost of goods sold.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**NOTE 5 - LIABILITY FOR EMPLOYEE RIGHTS UPON RETIREMENT**

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

The liability is funded in part from the purchase of insurance policies or by the establishment of pension funds with dedicated deposits in the funds. The amounts used to fund these liabilities are included in the Company's balance sheets under "Funds in respect of employee rights upon retirement." These policies are the Company's assets. However, under labor agreements and subject to certain limitations, any policy may be transferred to the ownership of the individual employee for whose benefit the funds were deposited. In the years ended December 31, 2016, 2017 and 2018, the Company deposited approximately \$164,000, \$166,000 and \$145,000, respectively, with insurance companies in connection with its severance payment obligations.

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

The amounts of severance pay expenses were approximately \$842,000, \$906,000 and \$781,000 for each of the years ended December 31, 2016, 2017 and 2018, respectively, of which approximately \$675,000, \$746,000 and \$620,000 in the years ended December 31, 2016, 2017 and 2018, respectively, were in respect of the Contribution Plans. Gain (loss) on amounts funded in respect of employee rights upon retirement totaled approximately (\$7,000), \$21,000 and \$46,000 for the years ended December 31, 2016, 2017 and 2018, respectively.

The Company expects to contribute approximately \$748,000 in the year ending December 31, 2019 to insurance companies in connection with its severance liabilities for its operations for that year, approximately \$604,000 of

which will be contributed to one or more Contribution Plans.

During the five-year period following December 31, 2018, the Company expects to pay future benefits to three employees upon each such employee's normal retirement age. The Company anticipates that the benefits payable will be approximately \$248,000.

## **NOTE 6 - COMMITMENTS**

### **a. Royalty Commitments**

The Company is obligated to pay royalties to NATI on proceeds from the sale of products developed from research and development activities that were funded, partially, by grants from NATI or its predecessor, the Office of the <sup>1</sup>Israeli Innovation Authority (IIA). At the time the grants were received, successful development of the related projects was not assured.

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

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

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

Royalty expenses to NATI or the IIA are included in the statement of operations as a component of the cost of revenues both in continuing and discontinued operations and were approximately \$288,000, \$1,384,000 and \$1,619,000 during the years ended December 31, 2016, 2017 and 2018, respectively.

At December 31, 2017 and 2018, the maximum total royalty amount payable by the Company under these funding arrangements is approximately \$42.2 million and \$41.9 million, respectively (without interest, assuming 100% of the funds are payable).

The Company is a party to certain research and license agreements. Under the agreements, the Company is obligated to pay royalties at varying rates from its future revenues. The aggregate royalties payable under all of the agreements is equal to a varying range of percentages of net sales of licensed products. Royalty expenses under the agreements are included in the statement of operations as a component of the cost of revenues both in continuing and discontinued operations and were approximately \$286,000, \$0 and \$0 during the years ended December 31, 2016, 2017 and 2018, respectively.

Under each agreement, the Company is also obligated to pay milestone, licensing and other payments to the counterparties of the agreement. The payments under the agreements are for varying amounts and are subject to varying conditions. If all of the contingencies with respect to milestone payments under the research and license agreements are met, the aggregate milestone payments total payable would be approximately \$14.3 million and would be payable, if at all, as the Company's projects progress over the course of a number of years. Milestone payments of \$300,000, \$0 and \$0 were made during the years ended December 31, 2016, 2017 and 2018, respectively.

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

#### **b. Subcontracting Agreements**

The Company has entered into sub-contracting agreements with several clinical providers and consultants in Israel, the United States and certain other countries in connection with its primary product development process. As of December 31, 2018, total commitments under said agreements were approximately \$18.8 million.

#### **c. Lease Agreements**

The Company is a party to a number of lease agreements for its facilities, the latest of which has been extended until 2021. The Company has the option to extend certain of such agreements on two additional occasions for additional five-year periods each, for a total of 10 additional years. Under the leases, the aggregate monthly rental payments are approximately \$63,000. As of December 31, 2018, the Company provided bank guarantees of approximately \$402,000, in the aggregate, to secure the fulfillment of its obligations under the lease agreements. The future minimum lease payments required under the operating leases for such premises are approximately \$758,000, \$758,000 and \$621,000, for fiscal years 2019 through 2021, respectively. Lease expenses totaled approximately \$1.0 million, \$775,000 and 783,000 for each of the years ended December 31, 2016, 2017 and 2018, respectively.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

**d. Vehicle Lease and Maintenance Agreements**

The Company entered into several three-year lease and maintenance agreements for vehicles which are regularly amended as new vehicles are leased. The current monthly lease fees aggregate approximately \$43,000. The expected lease payments for the years ending December 31, 2019, 2020 and 2021 are approximately \$474,000, \$333,000 and \$82,000, respectively.

**NOTE 7 - SHARE CAPITAL**

**a. Rights of the Company's Common Stock**

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

**b. Stock based compensation**

On December 14, 2006, the Board of Directors adopted the Protalix BioTherapeutics, Inc. 2006 Stock Incentive Plan, as amended (the "Plan"). The Plan has since been amended to, among other things, increase the number of shares of common stock available under the Plan to 23,841,655 shares. The grant of options to Israeli employees under the Plan is subject to the terms stipulated by Sections 102 and 102A of the Israeli Income Tax Ordinance. Each option grant is subject to the track chosen by the Company, either Section 102 or Section 102A of the Israeli Income Tax Ordinance, and pursuant to the terms thereof, the Company is not allowed to claim, as an expense for tax purposes, the amounts credited to employees as a benefit, including amounts recorded as salary benefits in the Company's accounts, in respect of options granted to employees under the Plan, with the exception of the work-income benefit component, if any, determined on the grant date. For Israeli non-employees, the share option plan is subject to Section 3(i) of the Israeli Income Tax Ordinance.

As of December 31, 2018, 7,303,119 shares of Common Stock remain available for grant under the Plan.

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

From January 1, 2016 through December 31, 2018, the Company granted options and shares of restricted stock to certain employees and non-employees as follows:

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

a) Below is a table summarizing all of the options grants to employees during the year ended December 31, 2018:

<b>Year of grant</b>	No. of options granted	Exercise price	Vesting period	Fair value at grant (U.S. dollars in thousands)	Expiration period
2018	4,000,000	\$ 0.56	4 years	\$ 1,200	10 years
2018	2,360,000	\$ 0.51	4 years	\$ 700	10 years

Set forth below are grants made by the Company to employees (including related parties) during the three-year period ended December 31, 2018 (such grants appear in the table above):



**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

On September 13, 2018, the Company's compensation committee approved the grant of 10-year options to purchase, in the aggregate, 6,360,000 shares of Common Stock, of which options to purchase 4,000,000 shares of Common Stock were granted to the Company's executive officers and options to purchase 2,360,000 shares of Common Stock were granted to other employees with an exercise price equal to \$0.56 per share and \$0.51 per share, respectively, under the Plan. The options vest over a four-year period in 16 equal quarterly increments. Vesting of the options granted to the executive officers is subject to acceleration in full upon a Corporate Transaction or a Change in Control, as those terms are defined in the Plan, and are subject to certain other terms and conditions. The Company estimated the fair value of the options on the date of grant using the Black-Scholes option-pricing model to be approximately \$1.9 million based on the following weighted average assumptions: share price equal to \$0.51; dividend yield of 0% for all years; expected volatility of 64.3%; risk-free interest rates of 2.9%; and expected life of six years.

b) The total unrecognized compensation cost of employee stock options at December 31, 2018 is approximately \$1,524,000. The unrecognized compensation cost of employee stock options is expected to be recognized over a weighted average period of 1.18 years.

The total cash received from employees as a result of employee stock option exercises for the years ended December 31, 2016, 2017 and 2018 was approximately \$14,000, \$0 and \$0, respectively. The Company did not realize any tax benefit in connection with these exercises.

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

During the three years ended December 31, 2018 there were no options granted by the Company to its consultants, directors, and other service providers. In addition, during the three years ended December 31, 2018, there were no option exercises by any of the Company's consultants, directors, and other service providers and, consequently, no shares of Common Stock were issued in connection with exercises of options by, nor was any cash received from, the Company's consultants, directors, and other service providers during such period.

3. A summary of share option plans, and related information, under all of the Company's equity incentive plans for the years ended December 31, 2016, 2017 and 2018 is as follows:

## a. Options granted to employees:

	Year ended December 31, 2016		2017		2018	
	Number of options	Weighted average exercise price	Number of options	Weighted Average Exercise Price	Number of options	Weighted average exercise price
Outstanding at beginning of year	6,952,293	\$ 3.363	4,884,211	\$ 3.617	4,729,617	\$ 3.604
Changes during the year:						
Granted					6,360,000	0.541
Forfeited and Expired	1,514,957	3.748	154,594	4.004	1,088,942	4.604
Exercised (*)	553,125	0.067				
Outstanding at end of year	4,884,211	\$ 3.617	4,729,617	\$ 3.604	10,000,675	\$ 1.547
Exercisable at end of year	3,498,492	\$ 4.296	4,457,461	\$ 3.696	3,944,863	\$ 3.065

(\*) The total intrinsic value of options exercised during the years ended December 31, 2016, 2017 and 2018, was approximately \$213,000, \$0 and \$0, respectively.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

b. Restricted stock granted to employees:

	Year ended December 31, 2016 Number of shares of restricted stock
Outstanding at beginning of year	127,874
Changes during the year:	
Vested	127,874
Forfeited	-
Outstanding at end of year	-

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

	Year ended December 31,					
	2016		2017		2018	
	Number of options/ restricted stock	Weighted average exercise price	Number of options/ restricted stock	Weighted average exercise price	Number of options/ restricted stock	Weighted average exercise price
Outstanding at beginning of Year	637,209	\$ 11.638	208,000	\$ 3.156	200,000	\$ 3.282
Changes during the year:						
Expired	429,209	15.748	8,000	0.001	50,000	3.02
Vested restricted stock						
Outstanding at end of year	208,000	3.156	200,000	3.282	150,000	3.37
Exercisable at end of year	170,500	\$ 3.109	200,000	\$ 3.282	150,000	\$ 3.37

d. The following tables summarize information concerning outstanding and exercisable options and restricted stock as of December 31, 2018:

December 31, 2018  
Options outstanding

Exercise prices	Number of options outstanding at end of year	Weighted average remaining contractual life	Options exercisable	
			Number of options exercisable	Weighted average remaining contractual life
n/a (Restricted Stock)			n/a	n/a
\$0.51	2,360,000	9.71	147,500	9.71
\$0.56	4,000,000	9.71	250,000	9.71
\$1.720	1,623,593	6.22	1,530,281	6.22
\$2.370	900,000	5.74	900,000	5.74
\$2.650	209,082	0.15	209,082	0.15
\$3.370	150,000	5.56	150,000	5.56
\$6.900	680,000	1.15	680,000	1.15
\$7.550	160,000	0.56	160,000	0.56
\$9.660	68,000	1.83	68,000	1.83
	10,150,675		4,094,863	

F-21

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

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

(U.S. dollars in thousands)	Year ended December 31,		
	2016	2017	2018
Research and development expenses	\$ 571	\$ 182	\$ 310
Selling, general and administrative expenses	417	155	204
	\$ 988	\$ 337	\$ 514

**c. Private and 144A Offerings**

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

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

On May 22, 2018, the Company agreed to a privately negotiated exchange with certain existing note holders to exchange \$3,423,000 aggregate principal amount of the Company's outstanding 2018 Notes for 2,613,636 shares of the Company's common stock and \$2.23 million in cash to cover outstanding principal and accrued interest on the exchanged 2018 Notes. See also note 8a.

**NOTE 8 - CONVERTIBLE NOTES**

**a. 4.5% Convertible Notes ("2018 Notes")**

On September 18, 2013, the Company completed a private placement of \$69.0 million in aggregate principal amount of Senior Convertible Notes (the “2018 Notes”), including \$9.0 million aggregate principal amount of 2018 Notes related to the initial purchaser’s over-allotment option, which was exercised in full. On September 15, 2018, the 2018 Notes matured and have been paid in full.

In connection with the completion of the offering of the 2018 Notes, the Company had entered into an indenture with The Bank of New York Mellon Trust Company, N.A., as trustee, governing the 2018 Notes. The 2018 Notes accrued interest at a rate of 4.50% per year, payable semiannually in arrears. In December 2016, \$54.1 million aggregate principal amount of 2018 Notes were exchanged for 2021 Notes and shares of common stock (see also note 8b) and in July 2017, \$9.0 million aggregate principal amount of 2018 Notes were exchanged for 2022 Notes as defined in note 8c (see also note 8c).

The initial conversion rate for the 2018 Notes was 173.6593 shares of the Common Stock for each \$1,000 principal amount of 2018 Notes (equivalent to an initial conversion price of approximately \$5.76 per share of the Common Stock), and was subject to adjustment for certain events but will not be adjusted for any accrued and unpaid interest.

On June 2018, the Company exchanged \$3.423 million aggregate principal amount of the Company’s 2018 Notes for 2,613,636 shares of Common Stock and approximately \$2.23 million in cash and delivered the necessary funds under the indenture governing the 2018 Notes to effectively discharge such notes, which was \$2.53 million. On September 15, 2018, the 2018 Notes matured and were paid in full.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

The following table sets forth total interest expense recognized for the years ended December 31, 2016, 2017 and 2018 related to the 2018 Notes:

(U.S. Dollars in thousands)	Year ended December 31,		
	2016	2017	2018
Contractual interest expense	\$ 2,943	\$ 501	\$ 139
Amortization of debt issuance costs and debt discount	421	71	15
Gain from early redemption			(32 )
Total	\$ 3,364	\$ 572	\$ 122

**b. 7.5% Convertible Notes (“2021 Notes”)**

On December 1, 2016, the Company entered into a note purchase agreement with institutional investors, which held part of the 2018 Notes (the “2016 Purchasers”), relating to the sale by the Company of \$22.5 million aggregate principal amount of 7.50% Senior Secured Convertible Notes due 2021 in a private placement pursuant to Section 4(a)(2) under the Securities Act of 1933, as amended (the “Securities Act”). Concurrently with the consummation of the private placement of the 2021 Notes, the Company entered into a privately negotiated exchange agreement (the “2016 Exchange Agreement”) with certain existing note holders identified therein to exchange \$54.1 million aggregate principal amount of the Company’s outstanding 2018 Notes for (i) \$40.186 million aggregate principal amount of 2021 Notes, (ii) 23,846,735 shares of Common Stock and (iii) cash, equal to the accrued and unpaid interest on the 2018 Notes and any fractional shares. The closing date of the purchase agreement and the 2016 Exchange Agreement was December 7, 2016. The issuance of the 2021 Notes and shares in the exchange and the private placement were made in reliance on the exemption from the registration requirements of the Securities Act pursuant to Section 4(a)(2) thereof. The net proceeds from the private placement were \$19.7 million, after deducting the placement agent’s fees and the Company’s estimated offering expenses.

In connection with the completion of the exchange and the private placement, the Company entered into an indenture (the “2016 Indenture”) with The Bank of New York Mellon Trust Company, N.A., as trustee, governing the 2021 Notes. The 2021 Notes accrue interest at a rate of 7.50% per year, payable semiannually in arrears on May 15 and November 15 of each year, beginning on May 15, 2017. A portion of the interest payable may be made in shares of Common Stock at the Company’s election. The Notes will mature on November 15, 2021.

On July 24, 2017, the Company entered into another note purchase agreement with certain institutional investors relating to the private issuance and sale by the Company of \$10.0 million in aggregate principal amount of its 2021 Notes. The 2021 Notes were issued pursuant to the 2016 Indenture dated (December 7, 2016). The net proceeds from this purchase agreement were \$9.5 million, after deducting the Company's offering expenses.

Holder may convert their 2021 Notes at any time. The initial conversion rate for the 2021 Notes is 1,176.4706 shares of the Common Stock for each \$1,000 principal amount of 2021 Notes (equivalent to an initial conversion price of approximately \$0.85 per share of the Common Stock). Upon conversion, the Company may settle the 2021 Notes by paying or delivering, as the case may be, cash, shares of Common Stock or a combination thereof, at the Company's election.

During the year ended December 31, 2018, note holders converted \$1.15 million aggregate principal amount of the 2021 Notes into a total of 1,537,415 shares of Common Stock and cash payments of approximately \$15,887, in the aggregate. As of December 31, 2018, a total of \$57.9 million aggregate principal amount of the 2021 Notes were outstanding.



**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

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

any or all of the 2021 Notes if the last reported sale price of the common stock for at least 20 trading days (whether a) or not consecutive) during the period of 30 consecutive trading days exceeds 150% of the conversion price on each applicable trading day, or

b) all of the 2021 Notes then outstanding if the aggregate principal amount of the 2021 Notes then outstanding is less than 15% of the aggregate principal amount of the notes issued.

No redemption was made during the years 2017 and 2018.

The 2021 Notes are guaranteed by the Restricted Subsidiaries (as defined in the 2016 Indenture) and are secured by a first-priority security interest in all of the present and after-acquired assets of the Company and each of the Restricted Subsidiaries (the “Collateral”), including, but not limited to, (i) 100% of the capital stock of the Guarantors (as defined in the 2016 Indenture) and each Restricted Subsidiary of the Company that is held by the Company or any Restricted Subsidiary, (ii) intellectual property, including all copyrights, copyright licenses, patents, patent licenses, software, trademarks, trademark licenses and trade secrets and other proprietary information, including, but not limited to, domain names, (iii) all cash, deposit accounts, securities accounts, commodities accounts and contract rights, (iv) all real property and leased property, subject to applicable minimum thresholds, as set forth in the 2016 Indenture, and (v) all other tangible and intangibles of the Company and the Guarantors. In connection with the grant of such liens, the Company entered into certain agreements with both Wilmington Savings Fund Society, FSB, as collateral agent in the United States, and with Altshuler Shaham Trusts Ltd., as security trustee in Israel. The 2016 Indenture restricts the ability of the Company, the Subsidiaries and any future subsidiaries to make certain investments, including transfers of the Company’s assets that constitute collateral securing the 2016 Notes, in its existing and future foreign subsidiaries, subject to certain exceptions.

Upon (i) the occurrence of a fundamental change (as defined in the 2016 Indenture) or (ii) if the Company calls the 2021 Notes for redemption as described below (either event, a “make-whole fundamental change”) and a holder elects to convert its 2021 Notes in connection with such make-whole fundamental change, the Company will, in certain circumstances, increase the conversion rate by a number of additional shares (the “Additional Shares”). In no event will

the conversion rate exceed the maximum conversion rate, which is 1,787.3100 shares per \$1,000 principal amount of 2021 Notes, which amount is inclusive of repayment of the principal of the 2021 Notes.

If a fundamental change occurs at any time, holders will have the right, at their option, to require the Company to purchase for cash any or all of the 2021 Notes, or any portion of the principal amount thereof, that is equal to \$1,000 or an integral multiple of \$1,000 in excess thereof, on a date of the Company's choosing that is not less than 20 calendar days nor more than 35 calendar days after the date of the applicable fundamental change company notice. The price the Company is required to pay for a 2021 Note is equal to 100% of the principal amount of such 2021 Note plus accrued and unpaid interest, if any, to, but excluding, the fundamental change purchase date.

For accounting purposes, since the terms of the 2018 Notes and the 2021 Notes are substantially different, the 2016 Exchange Agreement was considered as an extinguishment, which in essence means recording a gain due to the 2018 Notes that were exchanged for the 2021 Notes recorded at fair value as of the closing date. The gain on extinguishment of \$14.1 million was recognized.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

As the settlement upon conversion was subject to compliance with the listing standards of the NYSE American, until the Company's stockholders' approval was obtained, the Company was prohibited by these rules from issuing shares in excess of 20% of its outstanding shares (calculated as of December 1, 2016). The accounting guidance assumed that the conversion will be settled in cash and, as such, is precluded from equity classification for any part of the 2021 Notes that may have cash settlement. As such, that part of the conversion feature was accounted for as a derivative which is bifurcated from the debt host contract and was measured at fair value through the statement of operations until the Company's stockholders approved, in April 2017, the issuance of shares in excess of 20% of its outstanding shares. On April 12, 2017, the Company's stockholders approved the issuance of shares of the Company's Common Stock in excess of 20% of the Company's outstanding shares of Common Stock to settle conversion requests and pay interest on the Company's issued 2021 Notes. As a result, the Company reclassified the embedded derivative to additional paid in capital. During 2017, the measurement of the derivative resulted in a non-cash charge to the Company's statement of operations of \$38,061 thousand. The conversion feature of the 2021 Notes issued in July 2017 is accounted for as equity, which is bifurcated from the debt host contract. With respect to the remainder of the 2021 Notes, for which the conversion feature qualifies for equity classification (since upon conversion the Company at its election may settle the 2021 Notes by paying cash, shares of Common Stock or a combination of cash and shares of Common Stock) separate liability (debt) and equity (conversion option) components of such 2021 Notes were recorded. The Company measures the liability according to amortized cost using the effective interest method.

The Company prepared a valuation of the fair value of the 2021 Notes (a Level 3 valuation) for the issuance dates. The value of the 2021 Notes was estimated by implementing the binomial model. The liability component was valued based on the Income Approach. The following parameters were used:

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

The following table sets forth total interest expense recognized related to the 2021 Notes:

(U.S. Dollars in thousands)	Year Ended December 31,		
	2016	2017	2018
Contractual interest expense	\$313	\$4,434	\$4,359
Debt discount amortization	147	2,309	2,587
Gain on extinguishment	(14,063)		
Change in fair value of convertible note embedded derivative	6,473	38,061	
Interest payment in connection with conversions		3,918	234
Loss (Income) in connection with conversions		(1,643 )	245
Total	\$(7,130 )	\$47,079	\$7,425

#### c.4.5% Convertible Notes Due 2022 (“2022 Notes”)

On July 24, 2017, the Company entered into a privately negotiated exchange agreement (the “2017 Exchange Agreement”) with certain existing note holders identified therein to exchange \$9.0 million aggregate principal amount of the Company’s outstanding 2018 Notes for (i) \$8.55 million aggregate principal amount of the Company’s 4.5% convertible promissory notes due 2022, (ii) \$275,000 in cash consideration and (iii) cash, equal to the accrued and unpaid interest on the exchanged 2018 Notes.

As the terms of the 2018 Notes and the 2022 Notes were substantially different, the 2017 Exchange Agreement was considered an extinguishment of debt, which in essence means recording a loss due to the 2018 Notes that were exchanged for the 2022 Notes recorded at fair value as of the closing date. The Company recognized a loss of \$1.3 million due to the extinguishment.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

The Company prepared a valuation of the fair value of the 2022 Notes (a Level 3 valuation) for the issuance date. The value of the 2022 Notes was estimated by implementing the binomial model. The liability component was valued based on the Income Approach. The following parameters were used:

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

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

All of the 2022 Notes were converted during the year ended December 31, 2017 into 11,239,641 shares of Common Stock.

The following table sets forth total interest expense recognized related to the 2022 Notes:

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

**NOTE 9 - FAIR VALUE MEASUREMENT**

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

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

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

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

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

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

The fair value of the financial instruments included in the working capital of the Company is usually identical or close to their carrying value. The fair value of the convertible notes derivative is based on level 3 measurement.

The fair value of the \$57.9 million 2021 Notes as of December 31, 2018 is approximately \$56.6 million based on a level 3 measurement.

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**NOTE 9 - FAIR VALUE MEASUREMENT** (continued):

The Company prepared a valuation of the fair value of the 2021 Notes (a Level 3 valuation) as of December 31, 2018. The value of these notes were estimated by implementing the binomial model. The liability component was valued based on the Income Approach. The following parameters were used:

	2021 Notes	
Stock price (USD)	0.31	
Expected term	2.88	
Risk free rate	2.44	%
Volatility	75.94	%
Yield	13.34	%

**NOTE 10 - TAXES ON INCOME**

**a. The Company**

Protalix BioTherapeutics, Inc. is taxed according to U.S. tax laws. The Company's income is taxed in the United States at the rate of up to 27%.

On December 22, 2017, the Tax Cuts and Jobs Act (the "Act") was enacted into law. The new legislation represents fundamental and dramatic modifications to the U.S. tax system. The Act contained several key tax provisions that impacted the Company including the reduction of the maximum U.S. federal corporate income tax rate from 35% to 21%, effective January 1, 2018. Other significant changes under the Act included, among others, a one-time repatriation tax on accumulated foreign earnings, a limitation of net operating loss deduction to 80% of taxable income, and indefinite carryover of post-2017 net operating losses. The Act also repealed the corporate alternative minimum tax for tax years beginning after December 31, 2017. Losses generated prior to January 1, 2018 will still be subject to the 20-year carryforward limitation and the alternative minimum tax. Other impacts due to the Act included the repeal of the domestic manufacturing deduction, modification of taxation of controlled foreign corporations, a base erosion anti-abuse tax, modification of interest expense limitation rules, modification of limitation on deductibility of excessive executive compensation, and taxation of global intangible low-taxed income.

Modification of interest expense limitation rules under the Act provides generally that for taxable years 2018-2021 interest expense deduction shall be limited to 30% of the EBITDA and for taxable years 2022 onwards to 30% of EBIT. Disallowed interest deduction may be carried forward indefinitely. The Company believes that any potential impact (if applicable) of this limitation will be offset by utilization of available net operating losses.

U.S. GAAP requires that the impact of tax legislation be recognized in the period in which the law was enacted.

The Company believes that all future profits of its subsidiaries will be indefinitely reinvested or that there is no expectation to distribute any taxable dividends from these subsidiaries. The determination of the amount of the unrecognized deferred tax liability related to the undistributed earnings is estimated as an immaterial amount.

#### **b. Protalix Ltd.**

The Israeli Subsidiary is taxed according to Israeli tax laws:

##### **1. Tax rates**

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

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

In December 2016, the Economic Efficiency Law (Legislative Amendments for Implementing the Economic Policy for the 2017 and 2018 Budget Years), 2016 was published, introducing a gradual reduction in corporate tax rate from 25% to 23%. However, the law also included a temporary provision setting the corporate tax rate in 2017 at 24%. As a result, the corporate tax rate was 23% in 2018 and will be 23% in 2019 and thereafter.

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



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

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

F-27

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

**a. Reduced tax rates**

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

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

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

**b. Accelerated depreciation**

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

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

The Israeli Subsidiary’s entitlement to the benefits described above is subject to its fulfilling the conditions stipulated by the law, rules and regulations published thereunder, and the instruments of approval for the specific investment in an approved enterprise. Failure by the Israeli Subsidiary to comply with these conditions may result in the cancellation of the benefits, in whole or in part, and the Subsidiary may be required to refund the amount of the benefits with

interest. The Israeli Subsidiary received a final implementation approval with respect to its “Approved Enterprise” from the Investment Center.

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

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

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

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

**c. Tax losses carried forward to future years**

As of December 31, 2018, the Company had aggregate net operating loss (“NOL”) carry-forwards equal to approximately \$211 million that are available to reduce future taxable income as follows:

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

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

**1. The Company**

The Company's carry-forward NOLs, equal to approximately \$26 million (as of December 31, 2017, approximately \$23 million), may be restricted under Section 382 of the Internal Revenue Code ("IRC"). IRC Section 382 applies whenever a corporation with NOL experiences an ownership change. As a result of IRC Section 382, the taxable income for any post change year that may be offset by a pre-change NOL may not exceed the general IRC Section 382 limitation, which is the fair market value of the pre-change entity multiplied by the IRC long-term tax exempt rate.

Significant judgment is required in determining any valuation allowance recorded against deferred tax assets. In assessing the need for a valuation allowance, the Company considered all available evidence, including past operating results, the most recent projections for taxable income, and prudent and feasible tax planning strategies. The Company reassesses its valuation allowance periodically and if future evidence allows for a partial or full release of the valuation allowance, a tax benefit will be recorded accordingly.

**2. Protalix Ltd.**

At December 31, 2018, the Israeli Subsidiary had approximately \$185 million (as of December 31, 2017, approximately \$182 million) of carry-forward NOLs that are available to reduce future taxable income with no limited period of use.

**d. Deferred income taxes:**

The components of the Company's net deferred tax assets at December 31, 2017 and 2018 were as follows:

(U.S. dollars in thousands)	December 31,	
	2017	2018
In respect of:		

Timing Differences of Protalix Ltd.	\$11,761	\$6,678
Timing Differences of Protalix BioTherapeutics, Inc.	(426 )	(501 )
Net operating loss carry forwards	47,033	49,436
Valuation allowance	(58,368)	(55,613)
	-	-

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

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

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

**f. Tax assessments**

In accordance with the Income Tax Ordinance, as of December 31, 2018, all of Protalix Ltd.’s tax assessments through tax year 2013 are considered final.

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

Jurisdiction:	Years:
Israel	2014-2018
United States (*)	2014-2018

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

**PROTALIX BIOTHERAPEUTICS, INC.**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**NOTE 11 - SUPPLEMENTARY FINANCIAL STATEMENT INFORMATION**

**Balance sheets:**

(U.S. dollars in thousands)	December 31,	
	2017	2018
a. Other assets:		
Institutions	\$394	\$574
State of Israel (see note 6a)	195	190
Restricted deposit	623	561
Prepaid expenses	433	453
Assets of discontinued operation	215	
Sundry	74	99
	\$1,934	\$1,877

(U.S. dollars in thousands)	December 31,	
	2017	2018
b. Accounts payable and accruals – other:		
Payroll and related expenses	\$1,386	\$1,099
Interest payable	645	555
Provision for vacation	1,650	1,658
Accrued expenses	4,802	6,368
Royalties payable	301	369
Property and equipment suppliers	526	225
	\$9,310	\$10,274

**Statements of operations:**

(U.S. dollars in thousands)	December 31,		
	2016	2017	2018
Revenues from selling goods:			
Pfizer	\$5,226	\$12,181	\$5,320
Brazil	\$3,973	\$7,061	\$3,658
	\$9,199	\$19,242	\$8,978
Revenue from license and R&D services		\$1,836	\$25,262



**PROTALIX BIOTHERAPEUTICS, INC.  
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**NOTE 12 - RELATED PARTY TRANSACTIONS**

<b>(U.S. dollars in thousands)</b>	Year ended December 31,		
	2016	2017	2018
Compensation (including share based compensation) to the non-executive directors	\$ 560	\$ 499	\$ 467

**NOTE 13 - SUBSEQUENT EVENTS**

The Company has evaluated subsequent events through the date on which the consolidated financial statements were available to be issued and no subsequent events were identified.

F-31