

Protalix BioTherapeutics, Inc.  
Form 10-K  
March 12, 2015

**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**  
**<sup>x</sup>1934**

**For the fiscal year ended December 31, 2014**

**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)

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

**2 Snunit Street**

**Science Park**

**POB 455**

<b><u>Carmiel, Israel</u></b>	<b><u>20100</u></b>
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(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 MKT</b>

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

**None**

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

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

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

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

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

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

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

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

The aggregate market value of the voting common equity held by non-affiliates of the Registrant, as of June 30, 2014 was approximately \$179 million (based upon a per share price equal to \$3.65, the closing price for shares of the Registrant's common stock reported by the NYSE MKT for such date). Shares of common stock held by each officer, director and holder of 5% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other

purposes.

On March 1, 2015, approximately 93,603,819 shares of the Registrant's common stock, par value \$0.001 per share, were outstanding.

FORM 10-K

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## PART I

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

### CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

The statements set forth under the captions “Business,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Risk Factors,” and other statements included elsewhere in this Annual Report on Form 10-K, which are not historical, constitute “forward-looking statements” within the meanings of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, including statements regarding expectations, beliefs, intentions or strategies for the future. When used in this report, the terms “anticipate,” “believe,” “estimate,” “expect,” “can,” “continue,” “could,” “intend,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” and words or phrases of similar import, as they relate to our company or our subsidiaries or our management, are intended to identify forward-looking statements. 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:

- 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 result in the termination of such agreement which may have a material adverse effect on our company;

- risks related to the commercialization efforts for taliglucerase alfa in the United States, Israel, Brazil, Canada, Australia and other countries;

- risks related to the supply of drug product pursuant to our supply arrangement with Fiocruz;

the risk of significant delays in the commercial introduction of taliglucerase alfa in the United States, Brazil, Israel, Canada, Australia and other markets as planned;

risks related to the acceptance and use of taliglucerase alfa or any of our product candidates, if approved, by physicians, patients and third-party payors;

the risk that we will not be able to develop a successful sales and marketing organization for taliglucerase alfa in Israel, or for any other product candidate, in a timely manner, if at all;

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

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

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

delays in the approval or the potential rejection of any application filed with or submitted to the regulatory authorities reviewing taliglucerase alfa outside of the United States, Israel, Brazil, Canada, Australia and other countries in which taliglucerase alfa is already approved;

our ability to establish and maintain strategic license, collaboration and distribution arrangements, and to manage our relationships with Pfizer Inc., Fiocruz 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 our 2018 convertible notes, or any other indebtedness;

risks relating to our ability to finance our research programs, the expansion of our manufacturing capabilities and the ongoing costs in the case of delays in regulatory approvals for taliglucerase alfa outside of the United States, Israel, Brazil, Canada, Australia and other countries in which taliglucerase alfa is already approved;

delays in our preparation and filing of applications for regulatory approval of our other product candidates in the United States, the European Union and elsewhere;

- our expectations with respect to the potential commercial value of our product and product candidates;

the risk that products that are competitive to our product candidates may be granted orphan drug status in certain territories and, therefore, will be subject to potential marketing and commercialization restrictions;

- the impact of development of competing therapies and/or technologies by other companies;

any lack of progress of our research and development activities and our clinical activities with respect to any product candidate;

- the inherent risks and uncertainties in developing the types of drug platforms and products we are developing;

potential product liability risks, and risks of securing adequate levels of product liability and clinical trial insurance coverage;

- the possibility of infringing a third party's patents or other intellectual property rights;

the uncertainty of obtaining patents covering our products and processes and in successfully enforcing our intellectual property rights against third parties;



- risks relating to changes in healthcare laws, rules and regulations in the United States or elsewhere; and

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

Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced or late-stage clinical trials, even after obtaining promising earlier trial results or preliminary findings for such clinical trials. Even if favorable testing data is generated from clinical trials of a drug product, the U.S. Food and Drug Administration or 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, or ProCellEx. Using our ProCellEx system, we are developing 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. Our initial commercial focus has been on complex therapeutic proteins, including proteins for the treatment of genetic disorders, such as Gaucher disease and Fabry disease. With our experience, and having successfully developed Elelyso<sup>™</sup>, our first drug product, 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. We are now also applying the unique properties of our ProCellEx system for the oral delivery of therapeutic proteins.

The following table summarizes our current product candidates and our current projections regarding their respective stages of clinical development.

On May 1, 2012, the U.S. Food and Drug Administration, or the FDA, approved for sale our first commercial product, taliglucerase alfa for injection, which is being marketed in the United States and Israel under the brand name Elelyso, as 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 by the Brazilian National Health Surveillance Agency (Agencia Nacional de Vigilancia Sanitaria, or ANVISA) in March 2013, and by the Israeli Ministry of Health, or the Israeli MOH, in September 2012. It has also been approved by other regulatory agencies for other countries. Taliglucerase alfa is being marketed under the name Uplyso<sup>™</sup> in Brazil and certain other Latin American countries.

In August 2014, the FDA approved Elelyso for injection for pediatric patients and the Israeli MOH approved the pediatric indication in January 2015. Prior to the U.S. pediatric approval, Elelyso was approved for pediatric indications in Australia and Canada but in no other jurisdiction. In September 2014, CONITEC, the National Commission for Incorporation of Technologies in Brazil's Unified Healthcare System, announced that it had decided to give a positive funding recommendation for Uplyso in the treatment of adult patients with types 1 and 3 Gaucher disease, and established that Uplyso will be the first choice for treatment for new adult Gaucher patients in Brazil.

Since May 2012, taliglucerase alfa has been marketed in the United States by Pfizer Inc., or Pfizer, our commercialization partner, as provided in the exclusive license and supply agreement by and between Protalix Ltd., our wholly-owned subsidiary, and Pfizer, which we refer to as the Pfizer Agreement. We granted Pfizer an exclusive, worldwide license to develop and commercialize taliglucerase alfa under the Pfizer Agreement, but we retained those rights in Israel, and later in Brazil. We have agreed to a specific allocation between Protalix Ltd. and Pfizer of the responsibilities for the continued development efforts for taliglucerase alfa outside of Israel and Brazil. Protalix Ltd. has been marketing taliglucerase alfa in Israel since 2013 and in Brazil since January 2014.

On June 18, 2013, we entered into a Supply and Technology Transfer Agreement, or the Brazil Agreement, with Fiocruz, for taliglucerase alfa. The 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. Under the agreement, Fiocruz committed to purchase at least approximately \$40 million worth of taliglucerase alfa during the first two years of the term. Since the agreement went into effect, we have recorded revenues of approximately \$3.5 million for sales of taliglucerase alfa to Fiocruz in 2014 and, during the first quarter of 2015, we received a purchase order for approximately \$5.7 million of taliglucerase alfa out of which we have delivered approximately \$1.7 million of the product. In subsequent years, Fiocruz is required to purchase at least approximately \$40 million worth of taliglucerase alfa per year. We are not required to complete the final stage of the technology transfer until Fiocruz purchases at least approximately \$280 million worth of taliglucerase alfa.

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.

To facilitate the arrangement with Fiocruz, we and Pfizer agreed to an amendment of our exclusive license and supply agreement, which amendment provides for the transfer of the commercialization and other rights to taliglucerase alfa in Brazil back to us. As consideration for the transfer of the commercialization and supply rights, we agreed to pay Pfizer a maximum amount of approximately \$12.5 million from its net profits (as defined in the license and supply agreement) per year. Pfizer has also agreed to perform certain transitional services in Brazil on our behalf in connection with the supply of taliglucerase alfa to Fiocruz.

We will pay a fee equal to 5% of the net proceeds generated in Brazil to our agent for services provided in assisting us complete the Brazil Agreement pursuant to an agency agreement between us and the agent. The agency agreement will remain in effect with respect to the Brazil Agreement until the termination thereof.

We are cooperating with Pfizer to obtain marketing approval for taliglucerase alfa in additional countries and jurisdictions. In addition to those countries in which taliglucerase alfa has been approved, marketing authorization applications have been filed in other countries.

Currently, patients are being treated with taliglucerase alfa on a commercial basis in the United States, Brazil, Israel and Chile.

In addition to taliglucerase alfa, we are developing an innovative product pipeline using our ProCellEx protein expression system. Our product pipeline currently includes, among other candidates:

(1) PRX-102, or alpha-GAL-A, a therapeutic protein candidate for the treatment of Fabry disease, a rare, genetic lysosomal disorder in humans, currently in an ongoing phase I/II clinical trial. We expect to report interim efficacy and safety results for the 1 mg/kg dose group of the trial during the third quarter of 2015 and to report final efficacy and safety results for the 0.2mg, 1 mg and 2mg/kg dose groups of the trial during the fourth quarter of 2015.

(2) PRX-106, our oral antiTNF product candidate which is being developed as an orally-delivered anti inflammatory treatment using plant cells as a natural capsule for the expressed protein. We expect to initiate a proof of concept efficacy study during 2015.

(3) 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. We expect to initiate a proof of concept efficacy study during 2015.

(4) PRX-112, an orally administered glucocerebrosidase enzyme for the treatment of Gaucher patients utilizing oral delivery of the recombinant GCD enzyme produced and encapsulated within carrot cells. PRX-102 has been the subject of successful proof of concept clinical trials, as described below, and we intend to focus our efforts on a new formulation of the treatment during 2015.

Except for the rights to commercialize taliglucerase alfa worldwide (other than Brazil and Israel), which we licensed to Pfizer, we hold the worldwide commercialization rights to all of our proprietary development candidates. We have built an internal marketing team designed to serve the Israeli and Brazilian market for taliglucerase alfa and we intend to establish internal commercialization and marketing teams for our other product candidates in North America, the European Union and in other significant markets, including Israel, subject to required marketing approvals, as the need arises. In addition, we continuously evaluate potential strategic marketing partnerships as well as collaboration programs with biotechnology and pharmaceutical companies and academic research institutes.

## **Our Strategy**

In January 2015, we announced our newly implemented strategy for accelerated growth. The strategy centers around prioritizing existing and new pipeline candidates to focus on clinically superior products that offer a clear competitive advantage over existing treatments. The strategy was the culmination of two month of intensive review by our management of the company's internal resources and of the markets in which we think we can operate. The following highlights the details of the strategic plan.

**PRX-102 for the Treatment of Fabry disease.** PRX-102 is designed to be an improved enzyme replacement therapy product for the treatment of Fabry disease given its potential for clinically superior outcomes and enhanced safety when compared to currently marketed enzyme replacement therapies. The product candidate remains a key focus for our company, and we intend to aggressively push PRX-102 through clinical development. Interim efficacy and safety data from our ongoing phase I/II trial are described in this Annual Report.

**Oral Anti-TNF (PRX-106) Anti Inflammatory.** Oral anti-TNF represents a novel mode of administering a recombinant anti-TNF protein. We plan to initiate clinical efficacy trials of Oral Anti-TNF during 2015. Upon reviewing the proof of concept (POC) data, expected in early 2016, we intend to collaborate with a well-suited partner for further development.

**AIR DNase (PRX-110) for Cystic Fibrosis.** AIR DNase 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. The product candidate has demonstrated improved disease parameters in animal models and human sputum testing when compared to the currently marketed product. We plan to initiate clinical efficacy trials of AIR DNase for the treatment

of Cystic Fibrosis (CF) during 2015. Upon reviewing the results of the trial, expected in early 2016, we intend to collaborate with a well-suited partner for further development.

**Oral GCD (PRX-112) for Gaucher Disease.** Oral GCD represents a novel mode of administering taliglucerase alfa. The initial clinical data generated for this compound in pre-clinical and clinical trials is promising. In 2015, we intend to focus on improving the product candidate's formulation and delivery in order to transform it into a commercially viable product.

**Potential Pipeline Candidates.** We aim to expand our pipeline by leveraging the advantages of our proprietary ProCellEx<sup>®</sup> protein expression technology. The focus is expected to be on biologics with 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.

**Elelyso<sup>™</sup> for Gaucher Disease.** We anticipate continuing to increase market share in Israel. Additionally, our management intends to continue to work closely with Pfizer, our collaboration partner, and with the Brazilian government, to increase sales globally.

## Industry Overview

Recombinant proteins have revolutionized the treatment of a variety of diseases and disorders. Recombinant proteins are forms of human proteins that are produced, or expressed, using a mammalian, plant, bacterial or yeast cell as a production engine. In the early 1970s, a number of key scientific breakthroughs, including, among others, the demonstration of genetic engineering and genetic sequencing techniques, as well as the synthesis of genes, led to the advancement of recombinant protein technology. As a result, the market for pharmaceutical therapeutics has undergone a transformation as recombinant proteins and other biologic products have become an increasingly significant portion of the global drug market and the focus of research worldwide. The IMS Institute for Healthcare Informatics reports that global biologic spending was \$169 billion in 2012 and anticipated to reach \$221 billion in 2017 (Report by the IMS Institute for Healthcare Informatics, Nov. 2013).

Mammalian cell-based systems are the current industry standard for expression of recombinant therapeutic glycoproteins (complex proteins that contain sugar residues), including catalytic enzymes and monoclonal antibodies. Mammalian cell-based systems were first introduced in the late 1980s and are currently used to produce 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>. 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. The cells most often used in connection with mammalian cell-based protein expression are Chinese hamster ovary (CHO) cells.

Mammalian cell-based expression 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 glycosylation (the addition of sugar residues to a protein which is necessary to enable specific biological activity by the protein). 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. Due to their significant advantages, 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.

Despite the utility and widespread use of mammalian cell-based systems, they are subject to a number of disadvantages. CHO cells and other mammalian cells are highly sensitive and can only be grown under near perfect conditions, requiring highly complex, expensive, stainless steel bioreactors which tightly regulate the required temperature, pH and oxygen levels. As a result, such bioreactor systems are very costly and complicated to operate. CHO cells and other mammalian cells are also susceptible to viral infections, including human viruses, and several cases of viral contamination have occurred recently. 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. In addition, mammalian cell-based expression systems require large quantities of sophisticated and expensive growth medium to accelerate the expression process.

Several companies and research institutions have explored alternatives to mammalian cell-based production technologies that overcome some of these disadvantages, focusing primarily on 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.

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

ProCellEx is our proprietary production system. We have developed ProCellEx based on our plant cell culture technology for the development, expression and manufacture of recombinant proteins. ProCellEx 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 protein expression system does not involve mammalian or animal components or transgenic field-grown, whole plants at any point in the production process. As a result, through our ProCellEx protein expression system, we believe that we can develop recombinant therapeutic proteins yielding substantial cost advantages, accelerated development and other competitive benefits when compared to mammalian cell-based protein expression systems.



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

We have successfully demonstrated the feasibility of our ProCellEx system through: the FDA's approval of taliglucerase alfa; the clinical and preclinical studies we have performed to date, including the positive efficacy and safety data in our clinical trials for both Elelyso and PRX102 for the treatment of Fabry disease; preclinical results in well-known models in our enzyme for each of Fabry disease, DNase and antiTNF; and 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 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.

We are also using our ProCellEx system to produce active recombinant proteins through oral administration of plant cells expressing biotherapeutic proteins. In such method, an enzyme is naturally encapsulated within carrot 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 the enzyme in active form to the bloodstream. With initial proof of concept now demonstrated, 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 in early clinical trials of oral GCD in Gaucher patients.

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

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

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

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**Biologic Optimization.** Our ProCellEx protein expression system has internal capabilities developed to improve the biologic dynamics of the expressed protein. For example, the proteins produced through our system have uniform glycosylation 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 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 U.S. and international composition of matter patents for taliglucerase alfa, PRX-102 and certain of our other product candidates.

**Broad Range of Expression Capabilities.** Our ProCellEx protein expression system 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 (Chinese Hamster Ovary) 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.** Our ProCellEx system 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. 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.

***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. As a result, the risk of contamination of our products under development and the potential risk of viral transmission from our products 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 our ProCellEx system compared to mammalian cell-based expression systems.

***Potential ability to administer active therapeutic enzymes orally.*** We are using our ProCellEx system to produce active recombinant proteins through oral administration of plant cells expressing biotherapeutic proteins. 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, 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 anti TNF, and early clinical trials of oral GCD in Gaucher patients.

## **Elelyso, Our First Commercial Product**

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 the Israeli MOH approved the pediatric indication in January 2015. Prior to the U.S. pediatric approval, Elelyso was approved for pediatric indications in Australia and Canada but in no other jurisdiction.

We believe that taliglucerase alfa has the potential to offer patients and healthcare payors an effective and cost efficient treatment of Gaucher disease compared to the currently available ERTs.

## **Gaucher Disease Background**

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). The normal degradation products of GlcCer are glucose and ceramide, which are easily excreted by the cells through normal biological processes. Patients with Gaucher disease lack or otherwise have dysfunctional GCD and, accordingly, are not able to break down GlcCer. The absence of an active GCD enzyme leads to the accumulation of GlcCer in lysosomes of certain white blood cells called macrophages. Macrophages affected by the disease become highly enlarged due to the accumulation of GlcCer and are referred to as “Gaucher cells.” Gaucher 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.

## **Current Treatments for Gaucher Disease**

The standard of care for Gaucher disease is enzyme replacement therapy using recombinant GCD to replace the mutated or deficient natural GCD enzyme. It is estimated that there are approximately 12,000 people suffering from Gaucher disease worldwide, but only approximately 6,000 patients are undergoing treatment. 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<sup>®</sup>, enzyme replacement therapies commercialized by Genzyme Corporation (acquired by Sanofi), or Genzyme, and Shire plc, or Shire, respectively, are the only recombinant GCDs currently available on the market for the treatment of Gaucher disease. As enzyme replacement therapy does not cure the genetic disorder, but rather provides an external source for transfusion of the missing or mutated enzyme, Gaucher patients generally receive the treatment over their entire lifetime. According to public reports by Sanofi, consolidated sales of Cerezyme during the year ended December 31, 2014 were €715 million (or approximately \$865 million), a growth of approximately 8% compared to the same period in 2013. Shire reported annual worldwide sales of VPRIV of approximately \$367 million in 2014, a growth of 7% compared to VPRIV's sales in 2013.

In addition, Cerdelga<sup>®</sup> (eliglustat) is a substrate reduction therapy for Gaucher disease marketed by Sanofi. Cerdelga was approved for marketing by the FDA in August 2014 and by the European Commission in January 2015.

Cerezyme is produced through a mammalian cell-based protein expression process in CHO cells and VPRIV is produced using a human cancer cell line. There are no known severe side effects to the use of Cerezyme or VPRIV, and Cerezyme's approved use over the past decade suggests that it is an effective treatment of Gaucher disease. However, Cerezyme and VPRIV are both subject to the limitations of most mammalian cell-based therapeutic proteins, including lengthy and costly production processes and contamination risks.

Zavesca (miglustat), which is marketed by Actelion Ltd., or Actelion, 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, Zavesca's use has been limited with respect to treating Gaucher disease. However, Zavesca is also used to treat other rare disorders. Actelion has reported total sales of Zavesca of approximately CHF 103 million (approximately \$104 million) in 2014, an increase of approximately 8% compared to sales in 2013.

## **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 an improved version of the currently marketed Fabry disease enzymes, Fabrazyme<sup>®</sup> and Replagal<sup>®</sup>, 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. We believe that the treatment of Fabry disease is a specialty clinical niche with the potential for high growth.

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

Fabry disease is characterized by subnormal or absent enzymatic activity of alpha-GAL-A, a lysosomal enzyme which primarily catalyses the hydrolysis of terminal alpha-galactosyl groups of glycolipids, mainly the glycosphingolipid globotriaosylceramide (Gb3). The accumulation of Gb3 in body tissues results in Fabry disease. The ultimate consequence of glycosphingolipid deposition in the vasculature and other tissues is end-organ failure, particularly of the kidney, but also of the heart and cerebrovascular system. In addition, involvement of the central, peripheral and autonomic nervous systems results in episodes of pain and impaired peripheral sensation. Fabry disease affects approximately 8,000 people globally. In PRX-102, the prh-alpha-GALA, naturally occurring as a homodimer, is PEGylated and cross-linked to support and reinforce the homodimeric structure, which is crucial for the enzymatic activity of this enzyme. PRX-102 has been shown to be taken up by Fabry patients' cells where it localizes to the lysosome, in which Gb3 accumulates. PRX-102 is characterized by higher stability under physiologically relevant conditions, and extended circulation residence time as compared to current ERTs for Fabry disease.

### ***Current Treatments for Fabry Disease***

Currently there are two drugs available on the market to treat Fabry disease. Fabrazyme, marketed by Genzyme, is approved for the treatment of Fabry disease in the United States and the European Union. Sanofi reported €460 million (approximately \$557 million) in worldwide sales of Fabrazyme in 2014, a growth of 23% compared to 2013. The other approved drug for the treatment of Fabry disease in the European Union is Replagal, which is marketed by Shire. Shire reported \$500 million in sales of Replagal in 2014, an increase of 7% compared to 2013. According to public reports by Shire, during 2012 Shire withdrew its Biologics License Application (BLA) for Replagal with the FDA.

***PRX-102 Development Program***

In February 2015, we announced the completion of enrollment in our phase I/II clinical trial in adult Fabry patients. The phase I/II clinical trial is a worldwide, multi-center, open label, dose ranging study to evaluate the safety, tolerability, pharmacokinetics and exploratory efficacy parameters of PRX-102 in adult Fabry patients. There were 18 adult Fabry patients (11 male and 7 female) enrolled in the trial, each in one of three dosing groups, 0.2 mg/kg, 1mg/kg and 2mg/kg. Each patient receives intravenous infusions of PRX-102 every two weeks for 12 weeks, with a six-month efficacy follow up period. All patients that completed the trial have opted to continue to receive PRX-102 in an open-label extension trial.

In January and February 2015, we announced positive interim efficacy and safety data from the study. PRX-102 demonstrated meaningful clinical benefits across the following key disease parameters already in the low dose of 0.2 mg/kg:

- Major reduction in Gb3 in Renal Peritubular Capillaries;
- Significant improvement in all pain parameters;
- Stabilization of cardiac and kidney function with favorable trends; and
- Low level of antibody formation.

The interim efficacy analysis includes six patients enrolled in the 0.2mg/kg dose group at six months of treatment (for Gb3 in renal peritubular capillaries n=5). The interim safety analysis includes 12 patients; six patients enrolled in the 0.2mg/kg dose group and six patients enrolled in the 1mg/kg dose group.



Based on an analysis of kidney biopsies with randomized blinded scoring, PRX-102 demonstrated a major reduction from baseline in renal peritubular capillary Gb3 using both the quantitative Barisoni Lipid Inclusion Scoring System (BLISS) and the semi quantitative method. Using the BLISS method, a reduction in the rate of 82.2% for males, 65.4% for females and 75.5% for males and females combined were observed. Absolute change from baseline was -4.5, -1.2 and -3.2, respectively. Applying the semi quantitative scoring method, commonly used by approved enzyme replacement therapies, PRX-102 demonstrated a reduction of 69.6% in abnormal capillary score.

Using the well-accepted Brief Pain Inventory scale, a 100% reduction in pain at its worst, a 60.0% reduction in mean severity, and 78.8% reduction on mean interference (which includes walking, working, sleeping, enjoyment of life and others) were observed. In addition to a 100% reduction in worst pain, all patients also reported a 100% reduction in mean interference, with the exception of one patient who experienced a 33.3% reduction. See Figure 1.

**Figure 1. Improvement in Brief Pain Inventory (BPI)**

Reductions of plasma Lyso-Gb3 and plasma Gb3 concentrations were also observed. Females (n=2) demonstrated a -2.4 ng/mL mean change in Lyso-Gb3 and a -0.4 µg/mL mean change in plasma Gb3. Males (n=4) demonstrated a -96.2 ng/mL and a -1.3 µg/mL change, respectively. All patients demonstrated a reduction in absolute Lyso-Gb3 concentration and all patients demonstrated a reduction in Gb3 except for one patient. See Figure 2.

**Figure 2. Semi Quantitative Method**

A meaningful reduction in the total score of Mainz Severity Score Index (MSSI), which looks at general, neurological, cardiovascular and renal parameters, was also demonstrated, with a reduction in all parameters included in MSSI.

The leading causes for death of Fabry patients include cardiovascular disease and renal failures. All patients that participated in the trial exhibited stable cardiac and kidney function, with favorable trends after only six months, as measured by left ventricular mass (LVM), left ventricular mass index (LVMI), ejection fraction (EF), estimated glomerular filtration rate (eGFR) and urine protein. See Figures 3 and 4.

**Figure 3. Stability of Cardiac Parameters by MRI**

**Figure 4. Stable Kidney Functions**

The safety analysis for adverse events represents a total of 6.7 patient years. PRX-102 was well tolerated, with the majority of events being mild and moderate. Only one of the 12 patients evaluated for safety experienced hypersensitivity and discontinued per protocol. For this patient, anti PRX-102 IgG was negative and anti PRX-102 IgE was positive at baseline.

Six patients receiving the 0.2mg/kg dose and two patients receiving the 1m/kg dose were evaluated for antibody formation. Of these eight patients, only two patients, or 33% of the 0.2 mg/kg dose cohort, developed antibodies. All adverse events experienced by these patients were deemed by the investigators to be unrelated to PRX-102.

PRX-102 has a significantly longer circulatory half-life ( $T_{1/2}$ ) of approximately 60 hours, and a substantially higher area under the curve (AUC) of approximately 70,000 ng/mL\*hour for the 0.2mg/kg dose, when compared to currently marketed enzyme replacement therapies. These enhanced pharmacokinetic benefits are believed to be the result of the chemical modifications made to PRX-102, including cross-linking and covalent bonding to make the enzyme a more stable homo-dimer. See Figures 5 and 6.

**Figure 5. Improved Pharmacokinetics** **Figure 6. Area under the Curve (AUC)**

We expect to report interim results from the 1mg/kg cohort in the third quarter of 2015, and full top-line results from all dosing cohorts in the fourth quarter of 2015. We intend to request an end of phase II meeting with the FDA in the fourth quarter of 2015, and anticipate initiating a phase III pivotal trial in early 2016.

### **PRX-106; Oral antiTNF as an Anti Inflammatory**

Our oral antiTNF product candidate is a recombinant antiTNF (Tumor, Necrosis Factor) protein that we are expressing through ProCellEx. AntiTNF drugs represent the biggest category of biological drugs in the world today with combined sales of over \$20 billion a year.

Oral antiTNF is a plant cell-expressed form of the fused protein that is naturally encapsulated within carrot 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 injectable therapy. 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.

We are currently developing oral antiTNF an orally-administered anti inflammatory using plant cells as a natural capsule for the expressed protein. In preclinical studies, oral PRX-106 alleviated immune-mediated hepatitis and reduced interferon gamma levels in a concanavalin A (ConA) inflammatory mouse model. Additionally, oral administration of PRX-106 alleviated immune mediated colitis in a well-established mouse model, promoting serum levels of anti-inflammatory IL-10 and regulatory T-cells.

pr-antiTNF is a plant cell-expressed recombinant fusion protein made from the binding domain of the human TNF receptor (TNFR), fused to the Fc component of a human antibody domain. It has an identical amino acid sequence to Enbrel and our in vitro and preclinical animal studies have demonstrated that pr-antiTNF exhibits similar or better activity to Enbrel. See Figure 7.

### **Figure 7. IBD Animal Model**

We are now conducting additional preclinical studies on oral antiTNF for several attractive indications, and we plan to initiate clinical efficacy trials of oral anti TNF during 2015. Upon reviewing the proof of concept (POC) data, expected in early 2016, we intend to collaborate with a well-suited partner for further development.

***PRX-110; AIR DNase for the Treatment of Cystic Fibrosis***

PRX-110, or AIR DNase, is our plant cell recombinant form of human deoxyribonuclease I (DNase I) that we are developing for the treatment of Cystic Fibrosis, to be administered by inhalation. DNase I cleaves extracellular DNA and thins the thick mucus that accumulates in the lungs of Cystic Fibrosis patients. Currently, Pulmozyme® is the only DNase I commercially available, with annual sales of approximately \$626 million in sales for 2014, according to public reports by F. Hoffman-La Roche Ltd.

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

AIR DNase 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. The product candidate has demonstrated improved disease parameters in animal and human models sputum testing when compared to the currently marketed product. See Figure 8.

**Figure 8. Rheology Data Analysis in in human sputum samples**

We plan to initiate clinical efficacy trials of AIR DNase for the treatment of Cystic Fibrosis during 2015. Upon reviewing the results of the trial, expected in early 2016, we intend to collaborate with a well-suited partner for further development.

***PRX-112; Orally Administered GCD for the Treatment of Gaucher Disease***

We are developing PRX-112, an orally-delivered glucocerebrosidase (GCD) enzyme for the enzyme replacement therapy treatment of Gaucher disease. In 2015, our focus with respect to oral GCD, will be on improving oral GCD's formulation and delivery in order to transform the product candidate into a commercially viable product.

***Oral GCD Development Program***

In February 2015, the last Gaucher patient was treated in our phase IIa clinical trial of oral GCD. The phase IIa clinical trial was a 28-day open-label, sequential dose escalation study to evaluate the safety of PRX-112, and study the dose dependent pharmacokinetics of PRX-112 in naïve adult Gaucher patients. The primary objective of the trial was to measure the safety of oral GCD in Gaucher patients. Additional objectives included an evaluation of oral GCD's pharmacokinetic profile and exploratory endpoints. The trial covered 17 naïve adult Gaucher patients. Subjects receive once daily oral administrations of PRX-112 for five consecutive days at each dose, with a two-day washout period between doses.

An initial analysis of the results demonstrates that oral GCD was well tolerated. No patient discontinued the study prematurely, there were no drug-related serious adverse events (SAE) reported and no treatment-induced antibodies were detected in any of the patients participating in the trial. Four patients experienced adverse reactions, all of which were transient in nature, mild and moderate and the patients that experienced the adverse reactions recovered without

further events. Active GCD enzyme was detected in the blood circulation of 10 out of the 17 participants in the trial. In addition, elevated platelet levels were observed in 10 out of the 17 participants in the trial.

We intend to focus our efforts on a new formulation of the treatment during 2015 in order to prepare a viable solution for further clinical development.

### ***Phase I Trial Data***

We completed a phase I clinical trial of oral GCD, which was an exploratory, open label study to evaluate the safety and pharmacokinetics of oral GCD in Gaucher patients. Patients received re-suspended lyophilized carrot cells in a single oral administration during the first segment of the trial and three consecutive daily administrations during the second segment of the trial. The primary objective of the trial was to measure the safety of oral GCD in Gaucher patients. Additional objectives included an evaluation of oral GCD's pharmacokinetic profile and exploratory endpoints. The results demonstrate that oral GCD was well tolerated across all three doses tested. No patient discontinued the study prematurely, there were no drug related serious adverse events (SAE) reported and no treatment-induced antibodies were detected in any of the patients participating in the trial. All adverse reactions were transient in nature, mild and moderate and the patients that experienced the adverse reactions recovered without further events. One patient experienced nausea related to treatment and two patients experienced mild dizziness and dizziness, which was possibly related to treatment.

Pharmacokinetic (PK) studies revealed that active GCD enzyme was detected in the patients' blood circulation, measured in the well-established assay in leucocytes of Gaucher patients, following oral administration of oral GCD. C max analysis showed an average increase of over 100% in enzymatic activity from base line, with an increase ranging from approximately 50% to 350% among the different, individual patients in the study. In general, the PK profile of oral GCD has a pattern of continuous enzyme presence over approximately 30 hours from administration. Platelet levels in 3 out of 8 thrombocytopenic Gaucher patients tested showed meaningful, rapid and unexpected improvement in platelet count after short-term treatment with oral GCD. The data demonstrates platelet count increases ranging from 27% to 78% from base line. Thus, with a daily oral administration of oral GCD, we expect to achieve a steady state level of active GCD enzyme in the blood circulation of patients similar to the physiological state in healthy individuals.

Platelet levels in 3 out of 8 thrombocytopenic Gaucher patients tested showed meaningful, rapid and unexpected improvement in platelet count after short-term treatment with Oral GCD. The data demonstrates platelet count increases ranging from 27% to 78% from base line.

### **Commercialization Agreement for taliglucerase alfa**

On November 30, 2009, Protalix Ltd. and Pfizer entered into the Pfizer Agreement pursuant to which Pfizer was granted an exclusive, worldwide license to develop and commercialize taliglucerase alfa. Under the terms and conditions of the Pfizer Agreement, Protalix Ltd. retained the right to commercialize taliglucerase alfa in Israel and Brazil. In connection with the execution of the Pfizer Agreement, Pfizer made an upfront payment to Protalix Ltd. of \$60.0 million in connection with the execution of the agreement and subsequently paid Protalix Ltd. an additional \$30.0 million milestone payment. In addition to the milestone payments, Protalix Ltd. is eligible to payments equal to 40% of the net profits earned by Pfizer on sales of taliglucerase alfa (or share 40% of the net loss). In calculating the



net profits, there are certain agreed upon limits on the amounts that may be deducted from gross sales for certain expenses and costs of goods sold. Protalix Ltd. retained the manufacturing rights to taliglucerase alfa, and Pfizer and Protalix Ltd. agreed to a specific allocation of the responsibilities for the continued development efforts for taliglucerase alfa prior to its approval. Protalix Ltd. will manufacture all of the taliglucerase alfa needed for all purposes under the agreement and Pfizer will purchase the taliglucerase alfa from Protalix Ltd., subject to certain terms and conditions. The Pfizer Agreement also provides for reimbursement by Pfizer of certain costs to be incurred by Protalix Ltd.

We will be subject to a withholding tax on the U.S. revenue source portion of the payments made to us for our share of Pfizer's in net profits under the Pfizer Agreement. Currently, the withholding tax rate is 15%.

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

We entered into the Brazil Agreement with Fiocruz in June 2013, which 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. Under the agreement, Fiocruz committed to purchase at least approximately \$40 million worth of taliglucerase alfa during the first two years of the term. Since the agreement went into effect, we have recorded revenues of approximately \$3.5 million for sales of taliglucerase alfa to Fiocruz in 2014 and, during the first quarter of 2015, we received a purchase order for approximately \$5.7 million of taliglucerase alfa out of which we have delivered approximately \$1.7 million of the product. In subsequent years, Fiocruz is required to purchase at least approximately \$40 million worth of taliglucerase alfa per year. We are not required to complete the final stage of the technology transfer until Fiocruz purchases at least approximately \$280 million worth of taliglucerase alfa. If Fiocruz fails to comply with certain of its purchase commitments under the agreement, we may terminate the agreement, and all of our rights to the technology will be returned.

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.

To facilitate the arrangement with Fiocruz, we and Pfizer agreed to an amendment of our exclusive license and supply agreement, which amendment provides for the transfer of the commercialization and other rights to taliglucerase alfa in Brazil back to us. As consideration for the transfer of the commercialization and supply rights, we agreed to pay Pfizer a maximum amount of approximately \$12.5 million from its net profits (as defined in the license and supply agreement) per year. Pfizer has also agreed to perform certain transitional services in Brazil on our behalf in connection with the supply of taliglucerase alfa to Fiocruz.

We will pay a fee equal to 5% of the net proceeds generated in Brazil to our agent for services provided in assisting us complete the Brazil Agreement pursuant to an agency agreement between us and the agent. The agency agreement will remain in effect with respect to the Brazil Agreement until the termination thereof.

## **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, 2014, we hold, or have license rights to 64 patents and 95 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. As of December 31, 2014, we hold, with a third party, one joint patent and one joint patent application, and licensed rights to two patents.

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

As of December 31, 2014, our patent portfolio consists 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 have been issued 19 patents in the United States, Australia, the European Union, Israel, Canada, the Czech Republic, Hungary, Japan, Poland, Mexico, Hong Kong, India and Korea, and hold three pending patent applications. Among other things, the patents cover the methods that we use for culturing and harvesting plant cells and/or tissues in consecutive cycles. Of the issued patents in this family, 13 are expected to expire in 2017 and six are expected to expire in 2025.

With respect to our ProCellEx protein expression system, we hold four issued patents and 13 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 are expected to expire in 2028.

We hold a patent family containing 23 issued patents in India, South Africa, Russian Federation, Australia, China, the United States, Ukraine, Singapore, Japan, Europe, Hong Kong, Mexico, Korea Canada, Brazil and Israel and 13 patent applications 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 are expected to expire in 2024.

We hold a patent family containing four 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 hold a patent family containing four issued patents in South Africa, Australia and Singapore, and seven pending patent applications 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 are expected to expire in 2026.

We hold a patent family containing three granted patents in the United States, South Africa and Australia, and five pending patent applications 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 are expected to expire in 2028.

We hold a patent family containing 11 pending patent application 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 hold a patent family containing three granted patents in Europe, New Zealand and South Africa and 16 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 are expected to expire in 2031.

We hold a patent family containing two pending patent applications relating to therapeutic proteins with stabilized quaternary structure. 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 hold a patent family containing one granted patent in Europe and two pending patent applications relating to multimeric protein structures of glucocerebrosidase and to uses thereof in treating Gaucher disease. The issued patent and any patent applications to issue in the future based on the patent applications in this patent family, if at all, are expected to expire in 2031.

We hold three patent families containing eight 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 hold two PCTs and 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.

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.

With respect to taliglucerase alfa, we have licensed the rights to two patents from Virginia Tech Intellectual Properties, Inc., or Virginia Tech, that are expected to expire in 2016.

· We co-own a PCT that covers use of plant cells expressing a TNF alpha polypeptide inhibitor in therapy.

We hold two patent families relating to oral delivery of plant cells comprising recombinant glucocerebrosidase for the treatment of Gaucher disease. The patents to issue in the future based on patent application in this patent family, if at all, are expected to expire in 2033 and 2035.

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. Under the terms of the agreement, 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.

In January 2005, Protalix Ltd. entered into a license agreement with Virginia Tech University, pursuant to which we received a non-exclusive worldwide license to make, have made, use, sell, offer for sale and import certain of Virginia Tech's patents. As consideration for the license, we made a one-time license fee payment to Virginia Tech, and we are obligated to make royalty payments equal to varying low, single-digit percentages of net sales of licensed products by Protalix Ltd., its subsidiaries and/or their affiliates. Upon commercialization of a licensed product, the royalty payment is subject to a low, annual minimum amount. In addition, we were obligated to make milestone payments equal to \$150,000, in the aggregate, upon the achievement of certain milestones, which milestone payments have been satisfied. We have the right to grant sublicenses under the agreement.

Our license agreement with Virginia Tech remains in effect until the earlier of the expiration of the last patent under the agreement or 10 years after the first commercial sale of any licensed product. Virginia Tech may terminate the agreement upon written notice to us that we are in material breach of our obligations under the agreement if we are unable to remedy such material breach within a fixed number of days after we receive such notice, which number may be doubled if we are making good faith efforts to achieve a cure and the extension will not increase the damages suffered by Virginia Tech. We have the right to terminate the agreement at any time upon prior written notice delivered an agreed-upon number of days prior to the date of termination.

## Manufacturing

We are obligated to manufacture all of the taliglucerase alfa drug product needed under the Pfizer Agreement, subject to certain terms and conditions. Our drug product candidates, including 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 use our current facility, which has approximately 20,000 sq/ft of clean rooms built according to industry standards, to develop, process and manufacture taliglucerase alfa and other recombinant proteins. We intend to use our current manufacturing space to produce all of the taliglucerase alfa we need in the near future, included the taliglucerase alfa to be purchased by Pfizer. 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. Current capacity of our facility can serve all of our current and expected commercial and clinical needs, and may be sufficient to serve our production needs for the commercialization of PRX-102.

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

We have engaged a contract manufacturer in Europe to act as an additional source of fill and finish activities for taliglucerase alfa. According to our agreement with Pfizer, Pfizer will be responsible for the fill and finish activities for taliglucerase alfa. We have engaged other contract manufacturers to perform fill/finish activities for PRX-102 and for our oral treatment of Gaucher disease.

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 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 and our 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.

We specifically face competition from companies with approved treatments of Gaucher disease. In addition to Elelyso, there are two other ERTs for the treatment of Gaucher disease; Cerezyme which is marketed by Genzyme (acquired by Sanofi) and VPRIV, which is marketed by Shire. To a much lesser extent, we also compete with Actelion. In addition, Sanofi has commercialized Cerdelga, a substrate reduction therapy for Gaucher disease. Cerdelga was approved for marketing by the FDA in August 2014 and by the European Commission in January 2015.



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. In 2012, Shire withdrew its BLA for Replagal in the United States. In addition, we are aware of other clinical stage, early clinical stage and experimental drugs which are being developed for the treatment of Fabry disease by Amicus Therapeutics and other companies.

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.

Several biogeneric companies are pursuing the opportunity to develop and commercialize follow-on versions of other currently marketed biologic products, including growth factors, hormones, enzymes, cytokines and monoclonal antibodies, which are areas that interest us. These companies include, among others, Novartis AG/Sandoz Pharmaceuticals, BioGeneriX AG, Stada Arzneimittel AG, BioPartners GmbH and Teva Pharmaceutical Industries Ltd. or Teva. 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>Affiliation</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)
Professor Aaron Ciechanover, M.D., D.Sc.	Laureate of the Nobel Prize in Chemistry
	Distinguished research Professor at the Cancer and Vascular Biology Research Center of the Rappaport Research Institute and Faculty of Medicine at the Technion, Israel's Institute of Technology
	American Academy of Arts and Sciences, Member

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

Alexander Levitzki,  
Ph.D.

1990 Rothschild Prize in Biology

2002 Hamilton-Fairley Award, European Society of Medical Oncology

2005 Wolf Prize for Medicine

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

Institute Professor and the Lita Annenberg Hazen Professor of Immunochemistry at the Skaggs Institute for Chemical Biology of The Scripps Research Institute

1978 Parke-Davis Award

1990 The San Marino Prize

1995 Wolf Prize in Chemistry

Richard Lerner,  
M.D.

1996 California Scientist of the Year Award

2002 University of California Presidential Medal

Member, Royal Swedish Academy of Sciences

Member, United States National Academy of Sciences

#### 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, 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 intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. For a fast track product, the FDA may consider for review on a rolling basis sections of the NDA before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA as they become available and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. We used the rolling submission option for our taliglucerase alfa NDA, which we completed in April 2010.

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

Medicare is the federal healthcare program for those who are (i) over 65 years of age, (ii) disabled, (iii) suffering from end-stage renal disease or (iv) suffering from Lou Gehrig's disease. Medicare consists of part A, which covers inpatient costs, part B, which covers services by physicians and laboratories, durable medical equipment and certain drugs, primarily those administered by physicians, and part D, which provides drug coverage for most prescription

drugs other than those covered under part B. Medicare also offers a managed care option under part C. Medicare is administered by CMS. In contrast, Medicaid is a state-federal healthcare program for the poor and is administered by the states pursuant to an agreement with the Secretary of Health and Human Services. Most state Medicaid programs cover most outpatient prescription drugs.

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

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

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

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

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

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

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

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

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

A licensure framework for follow-on biologic products; and

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

## International Regulation



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

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

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

## Israeli Government Programs

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

## General Corporate Tax Structure in Israel

The income of Protalix Ltd., other than income from “Approved Enterprises,” is taxed in Israel at the regular rates which were 25% in 2012 and 2013 and 26.5% for 2014 and thereafter.

Capital gains on the sale of assets are subject to capital gain tax according to the corporate tax rate in effect for the year of selling the assets.

In addition to the corporate taxes in Israel, we are subject to a withholding tax on the U.S. revenue source portion of the payments made to us for our share of Pfizer’s net profits under the Pfizer Agreement. The withholding tax rate is 15%. See “Business—Commercialization Agreement.”

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

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

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

Investment Law prior to its amendment as well as the relevant changes contained in the new legislation.

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

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

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

<b>Percent of Foreign Ownership</b>	<b>Rate of Reduced Tax</b>
0-49%	25%
49-74%	20%
74-90%	15%
90-100%	10%

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

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

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

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

Under the Investment Law, the approval of the 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:

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

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

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

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

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

To date, Protalix Ltd. has received grants from the OCS for the financing of a portion of its research and development expenditures in Israel. As of December 31, 2014, the OCS approved grants in respect of Protalix Ltd.'s continuing operations totaling approximately \$36.8 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 the OCS through payments of royalties at a rate of 3% to 6% of the revenues generated from an OCS-funded project, depending on the period in which revenues were generated. As of December 31, 2014, Protalix Ltd. either paid or accrued royalties payable of \$5.6 million and Protalix Ltd.'s contingent liability to the OCS with respect to grants received was approximately \$30.0 million.

Under the Israeli Law for the Encouragement of Industrial Research and Development, 1984, and related regulations, or the Research Law, recipients of grants from the OCS 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 the OCS-financed technologies and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the approval of the OCS' Research Committee. Protalix Ltd. may not receive the required approvals for any proposed transfer and, if received, Protalix Ltd. may be required to pay the OCS 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 the OCS, the amount of time that has elapsed between the date on which the know-how was transferred and the date on which the OCS 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 the OCS. 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, the Research Committee to allow the transfer outside of Israel of know-how derived from an approved program and the related manufacturing rights. In general, the Research Committee may approve transfer of know-how in limited circumstances 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 the OCS an amount, in cash, as set forth in the Research Law. 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 the OCS as set forth in the Research Law.

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 the OCS 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 OCS funding and there is no restriction on the export of products manufactured using technology developed with OCS 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.” OCS 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 & Samara 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 the OCS. Furthermore, the research and development projects must be for the promotion of the company and carried out by or on behalf of the company seeking such tax deduction. However, the amount of such deductible expenditures is reduced by the sum of any funds received through government grants for the finance of such scientific research and development projects. Expenditures not so approved are deductible over a three-year period.

#### Employees

As of December 31, 2014, we had 234 employees, of whom 32 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 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 Our Financial Condition and Capital Requirements**

**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 shareholders.**

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 payments we have received in connection with our license and supply agreement with Pfizer. For the years ended December 31, 2014, 2013 and 2012, we had net losses of \$29.9 million, \$27.8 million and \$11.6 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. Our lead product was first approved for marketing by the FDA in May 2012, by the Israeli MOH in September 2012 and, subsequently, in certain other countries. We fund all of our operations and capital expenditures from the revenues we generate from sales of taliglucerase alfa supplemented with our cash on hand, other licensing fees and grants and the net proceeds of any equity or debt offerings. Based on our current plans 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 seek additional financing to implement and fund product development, preclinical studies and clinical trials for the drugs in our pipeline, as well as additional drug candidates and other research and development projects. 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. Any additional source of financing will likely involve the issuance of our equity securities, which will have a dilutive effect on our shareholders.

## **Risks Related to the Commercialization of taliglucerase alfa**

### **We cannot predict the share in net income we will receive from Pfizer's sales of taliglucerase alfa.**

Taliglucerase alfa has been approved for marketing in the United States, Israel, Brazil and other territories. Otherwise, we have no other products approved for marketing. As we have invested a significant portion of our efforts and financial resources in the development of taliglucerase alfa, our ability to generate product revenue depends heavily on the successful commercialization of taliglucerase alfa. Under the Pfizer Agreement, Pfizer holds an exclusive worldwide license to develop and commercialize taliglucerase alfa, except in Israel and Brazil. Sales of taliglucerase alfa worldwide (except Israel and Brazil) are dependent upon Pfizer's sales and marketing efforts, which we do not control and may not be able to effectively influence, and on the actions and decisions of foreign regulatory authorities. Upon the approval of taliglucerase alfa in additional markets, if at all, Pfizer may experience delays in, or be unable to achieve, the commercial introduction of taliglucerase alfa in those markets, which would have a material adverse effect on our business, results of operations and financial condition.

Our future revenues under our collaboration with Pfizer from Pfizer's sales of taliglucerase alfa will depend on a number of factors, including:

- the number of Gaucher patients who will be treated with taliglucerase alfa;
- the willingness of Gaucher patients to switch from other ERTs to taliglucerase alfa;
- competition from Cerezyme, VPRIV and Cerdelga, and other current or future approved treatments of Gaucher disease;
- Pfizer's efforts under the Pfizer Agreement and the effectiveness of Pfizer's commercial strategy and its execution of that strategy, including its pricing strategy and the effectiveness of its efforts to obtain adequate third-party reimbursements;

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- obtaining marketing approvals and reimbursement from additional regulatory authorities;
- a continued acceptable safety and efficacy profile of our product candidates following approval;
- the successful audit of our facilities by additional regulatory authorities;
- maintaining the cGMP compliance of our manufacturing facility or establishing manufacturing arrangements with third parties; and
- the capacity of physicians and health care providers to provide treatment to Gaucher patients.

We cannot accurately predict the amount of revenues we will generate under our collaboration with Pfizer in future periods, if any. Any failure to commercialize taliglucerase 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.

The market share and/or other indicators of market acceptance of taliglucerase alfa may not meet the expectations of investors or public market analysts, which would have a material adverse effect on our business, results of operations and financial condition and the market price of our common stock would likely decline.

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

Uplyso was first approved for marketing in Brazil in March 2013. Under our Supply and Technology Transfer Agreement with Fiocruz, we are not required to complete the final stage of the technology transfer for the production of Uplyso until Fiocruz purchases at least approximately \$280 million worth of Uplyso. However, we do not control and may not be able to effectively influence Fiocruz's ability to distribute Uplyso in Brazil. With respect to the first required purchase amount, we have recorded revenues of approximately \$3.5 million for sales of Uplyso to Fiocruz in 2014 and, during the first quarter of 2015, we received a purchase order for approximately \$5.7 million of Uplyso out of which we have delivered approximately \$1.7 million of the product. If Fiocruz fails to comply with the purchase requirements of the Supply and Technology Transfer Agreement, we may terminate the agreement and market Uplyso in Brazil on our own or through Pfizer. 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.

We 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 Fiocruz to distribute Uplyso in Brazil, or the experience of significant delays in doing so, may have a material adverse effect on our business, results of operations and financial condition.

**If safety issues regarding taliglucerase alfa that were not known at the time of approval are discovered, or if we or Pfizer fail to comply with continuing U.S. and applicable foreign regulations, commercialization efforts for**

**taliglucerase alfa could be adversely affected and taliglucerase alfa could lose its approval or its sales could be suspended.**

Drug products remain subject to continuing regulatory oversight after they are approved for marketing, including the review of additional safety information. Drugs are more widely used by patients once approved for sale and, therefore, side-effects and other problems may be observed after approval that were not seen or anticipated, or were not as prevalent or severe, during clinical trials or nonclinical studies. The subsequent discovery of previously unknown problems with a product could negatively affect commercial sales of the product, result in restrictions on the product or lead to the withdrawal of the product from the market. The reporting of adverse safety events involving taliglucerase alfa or public speculation about such events could cause our stock price to decline or experience periods of volatility and may have a material adverse effect on our business, results of operations and financial condition.

If we or Pfizer fail to comply with applicable continuing regulatory requirements, we or Pfizer may be subject to fines and/or criminal prosecutions, and taliglucerase may become subject to suspension or withdrawal of regulatory approval, product recalls and seizures and operating restrictions. In addition, the manufacturers we and Pfizer engage to produce taliglucerase alfa and the manufacturing facilities in which taliglucerase alfa is made are subject to periodic review and inspection by the FDA and foreign regulatory authorities. If problems are identified during the review or inspection of these manufacturers or manufacturing facilities, it could result in our inability to use the facility to make our product or a determination that inventories are not safe for commercial sale, which may have a material adverse effect on our business, results of operations and financial condition.

**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 taliglucerase alfa or any of our other product candidates, if approved for marketing. Future acceptance and use of taliglucerase alfa or any of our other 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.

Because we expect sales of taliglucerase alfa to generate substantially all of our product revenues for the foreseeable future, any lack of market acceptance of taliglucerase alfa would have a material adverse effect on our business, results of operations and financial condition.

**If the market opportunities for taliglucerase alfa or our other product candidates 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 taliglucerase alfa or any of our other product candidates, if approved, in all territories which could diminish our sales or affect our ability to sell taliglucerase alfa or any other products profitably.**

Market acceptance and sales of taliglucerase alfa or any of our other product candidates, if approved, will depend on worldwide coverage and reimbursement policies. 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. Although, to date taliglucerase alfa is covered and reimbursed in all the approved territories, coverage might not be available for taliglucerase alfa or any of our other product candidates, if approved, in all territories. 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 taliglucerase alfa, or any other approved product, if any, 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 taliglucerase alfa in the United States, as well as marketing activities in the United States related to any other products for which we obtain regulatory approval, 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or 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.

The Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including health care fraud, and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private third-party payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services.

We are unable to predict whether we could be subject to actions under any of these or other fraud and abuse laws, or the impact of such actions. Moreover, to the extent that taliglucerase alfa, or any of our products, if approved for marketing, will be sold in a foreign country, we and our collaborators, including Pfizer, may be subject to similar foreign laws and regulations. If we or any of our 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 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 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, we have commenced a phase III clinical trial in connection with only one drug candidate, taliglucerase alfa, which trial was completed in August 2009. These operations provide a limited basis for investors to assess our ability to commercialize our drug candidates and whether to invest in our company.

**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. 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.

**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. Pfizer holds an exclusive, worldwide right to develop and commercialize taliglucerase alfa worldwide, except in Israel and Brazil. If we decide to market any of our other products directly, if any, we must 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 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.**

While we do sell directly taliglucerase alfa in Israel and Brazil and we intend to build a sales force to market other product candidates at least in certain regions 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 develop. We may pursue arrangements regarding the sales and marketing and distribution of one or more of our product candidates, such as our current license and supply agreement with Pfizer for taliglucerase alfa, 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.

**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 is 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 20 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 of follow-up 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.

**We currently depend heavily on the success of taliglucerase alfa, our first commercial product. Any failure to successfully commercialize taliglucerase 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 have invested a significant portion of our efforts and financial resources in the development of taliglucerase alfa. Our ability to generate product revenue, depends heavily on the successful development and commercialization of taliglucerase alfa. Pfizer holds an exclusive worldwide license to develop and commercialize taliglucerase alfa, except in Israel and Brazil. The successful commercialization of taliglucerase alfa will depend on several factors, including the following:

- obtaining marketing approvals and reimbursement from additional regulatory authorities;
- the successful audit of our facilities by additional regulatory authorities;

maintaining the cGMP compliance of our manufacturing facility or establishing manufacturing arrangements with third parties;

- Pfizer's efforts under the Pfizer Agreement;
- Fiocruz's activities in Brazil;
- Fiocruz's purchasing the minimum quantities under the Technology Transfer Agreement;
- our marketing efforts in Israel;
- a continued acceptable safety and efficacy profile of taliglucerase alfa;
- the availability of reimbursement to patients from healthcare payors for taliglucerase alfa; and
- other risks described in these Risk Factors.

Any failure to successfully commercialize taliglucerase 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.

**If we are unable to develop and commercialize our other 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.

**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 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 trials. We may encounter problems that cause us to abandon or repeat preclinical studies or clinical trials. Companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials. Data obtained from tests are susceptible to varying interpretations which may delay, limit or prevent regulatory approval. Failure or delay in the commencement or completion of our clinical trials may be caused by several factors, including:

- unforeseen safety issues;
- determination of dosing issues;
- lack of effectiveness during clinical trials;
- slower than expected rates of patient recruitment;
- 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 may 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.

**If the results of our clinical trials do not support our claims relating to any 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 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. 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 may involve a specific and small patient population. 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 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.

**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 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 any of our 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.

**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 or experiencing adverse clinical events, which may or may not be judged related to our drug candidates under evaluation. The discontinuation of patients in any one of our studies may cause the results from that 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 our NDA and other marketing applications, and our introduction of new drugs, if any, may be delayed which could impair our clinical development programs and would have a material adverse effect on our business and results of operations. The collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators also assist our competitors, our competitive position could be harmed.

**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, the Israeli MOH, ANVISA and the IMB on behalf of the EMA 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, which would 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 and our other 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 have engaged other parties for our other 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 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.

We specifically face competition from companies with approved treatments of Gaucher disease. In addition to Elelyso, there are two other ERTs for the treatment of Gaucher disease; Cerezyme and VPRIV. To a much lesser extent, we also compete with Actelion. In addition, Cerdelga, Genzyme's orally-delivered small molecule drug for the treatment of Gaucher disease, was approved in 2014.

There are two approved ERTs for the treatment of Fabry disease; Fabrazyme and Replagal. Fabrazyme is available in the United States and the European Union. Replagal is available in the European Union. In 2012, Shire elected to withdraw its BLA for Replagal in the United States. In addition, we are aware of other clinical stage, early clinical stage and experimental drugs which are being developed for the treatment of Fabry disease.

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 iBio, Medicago and Greenovation Biotech GmbH, none of which are cell-based. Rather, such companies base their product development on transgenic plants or whole plants.

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 successfully manage our growth, there could be a material adverse impact on our business, results of operations and financial condition.**

We have grown rapidly and expect to continue to grow. 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 shareholders.

**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, chemists, biologists 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 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, financial condition and results of operations.



**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, financial condition and results of operations.

**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, financial condition and results of operations. In addition, the existence of a product liability claim could affect the market price of our common stock.

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

Increasing healthcare expenditures have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would result in changes in the U.S. healthcare system have been introduced or proposed in the U.S. Congress and in some state legislatures within the United States, including reductions in the pricing of prescription products and changes in the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products. Legislation passed in recent years has imposed certain changes to the way in which drugs, including our product candidates, are covered and reimbursed in the United States. For example, federal legislation and regulations have implemented new reimbursement methodologies for certain drugs, created a voluntary prescription drug benefit, Medicare Part D, and have imposed significant revisions to the Medicaid Drug Rebate Program. The PPACA imposes yet additional changes to these programs. We believe that legislation that reduces reimbursement for our product candidates could adversely impact how much or under what circumstances healthcare providers will prescribe or administer our products, 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 products, 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 net operating loss carryforwards, or “NOLs”, as of December 31, 2014, are equal to approximately \$138.8 million, of which approximately \$17 million may be restricted under Section 382 of the Internal Revenue Code of 1986, as amended, or the “Code.” Section 382 of the Code imposes limitations on a corporation’s ability to utilize NOLs to offset taxable income if the corporation experiences an “ownership change.” In general terms, an “ownership change” may result from transactions increasing the ownership of certain stockholders in the stock of a corporation by more than 50% over a three-year period. In the event that an ownership change has occurred, or were to occur, utilization of our NOLs would be subject to an annual limitation under Section 382, which is generally the fair market value of the pre-change entity multiplied by the long-term tax exempt rate, which is published monthly by the Internal Revenue Service.

**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 our subsidiary 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 which would have a material adverse effect on our business, results of operations and financial condition.

## Risks Related to Regulatory Matters

### **We are subject to extensive governmental regulation including the requirement of FDA or comparable approval before our drug candidates may be marketed.**

Both before and after approval of our drug candidates, 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, financial condition and results of operations.**

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 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 Biologic License Application (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 FDA's, the EMA's and foreign regulatory authorities' regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the drug candidate and requires substantial resources for research, development and testing. Taliglucerase alfa has been approved for marketing in the United States, Israel, Brazil, Mexico, Chile and Uruguay, and marketing applications are outstanding in other countries. Even if we comply with all the requests of regulatory authorities, the authorities may ultimately reject the marketing applications filed for taliglucerase alfa or that we file for our other product candidates in the future, if any, or we might not obtain regulatory clearance in a timely manner for taliglucerase alfa in certain countries or for any of our other drug candidates. 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, financial condition and results of operations. 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, financial condition and results of operations.

**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.

**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.

Foreign regulations regarding orphan drugs are similar to those in the United States but there are several conceptual differences. For example, the exclusivity period in the European Union is generally 10 years. The EMA/European Commission has granted orphan drug designation and exclusivity to VPRIV in the European Union. For this reason, CHMP has recommended that the EC not issue a Marketing Authorization for taliglucerase alfa in the European Union. Therefore, VPRIV has orphan market exclusivity in the European Union for a 10-year period commencing on its authorization in August 2010 which may have a material adverse effect on our business, results of operations and financial condition.

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. None of our currently developed 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 that 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.

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

**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, 2014, we had 94 pending patent applications and one joint pending patent application with a third party. 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, 2014, we hold, or have license rights to, 64 patents. If patent rights covering our products or technologies are not sufficiently broad, they may not provide us with sufficient proprietary protection or competitive advantages against competitors with similar products and technologies. Furthermore, if the U.S. Patent and Trademark Office or foreign patent offices issue patents to us or our licensors, others may challenge the patents or circumvent the patents, or the patent office or the courts may invalidate the patents. Thus, any patents we own or license from or to third parties may not provide any protection against our competitors and those who infringe upon our patents.

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

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

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

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

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

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

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

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

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

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

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

commercial sale of the relevant product.

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

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

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

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

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

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

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

**Because a certain portion of our expenses is incurred in New Israeli Shekels, or NIS, 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 the OCS. 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, we are prohibited from transferring the OCS-financed technologies and related intellectual property rights outside of the State of Israel, except under limited circumstances and only with the approval of the OCS' Research Committee. We may not receive the required approvals for any proposed transfer and, if received, we may be required to pay the OCS a portion of the consideration that we receive upon any sale of such technology by a non-Israeli entity. The scope of the support received, the royalties that we have already paid to the OCS, the amount of time that has elapsed between the date on which the know-how was transferred and the date on which the OCS 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 the OCS. 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, 2013 and 2014, we recorded grants totaling \$3.4 million and \$5.1 million from the OCS, respectively. The grants represent 10.4% and 17.2%, respectively, of our gross research and development expenditures for the years ended December 31, 2013 and 2014. 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.**

Most of our directors and none of our officers are residents of the United States, and 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.

### **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:

- Purchases of Uplyso by Fiocruz;
- Pfizer's and our commercialization efforts for Elelyso;
- the results of our ongoing studies regarding our product candidates;
- announcements regarding partnerships or collaborations by us or our competitors;
- 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.**

The market price of our common stock could drop significantly if our existing shareholders sell a large number of shares of our common stock or are perceived by the market as intending to sell them. All 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. At December 31, 2014, there were options to purchase common stock issued and outstanding and unvested restricted shares covering 7,465,025 shares of our common stock with a weighted average exercise price of \$3.96 per share. Also at December 31, 2014, there were 1,923,444 shares of common stock remaining available for future for issuance in connection with future grants of incentives under our amended 2006 stock incentive plan.

**Servicing our debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our debt.**

Our ability to pay interest on, or to make any scheduled payment of the principal of, the 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 indenture governing the Notes and the agreements governing future indebtedness may restrict us from adopting any of these alternatives. 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. The failure to generate sufficient cash flow or to effect any of these alternatives could significantly adversely affect the value of the Notes and our ability to pay amounts due under the Notes.

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

The outstanding Notes represent a significant amount of indebtedness and 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, financial condition and results of operations. For example, it could:

- make it more difficult for us to satisfy our financial obligations, including with respect to the Notes; result in an event of default 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 Notes surrendered to us by holders upon a fundamental change (as described in the indenture governing the Notes), which failure would result in an event of default with respect to the 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, financial condition and results of operations and our ability to meet our payment obligations under the Notes and our other indebtedness. Our ability to make payments with respect to the Notes and to satisfy any other debt obligations will depend 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.

**Any conversion of the Notes will dilute the ownership interest of our existing stockholders, including holders who had previously converted their notes.**

The conversion of some or all of the Notes 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 the Notes may encourage short selling by market participants because the conversion of the Notes could depress the price of our common stock.

**Our common stock is listed for 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 MKT 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 MKT 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 MKT 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, executive officers, principal shareholders and affiliated entities 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 shareholders.**

Our directors, executive officers, principal shareholders and affiliated entities beneficially own, in the aggregate, approximately 33% of our outstanding common stock. 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 shareholders. 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 shareholders. This could prevent the consummation of transactions favorable to other shareholders, such as a transaction in which shareholders might otherwise receive a premium for their shares over current market prices.

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

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

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

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

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

There have been other changing laws, regulations and standards relating to corporate governance and public disclosure in addition to the Sarbanes-Oxley Act, as well as new regulations promulgated by the Commission and rules promulgated by the national securities exchanges, including the NYSE MKT 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 shareholders. 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 shareholder 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 shareholders may impede a takeover of our company and may prevent a transaction that is favorable to our shareholders.

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.

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 \$85,000 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. We have leased the facility through 2016, subject to three options exercisable by us to extend the term for a five-year period, for an aggregate of 15 additional years. Upon the exercise of each option to extend the term of the lease, if any, the then current base rent shall be increased by 10%. We also lease an office in Ramat Gan, Israel, for approximately \$2,500 per month.

### Item 3. Legal Proceedings

We are not involved in any material legal proceedings.

### Item 4. Mine Safety Disclosures

Not applicable.

**PART II**

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

Our common stock began trading on the NYSE MKT (formerly, the American Stock Exchange) on March 12, 2007 under the symbol "PLX." Our common stock is also listed on the TASE under the symbol "PLX." The following table sets forth the quarterly high and low closing prices for our common stock on the NYSE MKT.

	Price Range	
	High	Low
Fourth Quarter 2014	\$2.65	\$1.80
Third Quarter 2014	\$3.60	\$2.37
Second Quarter 2014	\$4.84	\$3.65
First Quarter 2014	\$5.26	\$3.85
Fourth Quarter 2013	\$4.60	\$3.72
Third Quarter 2013	\$5.68	\$4.39
Second Quarter 2013	\$5.67	\$4.81
First Quarter 2013	\$6.15	\$5.03

These quotations reflect prices between dealers and do not include retained mark-ups, mark-downs and commissions and may not necessarily represent actual transactions. There were approximately 85 holders of record of our common stock at March 1, 2015. A substantially greater number of holders of our common stock are "street name" or beneficial holders, whose shares are held of record by banks, brokers and other financial institutions. To date, we have not declared or paid any cash dividends on our common stock. We do not anticipate paying any dividends on our common stock in the foreseeable future.

**STOCK PERFORMANCE GRAPH**

The following graph compares the cumulative total shareholder return data for our common stock from December 31, 2009 through December 31, 2014 to the cumulative return over such time period of (i) The NYSE MKT Composite Index and (ii) The Nasdaq Biotechnology Index. The graph assumes an investment of \$100 on December 31, 2009 in each of our common stock, the stocks comprising the NYSE MKT Composite 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, 2014, 2013 and 2012 and the selected consolidated balance sheet data as of December 31, 2014 and 2013, 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, 2011 and 2010 and the balance sheet data as of December 31, 2012, 2011 and 2010 are derived from audited financial statements not included in this Annual Report. The historical results presented below are not necessarily indicative of future results.

	Year Ended December 31,				
	2010	2011	2012	2013	2014
	(in thousands, except share and per share amounts)				
<b>Consolidated Statement of Operations Data:</b>					
Revenues	\$6,642	\$8,386	\$34,870	\$10,479	\$13,651
Our share in the Collaboration Agreement	4,602	(5,418 )	(446 )	1,034	1,509
Cost of revenues	4,383	1,525	8,144	5,428	9,053
Gross profit	6,861	1,443	26,280	6,085	6,107
Research and development expenses, net	29,951	31,043	28,689	24,816	21,650
Selling, General and administrative expenses	6,876	6,931	9,763	8,385	9,661
Financial income (expenses), net	968	2	554	(674 )	(4,739 )
Net loss	\$28,998	\$36,529	\$11,618	\$27,790	\$29,943
Net loss per share of common stock, basic and diluted	\$0.36	\$0.43	\$0.13	\$0.30	\$H.32
Weighted average number of shares of common stock used in computing net loss per share of common stock	80,960,300	84,645,364	90,845,901	92,368,138	92,891,846
<b>Consolidated Balance Sheet Data:</b>					
Cash and cash equivalents	\$35,900	\$27,001	\$52,035	\$86,398	\$54,767
All other assets	28,829	24,804	26,692	26,935	23,703
Total assets	64,729	51,805	78,727	113,333	78,470
Current liabilities	18,903	18,693	25,755	26,696	26,210
Total liabilities	76,052	77,882	82,084	140,279	134,071
Capital deficiency	11,323	26,077	3,357	26,946	55,601

## **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. Using our ProCellEx system, we are developing a pipeline of proprietary, clinically superior versions of recombinant therapeutic proteins that primarily target large, established pharmaceutical markets and that rely upon known biological mechanisms of action. Our initial commercial focus has been on complex therapeutic proteins, including proteins for the treatment of genetic disorders, such as Gaucher disease and Fabry disease. With our experience, and having successfully developed Elelyso, our first drug product, 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. Because we are primarily targeting biologically superior versions of highly active, well-tolerated and commercially successful therapeutic proteins, we believe our development process is associated with relatively less risk compared to other biopharmaceutical development processes for completely novel therapeutic proteins. We are now also applying the unique properties of our ProCellEx system for the oral delivery of therapeutic proteins.

On May 1, 2012, the U.S. Food and Drug Administration, or the FDA, approved for sale our first commercial product, taliglucerase alfa for injection, which is being marketed in the United States and Israel under the brand name Elelyso, as 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 by ANVISA in March 2013, by the Israeli MOH in September 2012 and by other regulatory agencies in other countries. Taliglucerase alfa is being marketed under the name Uplyso in Brazil and certain other Latin American countries.

In August 2014, the FDA approved Elelyso for injection for pediatric patients and the Israeli MOH approved the pediatric indication in January 2015. Prior to the U.S. pediatric approval, Elelyso was approved for pediatric indications in Australia and Canada but in no other jurisdiction. In September 2014, CONITEC announced that it had decided to give a positive funding recommendation for Uplyso in the treatment of adult patients with types 1 and 3 Gaucher disease, and established that Uplyso will be the first choice for treatment for new adult Gaucher patients in Brazil.

Taliglucerase alfa is our proprietary, recombinant form of GCD that is produced or expressed through ProCellEx. Taliglucerase alfa is the first plant cell-based recombinant therapeutic protein to be approved by the FDA or by the regulatory authorities with jurisdiction over any substantial market. Gaucher disease is a rare and serious lysosomal storage disorder with severe and debilitating symptoms. Gaucher patients suffer from mutations in or deficiencies of GCD, an enzyme that is naturally found in human cells.

Since May 2012, taliglucerase alfa has been marketed in the United States by Pfizer Inc., or Pfizer, our commercialization partner, as provided in the exclusive license and supply agreement by and between Protalix Ltd., our wholly-owned subsidiary, and Pfizer, which we refer to as the Pfizer Agreement. We granted Pfizer an exclusive, worldwide license to develop and commercialize taliglucerase alfa under the Pfizer Agreement, but we retained those rights in Israel, and later in Brazil. We have agreed to a specific allocation between Protalix Ltd. and Pfizer of the responsibilities for the continued development efforts for taliglucerase alfa outside of Israel. Protalix Ltd. has been marketing taliglucerase alfa in Israel since 2013 and in Brazil since January 2014.

On June 18, 2013, we entered into a Supply and Technology Transfer Agreement, or the Brazil Agreement, with Fiocruz, for taliglucerase alfa. The 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. Under the agreement, Fiocruz committed to purchase at least approximately \$40 million worth of taliglucerase alfa during the first two years of the term. Since the agreement went into effect, we have recorded revenues of approximately \$3.5 million for sales of taliglucerase alfa to Fiocruz in 2014 and, during the first quarter of 2015, we received a purchase order for approximately \$5.7 million of taliglucerase alfa out of which we have delivered approximately \$1.7 million of the product. In subsequent years, Fiocruz is required to purchase at least approximately \$40 million worth of taliglucerase alfa per year. We are not required to complete the final stage of the technology transfer until Fiocruz purchases at least approximately \$280 million worth of taliglucerase alfa.

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.

To facilitate the arrangement with Fiocruz, we and Pfizer agreed to an amendment of our exclusive license and supply agreement, which amendment provides for the transfer of the commercialization and other rights to taliglucerase alfa in Brazil back to us. As consideration for the transfer of the commercialization and supply rights, we agreed to pay Pfizer a maximum amount of approximately \$12.5 million from its net profits (as defined in the license and supply agreement) per year. Pfizer has also agreed to perform certain transitional services in Brazil on our behalf in connection with the supply of taliglucerase alfa to Fiocruz.

We will pay a fee equal to 5% of the net proceeds generated in Brazil to our agent for services provided in assisting us complete the Brazil Agreement pursuant to an agency agreement between us and the agent. The agency agreement will remain in effect with respect to the Brazil Agreement until the termination thereof.

We are cooperating with Pfizer to obtain marketing approval for taliglucerase alfa in additional countries and jurisdictions. In addition to those countries in which taliglucerase alfa has been approved, marketing authorization applications have been filed in other countries.

Currently, patients are being treated with taliglucerase alfa on a commercial basis in the United States, Brazil, Israel and Chile. In addition taliglucerase alfa is currently being provided to Gaucher patients under special access agreements or named patient provisions in certain countries.

In addition to taliglucerase alfa, we are developing an innovative product pipeline using our ProCellEx protein expression system. Our product pipeline currently includes, among other candidates:

(1) PRX-102, or alpha-GAL-A, a therapeutic protein candidate for the treatment of Fabry disease, a rare, genetic lysosomal disorder in humans, currently in an ongoing phase I/II clinical trial. We expect to report interim efficacy and safety results for the 1 mg/kg dose group of the trial during the third quarter of 2015 and to report final efficacy and safety results for the 0.2mg, 1 mg and 2mg/kg dose groups of the trial during the fourth quarter of 2015. We expect to enter into a pivotal phase III by early 2016.

(2) PRX-106, our oral antiTNF product candidate which is being developed as an orally-delivered anti inflammatory treatment for various inflammatory diseases using plant cells as a natural capsule for the expressed protein. We expect to initiate a proof of concept efficacy study during 2015 and announce results by early 2016.

(3) PRX-110, a proprietary plant cell recombinant human DNase under development for the treatment of cystic fibrosis, to be administered by inhalation. We expect to initiate a proof of concept efficacy study during 2015 and announce results by early 2016.

(4) PRX-112, an orally administered glucocerebrosidase enzyme for the treatment of Gaucher patients utilizing oral delivery of the recombinant GCD enzyme produced and encapsulated within carrot cells. PRX-102 has been the subject of successful proof of concept clinical trials, as described in Item 1, and we intend to focus our efforts on a new formulation of the treatment during 2015.

Except for the rights to commercialize taliglucerase alfa worldwide (other than Brazil and Israel), which we licensed to Pfizer, we hold the worldwide commercialization rights to all of our proprietary development candidates. We have built an internal marketing team designed to serve the Israeli and Brazilian market for taliglucerase alfa and we intend to establish internal commercialization and marketing teams for some of our other product candidates in certain regions, subject to required marketing approvals, as the need arises. 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. Most 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***

Currently, our source of revenues comes from sales of taliglucerase alfa pursuant to our license agreement with Pfizer, our sales of taliglucerase alfa in Israel and Brazil and from milestone payments under the Pfizer Agreement. We recognize revenue when the earnings process is complete, which is when revenue is realized or realizable and earned, there is persuasive evidence a revenue arrangement exists, delivery of goods or services has occurred, the sales price is fixed or determinable and collectability is reasonably assured.

We recognize revenue from milestone payments received pursuant to the Pfizer Agreement in accordance with guidance regarding revenue recognition and accounting for revenue arrangements with multiple deliverables. Pursuant to this guidance, we determine whether our arrangement with Pfizer involves multiple revenue-generating deliverables that should be accounted for as a combined unit of accounting or separate units of accounting for revenue recognition



purposes. If we determine that there are multiple units of accounting, the consideration from the arrangement is allocated among the separate units based on a relative fair value allocation. If the arrangement represents a single unit of accounting, the revenue is recognized over the performance obligation period. As the arrangement with Pfizer requires our continued involvement with respect to the proposed commercialization of taliglucerase alfa, the non-refundable, up-front license payments we received from Pfizer are deferred and recognized over the related performance period. We estimated the performance period of 14 years based on the date that the last relevant patent relating to taliglucerase alfa expires. The \$25.0 million milestone payment received in connection with the FDA's approval of taliglucerase alfa in the United States was considered to be a substantive milestone for purposes of revenue recognition, and, accordingly, was recorded as revenue during the period in which the milestone was achieved.

Under the terms and conditions of the Pfizer Agreement, we are entitled to 40% of the net profits or loss from sales of taliglucerase alfa by Pfizer and reimbursement of our certain related expenses we incur in connection with Pfizer's sales (other than those related to sales in Israel and Brazil). We hold all rights to taliglucerase alfa in Israel and Brazil. We recognize our share of net profit or loss under the Pfizer Agreement based on reports we receive from Pfizer summarizing the results of the collaborative activities under the agreement for the applicable period. Under the terms of the Pfizer Agreement, for its subsidiaries operating outside the United States, financial information is included based on the fiscal year ending November 30, while financial information for the U.S. entity is included based on the fiscal year ending December 31.

We recognize revenues received from the sale of a product when the sales price is fixed or determinable and collectability is reasonably assured. The revenues represent our cost with respect to the product sold.

We recognize net product revenue from our sales of Elelyso in Israel when persuasive evidence of an arrangement exists, the product has been delivered to the customer, title and risk of loss have passed to the customer, the price to the buyer is fixed or determinable and collection from the customer is reasonably assured. Product sale transactions are evidenced by customer purchase orders, customer contracts, invoices and/or the related shipping documents. Amounts collected from customers and remitted to governmental authorities, which represents value-added taxes related to Elelyso sales in Israel, are presented on a net basis in our Consolidated Statements of Operations, in that taxes billed to customers are not included as a component of net product revenues.

**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 – alpha-GAL-A	Phase I/II clinical trial, ongoing	Report interim efficacy and safety results for the 1 mg/kg dose group during the third quarter of 2015  Report final efficacy and safety results for the 0.2mg, 1 mg and 2mg/kg dose groups during the fourth quarter of 2015
PRX 106 – Oral antiTNF	Preclinical	Initiate proof of concept efficacy study
PRX-110 – AIR DNase	Preclinical	Initiate proof of concept efficacy study
PRX 112 – Oral Glucocerebrosidase	Phase IIa clinical trial	Develop new formulation

We anticipate incurring increasing costs in connection with the continued development of all four 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 the OCS. 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 and Development Law, 1984” in Item 1 of this Annual Report. There can be no assurance that we will continue to receive grants from the OCS in amounts sufficient for our operations, if at all.

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. While we are currently focused on advancing each of our product development programs, our future research and development expenses 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, financial condition and results of operations.”

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. The lengthy process of completing clinical trials and seeking regulatory approval 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.

For purposes of determining the fair value of the restricted shares of common stock granted to employees during the fiscal year ended December 31, 2013, our management used the fair value of our common stock which was the closing sale price of our common stock on the NYSE MKT on the date of grant.

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 described above has been 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.

***Year Ended December 31, 2014 Compared to the Year Ended December 31, 2013***

*Revenues*

We recorded revenue of \$13.7 million for the year ended December 31, 2014, an increase of approximately \$3.2 million, or 30%, compared to revenue of \$10.5 million for the year ended December 31, 2013. Revenues for the year ended December 31, 2014 include \$5.2 million of products sold in Israel and \$3.5 million in Brazil. Revenues also represent a pro rata amortization of the \$65.0 million upfront and milestone payments of \$1.1 million in each quarterly period.

*Our share in the Collaboration Agreement*

We recorded revenue of \$1.5 million as our share of net income in the collaboration under the Pfizer Agreement during the year ended December 31, 2014, an increase of approximately \$475,000, or 46%, compared to revenue of \$1.0 million recorded for the year ended December 31, 2013. Our share in the collaboration recorded for the year ended December 31, 2014 represents our 40% share of the net income generated during the period, which was primarily the result of revenues generated by Pfizer in the United States which exceeded the expenses during such period. Under the terms and conditions of the Pfizer Agreement, we record income or loss equal to 40% of the profit or loss realized from sales of taliglucerase alfa and related expenses incurred based on reports we receive from Pfizer summarizing the results of the collaborative activities under the Pfizer Agreement for the applicable period. Under the terms and conditions of the Pfizer Agreement, financial information of Pfizer's subsidiaries that operate outside the United States is included based on the fiscal year ending November 30, while financial information for the U.S. entity is included based on the fiscal year ending December 31.

*Cost of Revenues*

Cost of revenues was \$9.1 million for the year ended December 31, 2014, an increase of \$3.6 million, or 67%, compared to the cost of revenues of \$5.4 million for the year ended December 31, 2013. Cost of revenues for the year ended December 31, 2014 consists primarily of the costs of the \$1.1 million of products we delivered at cost to Pfizer under the Pfizer Agreement, write-down of inventory of \$1.7 million, and certain fixed costs relating to our manufacturing facility, including rent, depreciation, salary and maintenance expenses, amounting to approximately \$4.2 million, and to a much lesser extent, the direct cost of products we sold in Israel and Brazil for which revenues were recognized during the period. Cost of revenues for the years ended December 31, 2013 and 2014 include an aggregate of \$472,000 and \$1.1 million, respectively, in royalties payable to the OCS and to a certain academic institution in connection with gross sales of taliglucerase alfa during the period.

*Research and Development Expenses*

Research and development expenses were \$29.8 million for the year ended December 31, 2014, a decrease of \$3.6 million, or 11% from \$33.3 million for the year ended December 31, 2013. The decrease resulted primarily from a decrease of \$1.4 million in payroll and related expenses primarily due to a decrease in share-based compensation and a decrease of \$1.0 million in cost of 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.

*Selling, General and Administrative Expenses*

General and administrative expenses were \$9.7 million for the year ended December 31, 2014, an increase of \$1.3 million, or 15%, from \$8.4 million for the year ended December 31, 2013. The increase resulted primarily from sales and marketing expenses of approximately \$1.8 million, primarily in connection with sales in Brazil, which was partially offset by a decrease of \$383,000 in salaries expense.

*Financial Expenses and Income*

Financial expenses were \$4.7 million for the year ended December 31, 2014, compared to \$674,000 for the year ended December 31, 2013. Financial expenses resulted primarily from interest expense of \$3.1 million for the 4.5% convertible note and from the devaluation of the New Israeli Shekel against the U.S. dollar in the amount of \$1.3 million, which was partially offset by financial income which resulted primarily from interest earned on short term deposits.

*Year Ended December 31, 2013 Compared to the Year Ended December 31, 2012*

*Revenues*

We recorded revenue of \$10.5 million for the year ended December 31, 2013, an increase of approximately \$609,000, or 6%, compared to revenue of \$9.9 million for the year ended December 31, 2012, excluding the one-time \$25.0 million payment we received from Pfizer under the Pfizer Agreement in connection with the FDA's approval of taliglucerase alfa on May 1, 2012. The revenues represent our sales of taliglucerase alfa in Israel, the cost of products we deliver to Pfizer under the Pfizer Agreement and a pro rata amortization equal to \$1.1 million in each quarterly period resulting from the \$65.0 million upfront and milestone payments we received from Pfizer in 2009. The revenues for the year ended December 31, 2013 include \$5.0 million from products we sold in Israel.

### *Our share in the Collaboration Agreement*

We recorded revenue of \$1.0 million as our share of net income in the collaboration under the Pfizer Agreement during the year ended December 31, 2013, compared to the \$446,000 of loss recorded for the year ended December 31, 2012. Our share in the collaboration recorded for the year ended December 31, 2013 represents our 40% share of the net income generated during the period, which was primarily the result of revenues generated by Pfizer in the United States which exceeded the expenses during such period. Under the terms and conditions of the Pfizer Agreement, we record income or loss equal to 40% of the profit or loss realized from sales of taliglucerase alfa and related expenses incurred based on reports we receive from Pfizer summarizing the results of the collaborative activities under the Pfizer Agreement for the applicable period. Under the terms and conditions of the Pfizer Agreement, financial information of Pfizer's subsidiaries that operate outside the United States is included based on the fiscal year ending November 30, while financial information for the U.S. entity is included based on the fiscal year ending December 31.

### *Cost of Revenues*

Cost of revenues was \$5.4 million for the year ended December 31, 2013, a decrease of \$2.7 million, or 33%, compared to the cost of revenues of \$8.1 million for the year ended December 31, 2012. Cost of revenues for the year ended December 31, 2013 consists primarily of certain fixed costs relating to our manufacturing facility, including rent, depreciation, salary and maintenance expenses amounting to approximately \$4.9 million, and to a much lesser extent, the direct cost of products we sold in Israel and products we delivered to Pfizer for which revenues were recognized during the period. Cost of revenues for the years ended December 31, 2012 and 2013 include an aggregate of \$2.2 million and \$472,000, respectively, in royalties payable to the OCS and to a certain academic institution in connection with gross sales of taliglucerase alfa during the period. Prior to the FDA's approval of taliglucerase alfa, manufacturing costs related to taliglucerase alfa were classified as research and development expenses. Effective as of the FDA approval of taliglucerase alfa, we capitalize all manufacturing costs associated with taliglucerase alfa and expense such costs as cost of revenues, as applicable.

### *Research and Development Expenses*

Research and development expenses were \$33.3 million for the year ended December 31, 2013, a decrease of \$3.4 million, or 9.1% from \$36.7 million for the year ended December 31, 2012. The decrease resulted primarily from a decrease of \$2.1 million in payroll and related expenses primarily due to a decrease in share-based compensation and a decrease of \$1.2 million resulting from the winding down of certain clinical trials for taliglucerase alfa.



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.

#### *General and Administrative Expenses*

General and administrative expenses were \$8.4 million for the year ended December 31, 2013, a decrease of \$1.4 million, or 14%, from \$9.8 million for the year ended December 31, 2012. The decrease resulted primarily from a decrease of \$1.5 million in payroll and related expenses primarily due to a decrease in share-based compensation.

#### *Financial Expenses and Income*

Financial expense was \$674,000 for the year ended December 31, 2013, compared to financial income of \$554,000 for the year ended December 31, 2012. Financial expense resulted primarily from interest expense of \$1.0 million for the 4.5% convertible note which was partially offset by financial income which resulted primarily from interest earned on short term deposits.

### **Liquidity and Capital Resources**

#### *Sources of Liquidity*

As a result of our significant research and development expenditures and the lack of significant product sales revenue due to the recent launch of taliglucerase alfa in the United States and Israel, we have not been profitable and have generated operating losses since our inception. To date, we have funded our operations primarily with proceeds equal to \$31.3 million from the sale of shares of convertible preferred and ordinary shares of Protalix Ltd., and an additional \$14.1 million in connection with the exercise of warrants issued in connection with the sale of such shares, through December 31, 2008. In addition, on October 25, 2007, we generated gross proceeds of \$50 million in connection with an underwritten public offering of our common stock and on each of March 23, 2011 and February 22, 2012, we generated gross proceeds of \$22.0 million and \$27.2 million, respectively, in connection with underwritten public offerings of our common stock. We believe that the funds currently available to us as are sufficient to satisfy our capital needs for at least 12 months.

The following table summarizes our public funding sources since 2007:

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

In addition to the foregoing, on September 18, 2013, we completed a private placement of \$69.0 million in aggregate principal amount of 4.50% convertible notes due 2018, or the Notes, including \$9.0 million aggregate principal amount of Notes related to the offering's initial purchaser's over-allotment option, which was exercised in full.

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. Protalix Ltd. is also entitled to payments equal to 40% of the net profits earned by Pfizer on its global sales of taliglucerase alfa (except in Israel and Brazil). In calculating net profits there are certain agreed upon limits on the amounts that may be deducted from gross sales for certain expenses and costs of goods sold. 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.

#### *Cash Flows*

Net cash used in operations was \$29.2 million for the year ended December 31, 2014. The net loss for the year ended December 31, 2014 of \$29.9 million was further increased by a decrease of \$7.2 million in deferred revenues, but was partially offset by \$3.1 million in depreciation, \$1.4 million in financial expenses mainly due to exchange rate differences and share based compensation of \$1.2 million. Net cash used in investing activities for the year ended December 31, 2014 was \$1.0 million and consisted primarily of purchases of property and equipment.

Net cash used in operations was \$30.7 million for the year ended December 31, 2013. The net loss for the year ended December 31, 2013 of \$27.8 million was further increased by a decrease of \$7.2 million in deferred revenues and an increase of \$3.9 million in inventories, but was partially offset by share based compensation of \$4.1 million and \$3.5 million in depreciation. Net cash used in investing activities for the year ended December 31, 2013 was \$2.1 million and consisted primarily of purchases of property and equipment. Net cash provided by financing activities was \$66.9 million, consisting primarily of net proceeds from our offering of 2013 4.5% convertible notes.

*Future Funding Requirements*

We expect to continue to incur significant expenditures in the near future. We expect to continue to incur significant research and development expenses, including expenses related primarily to the clinical trials of PRX-102 and the advancement of our other product candidates into clinical trials.

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 factors, including the progress of Pfizer's commercialization efforts for taliglucerase alfa in the United States and other countries and, if anticipated marketing approvals of taliglucerase alfa are granted in other jurisdictions, the progress of Pfizer's global commercialization efforts for taliglucerase alfa, 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, 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. 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, 2012, 2013 or 2014.

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, 2012, 2013 or 2014.

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

We have no off-balance sheet arrangements as of December 31, 2013 and 2014.

### **Recently Issued Accounting Pronouncements**

Certain recently issued accounting pronouncements are discussed in Note 1(p) 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, 2014:

(U.S. dollars in thousands)	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Convertible notes	\$81,420	\$ 3,105	\$ 6,210	\$ 72,105	-
Operating lease obligations	\$3,944	\$ 1,519	\$ 2,425	-	-
Purchase obligations (1)	\$1,766	\$ 1,766			-
Certain clinical contract	\$1,226	\$ 981	\$ 245		-
Liability for employee rights upon retirement	\$2,253	-	-	-	\$ 2,253
Total	\$90,609	\$ 7,371	\$ 8,880	\$ 72,105	\$ 2,253

(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, 2014.

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 \$0.3 million and would be payable, if at all, as our projects progress over the course of a number of years. The royalty payments payable in connection with sales of each of our product candidates, if any, shall not exceed low, single-digit percentages of net sales of the product.

**Selected Quarterly Financial Data (unaudited)**

	Three Months Ended							
	2013				2014			
	(U.S. dollars in thousands)							
	March 31	June 30	Sept. 30	Dec. 31	March 31	June 30	Sept. 30	Dec. 31
Revenues	\$3,568	\$2,264	\$2,284	\$2,363	\$6,696	\$2,425	\$2,396	\$2,134
Net profit (loss) for the period	\$(4,321)	\$(6,837)	\$(5,747)	\$(10,885)	\$(7,345)	\$(6,119)	\$(8,010)	\$8,469
Earnings (loss) per share of common stock, basic and diluted	\$(0.05 )	\$(0.07 )	\$(0.06 )	\$(0.12 )	\$(0.08 )	\$(0.07 )	\$(0.09 )	\$(0.09 )

**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 income 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,		
	2012	2013	2014
Average rate for period	3.856	3.611	3.578
Rate at year-end	3.733	3.471	3.889

To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rate of the U.S. dollar against the NIS.

These measures, however, may not adequately protect us from material adverse effects due to the impact of inflation in Israel.

### **Interest Rate Risk**

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

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

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

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

None.

## Item 9A. Controls and Procedures

### Evaluation of Disclosure Controls and Procedures

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

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

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

### Management 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, 2014, the end of our fiscal year. Management based its assessment on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Management’s assessment included evaluation of elements such as the design and operating effectiveness of key financial reporting controls, process documentation, accounting policies and our overall control environment.

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

The effectiveness of our internal control over financial reporting as of December 31, 2014 has been audited by Kesselman & Kesselman, an independent registered public accounting firm, as stated in their report included herein.

#### Inherent Limitations on Effectiveness of Controls

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

#### Changes in internal controls

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15f and 15d-15f under the Exchange Act) that occurred during the year ended December 31, 2014 that have materially affected, or that are reasonably likely to materially affect, our internal control over financial reporting.

#### **Item 9B. Other Information**

None.

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## PART III

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

Our directors and executive officers, their ages and positions as of March 1, 2015 are as follows:

<b>Name</b>	<b>Age</b>	<b>Position</b>
<b>Directors</b>		
Shlomo Yanai	62	Chairman of the Board
Moshe Manor	58	Director, President and Chief Executive Officer
Amos Bar Shalev (1)(2)(3)	62	Director
Zeev Bronfeld (1)(2)(3)	63	Director
Yodfat Harel Buchris (1)(2)(3)	42	Director
Roger D. Kornberg, Ph.D.	67	Director
Aharon Schwartz, Ph.D.	72	Director
<b>Executive Officers</b>		
Einat Brill Almon, Ph.D.	55	Senior Vice President, Product Development
Yossi Maimon, CPA	44	Vice President, Chief Financial Officer, Treasurer and Secretary
Tzvi Palash	58	Chief Operating Officer
Yoseph Shaaltiel, Ph.D.	61	Executive VP, Research and Development

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(1) Member of Nominating Committee

(2) Member of Audit Committee

(3) Member of Compensation Committee

**Shlomo Yanai.** Mr. 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 a director of Lumenis Ltd. (NASDAQ:LMNS). Mr. Yanai served as President and Chief Executive Officer of 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 International Advisory Board, MBA Program of Ben-Gurion University of the Negev, 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 has 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<sup>®</sup> and Azilect<sup>®</sup>. Previously, he served as director of Teva Israel. Most recently, Mr. Manor serves on the Board of Directors of Kamedis Ltd. and Coronis Partners, and as Chairman of the Board of Directors of a startup company named 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. Mr. Bar Shalev served as a director of Protalix Ltd. from 2005 through January 31, 2008, and as our director from December 31, 2006 through January 31, 2008. Mr. Bar Shalev was not nominated for reelection at our annual meeting of shareholders on January 31, 2008. On July 14, 2008, our Board of Directors appointed Mr. Bar Shalev to serve on the board, at which time he was reappointed to the board of directors of Protalix Ltd. as well. Mr. Bar Shalev brings to us extensive experience in managing technology companies. Currently, Mr. Bar Shalev serves on the boards of directors of Ocure Ltd. and Velox Ltd., privately-held Israeli companies. From 2004 through 2013, Mr. Bar Shalev served as a director of Technorov Holdings (1993) Ltd. and managed its portfolio. In addition, he has served on the board of directors of Aposense Ltd. (TASE: APOS), an Israeli publicly-traded company listed on the TASE, since 2011, and 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 many other companies, including, among others, 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 31, 2006. From 2010 through July 2014, he served as the interim Chairman of our Board of Directors. Mr. Bronfeld brings to us vast experience in management and value building of biotechnology companies. Mr. Bronfeld is an experienced businessman who is involved in a number of biotechnology companies. He is a co-founder of Biocell Ltd. (TASE:BCEL), an Israeli publicly traded holding company specializing in biotechnology companies, and has served as its Chief Executive Officer since 1986. Mr. Bronfeld currently serves as a director of Biocell Ltd. and Macrocare Ltd. (NASDAQ: MCUR) and the as chairman of the board of directors of D.N.A. Biomedical Solutions Ltd. (TASE:DNA), 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 The Trendlines Group, Contipi Medical Ltd. and TransBiodiesel Ltd. From 2004 through 2012, Mr. Bronfeld served as a director of D. Medical Industries Ltd., a company that was dually-listed on the Nasdaq and the TASE. 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.

**Yodfat Harel Buchris.** Mrs. Harel Buchris has served as our director since June 2007. Commencing in February 2014, Mrs. Harel Buchris serves as the employer representative in Israel's National Labor Court and she currently serves on the board of directors of YP and 6 Partners Ltd., a Business Consulting and Investment Company. From 2006 to 2013, Mrs. Harel Buchris served as a Managing Director of Tamares Capital Ltd., a private investment group with interests in real estate, technology, manufacturing, leisure and media. At Tamares Capital, Mrs. Harel Buchris served as the Business Development Director and the head of the Israel office. Prior to joining Tamares Capital, from 2004 to 2006, she was the Head of the Medical Desk of Orbotech, Ltd. (NASDAQ:ORBK), a company providing high-tech inspection and imaging solutions for bare printed circuit board (PCB), flat panel display (FPD) and PCB assembly manufacturing worldwide. Prior to that, from 1994 to 2003, she was a Managing Director of Harel-Hertz Investment House Ltd., a business investment company with offices in Tel Aviv, Israel and Tokyo, Japan. In 2002,

Harel-Hertz Investment House became the Israeli representative office for ITX Corporation, a publicly-traded company in Japan. Mrs. Harel Buchris has served on the board of directors of Tamares Capital, Tamares Hotels, El Al, British Israel, Storewiz, N-trig, Secure Pharma, Siklu and Tamares Telecom. Mrs. Harel Buchris holds a B.A. in Communications and Political Science from Bar Ilan University and an executive M.B.A. from Bradford University, Great Britain. She has also completed programs in Mediation at Gome, Israel Mediation Center, Directors' Studies and Advanced Advertising and Marketing at the Israel Management Center. We believe Mrs. Harel Buchris' qualifications to serve on our Board of Directors include her experience in the management of Israeli and other businesses.

**Roger D. Kornberg, Ph.D.** Professor Kornberg has served as our director since February 2008. He has served as a director of OphthaliX Inc. (OTCBB:OPLI), since 2012 and of Biozone Pharmaceuticals, Inc. (otcqb:BZNE) since 2014. He served as a director of Teva (NASDAQ:TEVA, TASE:TEVA) from 2007 through 2013. He also serves as the Chief Scientist and a director of Biozone Pharmaceuticals. Professor Kornberg is a member of the U.S. National Academy of Sciences and the Winzer Professor of Medicine in the Department of Structural Biology at Stanford University, Stanford, California. He has been a member of the faculty of Stanford University since 1972. Prior to that, he was a professor at Harvard Medical School. Professor Kornberg is a renowned biochemist and in 2006 he was awarded the Nobel Prize in Chemistry in recognition for his studies of the molecular basis of eukaryotic transcription, the process by which DNA is copied to RNA. Professor Kornberg is also the recipient of several awards, including the 2001 Welch Prize, the highest award granted in the field of chemistry in the United States, and the 2002 Leopold Mayer Prize, the highest award granted in the field of biomedical sciences from the French Academy of Sciences. He received his B.S. in Chemistry from Harvard University in 1967 and his Ph.D. in Chemistry from Stanford University in 1972. He holds honorary degrees from universities in Europe and Israel, including the Hebrew University in Jerusalem, where he currently is a visiting professor. We believe Professor Kornberg's qualifications to serve on our Board of Directors include his expertise in chemistry and medicine and his experience in the academic arena.

**Aharon Schwartz, Ph.D.** Dr. Schwartz has retired from Teva (NASDAQ:TEVA, TASE: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 a number of life science companies, including BiolineRx Ltd. (NASDAQ:BLRX, TASE:BLRX), Yissum-the TTO of the Hebrew University of Jerusalem, DPharm Ltd. (TASE:DPRM), BioCancell Ltd. (TASE:BICL), CureTech Ltd. and Biomas Ltd., and a member of the board of directors of Alcobra Ltd. (NASDAQ:ADHD). Dr. Schwartz received his Ph.D. in organic chemistry in 1978 from the Weizmann Institute, 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 extensive experience in the life-science and pharmaceutical industry.

**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 then Senior Vice President, Product Development, and became our Senior Vice President, Product Development on December 31, 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 Biogenics Ltd., a company that developed an autologous platform for tissue-based protein drug delivery. Biogenics, based in Israel, is a wholly-owned subsidiary of 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. on October 15, 2006 as its Chief Financial Officer and became our Vice President and Chief Financial Officer on December 31, 2006. Prior to joining Protalix, from 2002 to 2006, he served as the Chief Financial Officer of Colbar LifeScience Ltd., 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. 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.

**Tzvi Palash.** Mr. Palash has served as Protalix Ltd.'s Chief Operating Officer since September 6, 2010. Prior to joining Protalix Ltd., from 2006 through 2010, Mr. Palash served as a General Manager of ColBar LifeScience Ltd. In that position, Mr. Palash served as a member of the Global Aesthetic Management Team at the Consumer Group of Johnson & Johnson. Prior to that, from 2001 through 2006, Mr. Palash served as the Vice President, Operations of ColBar LifeScience, and he has served in different positions at Teva. Mr. Palash has an M.Sc. in Biochemistry from the Hebrew University and a B.Sc. in Biology from the Tel Aviv University.

**Yoseph Shaaltiel, Ph.D.** Dr. Shaaltiel founded Protalix Ltd. in 1993 and has served as a member of our Board of Directors and as our Vice President, Research and Development since December 31, 2006. 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 seven 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.

#### **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 2014. 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% shareholders.



## **Audit Committee**

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 MKT and applicable rules and regulations of the Commission. Messrs. Bar Shalev and Bronfeld, and Mrs. Harel Buchris have been appointed by the Board of Directors to serve on the Audit Committee until their respective successors have been duly elected.

Our Audit Committee operates under a formal charter that governs its duties and conduct.

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 the Sarbanes-Oxley Act of 2002.

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.

Messrs. Bar Shalev and Bronfeld 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 MKT.

## **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 shareholder 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. Except for the compensation offered to our new President and Chief Executive Officer, we did not make any changes to the compensation of our executive officers. The Compensation Committee plans to convene later in 2015 to evaluate the current incentive plans and plan going forward, including updating its peer companies, as substantially all of the 2012 compensation milestones described below have expired and are no longer in effect.



The companies reviewed by the Compensation Committee in making compensation recommendations to our Board of Directors in 2012 include, among others, the following companies:

.	InterMune, Inc.
.	Vivus, Inc.
.	Biomarin Pharmaceutical Inc.
.	Rigel Pharmaceuticals, Inc.
.	Momenta Pharmaceuticals, Inc.
.	Nektar Therapeutics
.	Theravance, Inc.
.	Dendreon Corp.

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 an executive compensation report and 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 Chief Operating Officer, who we refer to collectively as the “Named Executive Officers,” are discussed herein. The above discussion does not include compensation granted to Dr. David Aviezer, our former President and Chief Executive Officer, as he retired from the Company in November 2014 and is no longer to the same compensation. On July 15, 2012, our Board of Directors adopted certain recommendations of the Compensation Committee regarding the compensation of our Named Executive Officers with no change in the base salary component.

**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 in the first quarter of the year, unless such bonus was, by its terms, made payable upon the achievement of a specific milestone. The Compensation Committee has not fixed a minimum or maximum award for any executive officer's annual discretionary bonus, unless specified in the officer's employment agreement.

Each of our executive officers is eligible for a discretionary annual bonus under his or her employment agreement. The Compensation Committee has not fixed a minimum or a maximum amount for any officer's annual discretionary bonus, nor is any executive officer entitled to a minimum or maximum bonus amount under his or her employment agreement.

On July 15, 2012, our Board of Directors adopted certain recommendations of the Compensation Committee regarding the compensation of our Named Executive Officers at that time, including the grant of certain incentive bonuses to be paid to them upon the achievement of a number of designated milestones, as set forth below. In addition, our Board of Directors approved the grant of restricted stock to our Named Executive Officers at that time, as described below, and to other members of our management team. The bonus amounts were determined by the Compensation Committee, in its discretion after review materials regarding peer companies, review with our legal counsel and review of materials provided by accounting firms.

The bonuses adopted by the Board of Directors in 2012 are as follows:

	Clinical Development Milestones per Clinical Product Candidate	Other Clinical Development Milestone for Clinical Product Candidate	Undisclosed Substantial Commercial Agreement	Entry into a Substantial Transaction	Entry into a Change in Control Transaction
Yoseph Shaaltiel, Ph.D.	\$ 170,000	\$ 120,000	\$ 180,000	TBD out of \$900,000	\$ 1,200,000
Einat Brill Almon, Ph.D.	\$ 150,000	\$ 100,000	\$ 170,000	TBD out of \$900,000	\$ 1,125,000
Yossi Maimon, CPA	\$ 35,000	\$ 10,000	\$ 450,000	TBD out of \$900,000	\$ 1,125,000
Tzvi Palash	\$ 70,000	\$ 20,000	\$ 100,000	TBD out of \$900,000	\$ 500,000

Substantially all of the milestones described above had a 24-month time limit for achievement and, as such, are currently expired. The Compensation Committee plans to convene later in 2015 to evaluate the current incentive plans and adopt new compensation goals going forward.

In addition to the bonuses granted to our Named Executive Officers, additional members of our management team are entitled to certain incentive bonuses payable upon the achievement of designated milestones. If we achieve agreed-upon advancements in the clinical development of each of certain designated product candidates during an agreed-upon amount of time immediately following the Board of Director's approval of the bonuses, our Named Executive Officers will be entitled to the amounts listed in the first two columns of the table set forth above. The amounts are payable upon achievement of the applicable milestone if, at such time, we have available an agreed-upon minimum cash balance. If we do not have the minimum cash balance, the bonuses will be considered earned, and will be payable when we next achieve the minimum cash balance.

The grants of restricted stock to the Named Executive Officers in 2012 at that time are as shown in the table immediately following this paragraph. The grants were made in accordance with the terms and conditions of our amended 2006 stock incentive plan.

Named Executive Officer	Number of Restricted Shares
Yoseph Shaaltiel, Ph.D.	210,000
Einat Brill Almon, Ph.D.	185,000
Yossi Maimon, CPA	185,000
Tzvi Palash	102,000

The restricted shares detailed above vest in 16 equal, quarterly increments over a four-year period, commencing upon the date of grant. In addition, each vested share is subject to a 24-month lock-up period, commencing upon the applicable vesting date. Immediately and automatically in the event of a Corporate Transaction or a Change in Control, all of the restricted shares listed above shall vest and the lock-up periods shall terminate, subject to certain exceptions.

***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.*** 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, stock option and other agreements with each of our Named Executive Officers, as amended, provide that all of the outstanding options and other securities granted by us to each Named Executive Officer are subject to accelerated vesting immediately upon a change in control of our company. As set forth above, our Board of Directors adopted certain recommendations of the Compensation Committee on July 15, 2012, regarding the compensation of our Named Executive Officers, including cash bonuses for Named Executive Officers if we complete a Corporate Transaction.

***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 in Section 11 of the Annual Report on Form 10-K for information regarding the compensation earned during the fiscal year ended December 31, 2014 by: our current President and Chief Executive Officer, our former 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 Chief Operating Officer, who we refer to collectively as the "Named Executive Officers."

## **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 Securities Exchange Act of 1934.*

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 10, 2015, by the members of the Compensation Committee of the Board of Directors.

*Amos Bar Shalev*

*Zeev Bronfeld*

*Yodfat Harel Buchris*

### **Summary Compensation Table**

The following table sets forth a summary for the fiscal years ended December 31, 2014, 2013 and 2012, respectively, of the cash and non-cash compensation awarded, paid or accrued by us or Protalix Ltd. to each of our current President and Chief Executive Officer, our former 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 Chief Operating Officer, 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 2014, 2013 and 2012 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 (2) Current President and Chief Executive Officer	2014	93,667		-	200,962	18,399	313,028
David Aviezer, Ph.D., MBA (3)	2014	443,840	400,000	(386,196 )	(138,728 )	100,109	419,025
Former President and Chief Executive Officer	2013	527,672	50,000	870,147	213,581	112,662	1,774,062
Yoseph Shaaltiel, Ph.D.	2012	493,960	675,000	860,963	1,101,142	99,080	3,230,145
Executive Vice President, Research and Development	2014	305,548	90,000	232,979	62,651	84,719	775,897
Einat Brill Almon, Ph.D.	2013	302,901	120,000	429,927	140,770	81,672	1,075,270
Senior Vice President, Product Development	2012	283,655	225,000	409,838	608,826	67,257	1,594,576
Yossi Maimon, CPA Vice President, Chief Financial Officer	2014	263,917	85,000	205,244	56,170	68,489	678,820
Tzvi Palash Chief Operating Officer	2013	261,505	100,000	378,745	126,208	66,600	933,058
	2012	244,716	215,000	361,048	547,846	67,763	1,436,373
	2014	299,090	225,000	205,244	56,170	74,493	859,997
	2013	292,096	110,000	378,745	126,208	67,739	974,788
	2012	268,618	157,500	361,048	544,199	58,231	1,389,596
	2014	233,669	50,000	113,161	11,413	74,520	482,763
	2013	231,668	20,000	208,822	72,055	72,105	604,650
	2012	216,451	35,000	199,064	152,240	66,274	669,029

- (1) Includes employer contributions to pension and/or insurance plans and other miscellaneous payments.
- (2) Mr. Manor commenced his tenure as our President and Chief Executive Officer as of November 1, 2014.
- (3) Dr. Aviezer's tenure as our President and Chief Executive Officer ended as of November 1, 2014.

### 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, 2014.

Name	Option Awards				Stock Awards	
	Number of Securities Underlying Unexercised Options	Number of Securities Underlying Unexercised Options	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock	Market Value of Shares or Units of Stock That Have Not Vested (\$)

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	Options Exercisable (#)	Unexercisable (#)				That Have Not Vested (#)	
Moshe Manor	56,250	843,750	2.37	9	/29/2024	—	—
David Aviezer	853,563	-	0.972	9	/10/2016		
	600,000	-	5.00	2	/7/2018		
	100,000	-	2.65	2	/25/2019		
	208,333	41,667	6.90	2	/25/2020		
						104,500	192,280
Yoseph Shaaltiel	122,162	-	0.001	6	/30/2016		
	263,728	-	5.00	2	/7/2018		
	50,000	-	2.65	2	/25/2019		
	120,833	24,167	6.90	2	/25/2020		
						91,875	169,050
Einat Brill Almon	311,272		5.00	2	/7/2018		
	108,333	21,667	6.90	2	/25/2020		
						80,938	148,926
Yossi Maimon	175,000		5.00	2	/7/2018		
	108,333	21,667	6.90	2	/25/2020		
						80,938	148,926
Tzvi Palash	160,000		7.55	8	/29/2020		
						44,625	82,110

### **Potential Payments upon Termination or Change-in-Control**

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. We do not provide any change in control benefits to our Named Executive Officers except for certain cash bonuses and the acceleration of the vesting periods for outstanding options and restricted stock, subject to certain conditions. Had we experienced a change of control on December 31, 2014, the value of the acceleration of the vesting period of Mr. Manor's options would be \$0; as of the same date all options held by each of our other Named Executive Officers were fully vested 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, had we experienced a change of control on December 31, 2014, the value of the acceleration of the shares of restricted stock held by each of Dr. Shaaltiel, Dr. Brill Almon, Mr. Maimon and Mr. Palash would be \$169,050, \$148,926, \$148,926, and \$82,110, respectively.

### **Employment Arrangements**

**Moshe Manor.** Mr. Manor joined Protalix Ltd. as its President and Chief Executive Officer pursuant to an employment agreement dated September 28, 2014. Pursuant to the employment agreement, his current monthly base salary is NIS 100,000 (approximately \$25,714) 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 MKT 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 the Company's 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 and a company phone. Mr. Manor is entitled to 24 working days of vacation.

**David Aviezer, Ph.D., MBA.** Dr. Aviezer originally served as Protalix Ltd.'s Chief Executive Officer on a consultancy basis pursuant to a Consulting Services Agreement between Protalix Ltd. and Agenda Biotechnology Ltd., a company wholly-owned by Dr. Aviezer. On September 11, 2006, Protalix Ltd. entered into an employment agreement with Dr. Aviezer pursuant to which he agreed to be employed as Protalix Ltd.'s President and Chief Executive Officer, which agreement supersedes the Consultancy Services Agreement. Dr. Aviezer served as our

President and Chief Executive Officer until November 2014. At the end of Dr. Aviezer's tenure as our President and Chief Executive Officer, his monthly base salary was NIS 148,000 (approximately \$38,056) and he was entitled to an annual bonus at the Board's discretion. The monthly salary was subject to cost of living adjustments from time to time. Dr. Aviezer was eligible under the employment agreement to receive a substantial bonus in the event of certain public offerings or acquisition transactions, which bonus shall be at the discretion of the Board, and certain specified bonuses in the event Protalix achieves certain specified milestones. In connection with the employment agreement, in addition to other options already held by Dr. Aviezer granted to Dr. Aviezer options to purchase 16,000 ordinary shares of Protalix Ltd. at an exercise price equal to \$59.40 per share, which we assumed as options to purchase 977,297 shares of our common stock at \$0.97 per share. Such options vest quarterly retroactively from June 1, 2006, over a four-year period. In addition, in 2008 we granted to Dr. Aviezer an option to purchase 600,000 shares of our common stock at an exercise price equal to \$5.00 per share. The option vests variably over a five-year period that commenced on January 1, 2008. In 2009, we granted Dr. Aviezer an option to purchase 100,000 shares of our common stock at an exercise price equal to \$2.65 per share. As of December 31, 2009, all of those options had fully vested. In 2010, we granted Dr. Aviezer an option to purchase 250,000 shares of our common stock at an exercise price equal to \$6.90 per share, which option vests quarterly over a three-year period commencing upon FDA approval of taliglucerase alfa, if at all, and on July 16, 2012, we granted Dr. Aviezer 418,000 restricted shares of common stock that vest quarterly in 16 equal increments over a four-year period. Dr. Aviezer's employment agreement was terminable by either party on 90 days' written notice for any reason and terminable by us for cause without notice. Dr. Aviezer was 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 and a company phone. Dr. Aviezer was entitled to 29 working days of vacation.

**Yoseph Shaaltiel, Ph.D.** Dr. Shaaltiel founded Protalix Ltd. in 1993 and currently serves as our Executive Vice President, Research and Development. Dr. Shaaltiel entered into an employment agreement with Protalix Ltd. on September 1, 2001. Pursuant to the employment agreement, his current monthly base salary is NIS 85,000 (approximately \$21,856) per month. The employment agreement is terminable by Protalix Ltd. on 90 days' written notice for any reason and we may terminate the agreement for cause without notice. In 2008 we granted to Dr. Shaaltiel an option to purchase 263,728 shares of our common stock at an exercise price equal to \$5.00 per share. The option vests variably over a five-year period that commenced on January 1, 2008. In 2009, we granted Dr. Shaaltiel an option to purchase 50,000 shares of our common stock at an exercise price equal to \$2.65 per share. As of December 31, 2009, all of those options had fully vested. In 2010, we granted Dr. Shaaltiel an option to purchase 145,000 shares of our common stock at an exercise price equal to \$6.90 per share, which option vests quarterly over a three-year period commencing upon FDA approval of taliglucerase alfa, if at all, and on July 16, 2012, we granted Dr. Shaaltiel 210,000 restricted shares of common stock that vest quarterly in 16 equal increments over a four-year period. 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 and a company phone. Dr. Shaaltiel is entitled to 29 working days of vacation.

**Einat Brill Almon, Ph.D.** Dr. Brill Almon joined Protalix Ltd. on December 19, 2004 as its Vice President, Product Development, pursuant to an employment agreement effective on December 19, 2004 by and between Protalix Ltd. and Dr. Brill Almon, and currently serves as our Senior Vice President, Product Development. Pursuant to the employment agreement, her current monthly base salary is NIS 73,500 per month (approximately \$18,899). She is also entitled to certain specified bonuses in the event that Protalix achieves certain specified clinical development milestones within specified timelines. In connection with the employment agreement, Protalix agreed to grant to Dr. Brill Almon options to purchase 7,919 ordinary shares of Protalix Ltd. at exercise prices equal to \$24.36 and \$59.40 per share, which we assumed as options to purchase 483,701 shares of our common stock at \$0.40 and \$0.97 per share. The options vest over four years. In addition, in 2008 we granted to Dr. Brill Almon an option to purchase 311,272 shares of our common stock at an exercise price equal to \$5.00 per share. The option vests variably over a five-year period that commenced on January 1, 2008. In 2009, we granted to Dr. Brill Almon an option to purchase 50,000 shares of our common stock at an exercise price equal to \$2.65 per share. As of December 31, 2009, all of those options had fully vested. In 2010, we granted Dr. Brill Almon an option to purchase 130,000 shares of our common stock at an exercise price equal to \$6.90 per share, which option vests quarterly over a three-year period commencing upon FDA approval of taliglucerase alfa, if at all, and on July 16, 2012, we granted Dr. Brill Almon 185,000 restricted shares of common stock that vest quarterly in 16 equal increments over a four-year period. 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 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.** Mr. Maimon joined Protalix Ltd. as its Chief Financial Officer pursuant to an employment agreement effective as of October 15, 2006 by and between Protalix Ltd. and Mr. Maimon and currently serves as our Chief Financial Officer. Pursuant to the employment agreement, his current monthly base salary is NIS 73,500 (approximately \$18,899) 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 connection with the employment agreement, Protalix agreed to grant to Mr. Maimon options to purchase 10,150 ordinary shares of Protalix Ltd. at an exercise price equal to \$59.40 per share, which we assumed as options to purchase 619,972 shares of our common stock at \$0.97 per share. The first 25% of such options shall vest on the first anniversary of the grant date and the remainder shall vest quarterly in 12 equal increments. In addition, in 2008 we granted to Mr. Maimon an option to purchase 175,000 shares of our common stock at an exercise price equal to \$5.00 per share. The option vests variably over a five-year period that commenced on January 1, 2008. In 2009, we granted to Mr. Maimon an option to purchase 50,000 shares of our common stock at an exercise price equal to \$2.65 per share. As of December 31, 2009, all of those options had fully vested. In 2010, we granted Mr. Maimon an option to purchase 130,000 shares of our common stock at an exercise price equal to \$6.90 per share, which option vests quarterly over a three-year period commencing upon FDA approval of taliglucerase alfa, if at all, and on July 16, 2012, we granted Mr. Maimon 185,000 restricted shares of common stock that vest quarterly in 16 equal increments over a four-year period. 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 and a company phone. Mr. Maimon is entitled to 29 working days of vacation.

**Tzvi Palash.** Mr. Palash joined Protalix Ltd. as its Chief Operating Officer pursuant to an employment agreement effective September 6, 2010 and currently serves as our Chief Operating Officer. Pursuant to the employment agreement, Mr. Palash's current monthly base salary is NIS 69,000 (approximately \$17,742) and Mr. Palash 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 connection with the employment agreement, we granted to Mr. Palash options to purchase 160,000 shares of our common stock with an exercise price equal to \$7.55 per share. The first 25% of such options vested on the first anniversary of the grant date and the remainder vest quarterly in 12 equal increments. In addition, on July 16, 2012, we granted Mr. Palash 102,000 restricted shares of common stock that vest quarterly in 16 equal increments over a four-year period. 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. Palash 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, a company laptop and lodging accommodations in the Carmiel area. Mr. Palash is entitled to 27 working days of vacation.

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

Our Board of Directors and a majority of our shareholders approved our 2006 Stock Incentive Plan on December 14, 2006. Our shareholders approved an amendment to the plan on June 17, 2012 and subsequently on November 10, 2014. There are 13,841,655 shares of our common stock reserved for issuance, in the aggregate, under the amended 2006 Stock Incentive Plan, 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, 2014, options to acquire 1,923,444 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 Internal Revenue Code, 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.

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) (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 Shareholders” 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 shareholders 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 shareholders 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, 2020. 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 Internal Revenue Code, 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 shareholder 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 2014. The fees to our current directors were paid by Protalix Ltd.

Name	Fees Earned or Paid in Cash (\$)	Option Awards	Total (\$)
Shlomo Yanai (1)	87,500	69,521	157,021
Zeev Bronfeld	113,000	—	113,000
Amos Bar Shalev	80,000	—	80,000
Yodfat Harel Buchris	80,000	—	80,000
Roger D. Kornberg	55,000	—	55,000
Aharon Schwartz (2)	5,555	—	5,555
Eyal Sheratzky (3)	68,888	—	68,888

(1) Mr. Yanai's tenure on our Board of Directors commenced on July 24, 2014. On that same date, the Board of Directors granted to Mr. Yanai a 10-year option to purchase 150,000 shares of our common stock with an exercise price of \$3.37 per share. The options vest over a three-year period; the first 50,000 shares vest on the first anniversary of the grant date and the remaining shares vest in eight equal quarterly increments over the subsequent two year period, subject to certain terms and conditions. The vesting of the options is accelerated in full upon a Corporate Transaction or a Change in Control, as those terms are defined in our amended 2006 Stock Incentive Plan. We estimated the fair value of the option on the date of grant using the Black-Scholes option-pricing model to be approximately \$193,000.

(2) Dr. Schwartz was elected to serve on our Board of Directors on November 10, 2014.

(3) Mr. Sheratzky's tenure on our Board of Directors ended on November 10, 2014.

Directors' fees paid to each of Zeev Bronfeld and Eyal Sheratzky 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 Messrs. Bar Shalev and Bronfeld and Mrs. Harel Buchris. 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

**Security Ownership of Certain Beneficial Owners and Management**

The following table sets forth information, as of March 1, 2015, 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 Chief Financial Officer and our Chief Operating Officer; 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 these tables, a person is deemed to be the beneficial owner of securities that can be acquired by such person within 60 days from March 1, 2015 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 93,603,819 shares of our common stock outstanding as of March 1, 2015.

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)	—	—

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Moshe Manor (2)	112,500	*
Amos Bar Shalev	1,680	*
Zeev Bronfeld (3)	2,162,481	2.3
Yodfat Harel Buchris (4)	137,424	*
Roger D. Kornberg, Ph.D. (5)	50,000	*
Aharon Schwartz	—	—
Einat Brill Almon, Ph.D. (6)	557,627	*
Yossi Maimon (7)	421,355	*
Tzvi Palash (8)	230,125	*
Yoseph Shaaltiel, Ph.D. (9)	1,176,936	1.3
All executive officers and directors as a group (11 persons) (10)	4,850,126	5.1
5% Holders		
Al-Rov (Israel) Ltd. (11)	4,915,383	5.3
Federated Investors Inc. (12)	10,270,101	11.0
Baillie Gifford & Co. (13)	6,510,158	7.0
Consonance Capital Management LP (14)	5,077,338	5.4

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\* less than 1%.

(1) Does not include 150,000 shares of our common stock underlying options that will not vest within 60 days of March 1, 2015.

(2) Consists of 112,500 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2015. Does not include 787,500 shares of our common stock underlying options that will not vest within 60 days of March 1, 2015.



- (3) Consists of shares of our common stock held directly by Mr. Bronfeld.
- (4) Represents shares held by YP & 6 Partners Ltd. Mrs. Harel Buchris is a director and shareholder of YP & 6 Partners Ltd. Mrs. Harel Buchris disclaims beneficial ownership of these shares except to the extent of her pecuniary interest therein.
- (5) Consists of 50,000 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2015.
- (6) Consists of 430,439 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2015 and 127,188 restricted shares of our common stock that have vested or will vest within 60 days of March 1, 2015. Does not include 10,833 shares of our common stock underlying options that will not vest within 60 days of March 1, 2015 and 57,813 restricted shares of our common stock that will not vest within 60 days of March 1, 2015.
- (7) Consists of 294,167 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2015 and 127,188 restricted shares of our common stock that have vested or will vest within 60 days of March 1, 2015. Does not include 10,833 shares of our common stock underlying options that will not vest within 60 days of March 1, 2015 and 57,813 restricted shares of our common stock that will not vest within 60 days of March, 2015.
- (8) Consists of 160,000 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2015 and 70,125 restricted shares of our common stock that have vested or will vest within 60 days of March 1, 2015. Does not include 31,875 restricted shares of our common stock that will not vest within 60 days of March 1, 2015.
- (9) Consists of 463,754 shares of our common stock held by Dr. Shaaltiel, 568,807 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2015 and 144,375 restricted shares of our common stock that have vested or will vest within 60 days of March, 2015. Does not include 12,083 shares of our common stock underlying options that will not vest within 60 days of March 1, 2015 and 65,625 restricted shares of our common stock that will not vest within 60 days of March 1, 2015.

(10) Consists of 2,765,339 shares of our common stock, 1,615,912 shares of our common stock issuable upon exercise of outstanding options within 60 days of March 1, 2015 and 468,875 restricted shares of our common stock that have vested or will vest within 60 days of March 1, 2015. Does not include 971,250 shares of common stock issuable upon exercise of outstanding options and 213,125 restricted shares of our common stock that will not vest within 60 days of March 1, 2015.

(11) The address is Alrov Tower, 46 Rothschild Blvd., Tel Aviv 66883, Israel. Consists of 4,229,337 shares of our common stock held by Al-Rov (Israel) Ltd., or Al-Rov Israel, and 686,046 shares of our common stock held by Techno-Rov Holdings (1993) Ltd., or Techno-Rov Holdings. Al-Rov Israel owns 100% of the outstanding shares of Al-Rov Technologies Holdings LTD, the holder of 80% of Techno-Rov Holdings.

(12) Based solely on a Schedule 13G/A filed on February 11, 2015 by Federated Investors, Inc. for December 31, 2014.

(13) Based solely on a Schedule 13G/A filed by Baillie Gifford & Co. on January 29, 2015 for December 31, 2014.

(14) Based solely on a Schedule 13G filed on February 17, 2015 by Consonance Capital Management LP for December 31, 2014.

## Equity Compensation Plan Information

The following table provides information as of December 31, 2014 with respect to the shares of our common stock that may be issued under our existing equity compensation plan.

Plan Category	A	B	C
	Number of Securities to be Issued Upon Exercise of Outstanding Options	Weighted Average Exercise Price of Outstanding Options	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column A)
Equity Compensation Plans Approved by Shareholders	6,833,159	\$ 3.38	1,923,444
Equity Compensation Plans Not Approved by Shareholders	631,866	\$ 10.24	-
Total	7,465,025	\$ 3.96	1,923,444

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

**Corporate Governance and Independent Directors**

In compliance with the listing requirements of the NYSE MKT, 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 MKT. 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 MKT as well as the independence standards set forth in the Sarbanes-Oxley Act of 2002 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, shareholder 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 Messrs. Bar Shalev and Bronfeld and Mrs. Harel Buchris are considered "independent" pursuant to the rules of the NYSE MKT and Section 10A(m)(3) of the Exchange Act. In addition, our Board of Directors has determined that at least two of 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. Bar Shalev, Mr. Bronfeld, Mrs. Harel Buchris, Dr. Kornberg, Dr. Schwartz and Mr. Yanai are "independent" pursuant to the rules of the NYSE MKT.

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. We have no formal policy regarding attendance by our directors at annual shareholders meetings, although we encourage such attendance and anticipate most of our directors will attend these meetings. Messrs. Bronfeld, Bar Shalev, Manor and Yanai, and Mrs. Harel Buchris attended our 2014 annual meeting of shareholders.

### **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 shareholder 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, 2014 and 2013 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,	
	2014	2013
Audit Fees	\$ 246,000	\$ 246,000
Audit Related Fees	\$ 10,000	\$ 10,000
Tax Fees	\$ 51,380	\$ 57,334
All Other Fees	\$ -	\$ 22,560

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

Prior to entering into the engagement letter with our independent registered accountants, our Audit Committee approved the 2014 audit fees. For fiscal year 2015, our Audit Committee has approved fees for certain permissible non-audit services to be rendered by our independent registered 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:

<sup>1</sup> *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>
Report of Independent Registered Public Accounting Firm	F-2
Consolidated Balance Sheets as of December 31, 2013 and 2014	F-3
Consolidated Statements of Operations for the years ended December 31, 2012, 2013 and 2014	F-4
Consolidated Statements of Changes in Capital Deficiency for the years ended December 31, 2012, 2013 and 2014	F-5
Consolidated Statements of Cash Flows for the years ended December 31, 2012, 2013 and 2014	F-6
Notes to Consolidated Financial Statements	F-8

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>ExhibiDate</b>	
3.1	Amended and Restated Articles of Incorporation of the Company	S-4	333-48677	3.4 March 26, 1998	
3.2	Article of Amendment to Articles of Incorporation dated June 9, 2006	8-A	001-33357	3.2 March 9, 2007	



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3.3	Article of Amendment to Articles of Incorporation dated December 13, 2006	8-A	001-33357	3.3	March 9, 2007
3.4	Article of Amendment to Articles of Incorporation dated December 26, 2006	8-A	001-33357	3.4	March 9, 2007
3.5	Article of Amendment to Articles of Incorporation dated February 26, 2007	8-A	001-33357	3.5	March 9, 2007
3.6	Article of Amendment to Articles of Incorporation dated December 17, 2014				X
3.7	Amended and Restated Bylaws of the Company				X
4.1	Form of Restricted Stock Agreement/Notice	8-K	001-33357	3.1	July 18, 2012

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4.2	Indenture, dated as of September 18, 2013, between Protalix BioTherapeutics, Inc. and The Bank of New York Mellon Trust Company, N.A., as Trustee	8-K	4.1	September 18, 2013
4.3	Form of 4.50% Convertible Note due 2018	8-K	001-333574.2	September 18, 2013
10.1	2006 Stock Incentive Plan, as amended	Def 14A	001-33357 Annex A	October 9, 2014
10.2	Employment Agreement between Protalix Ltd. and Yoseph Shaaltiel, dated as of September 1, 2004	8-K	001-33357 10.3	January 8, 2007
10.3	Employment Agreement between Protalix Ltd. and Einat Almon, dated as of December 19, 2004	8-K	001-33357 10.3	January 8, 2007
10.4	Employment Agreement between Protalix Ltd. and Yossi Maimon, dated as of October 15, 2006	8-K	001-33357 10.5	January 8, 2007
10.5†	License Agreement entered into as of April 12, 2005, by and between Icon Genetics AG and Protalix Ltd.	8-K/A	001-33357 10.6	September 20, 2007
10.6	Lease Agreement between Protalix Ltd. and Angel Science Park (99) Ltd., dated as of October 28, 2003 as amended on April 18, 2005	8-K	001-33357 10.9	January 8, 2007
10.7	Stock Option Award Agreement grant by and between the Company and Steven Rubin, dated as of December 31, 2006	10-K	001-33357 10.13	March 30, 2007
10.8	First Amendment to the December 31, 2006 Stock Option Award Agreement by and between the Company and Steven Rubin, effective as of February 28, 2007	10-K	001-33357 10.16	March 30, 2007
10.9	Scientific Advisory Board Agreement dated August 5, 2007 by and between the Company and Aaron Ciechanover, M.D.	8-K	001-33357 10.1	August 6, 2007
10.10	Unprotected Lease Agreement	10-K	001-33357 10.21	March 17, 2008

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10.11	Exclusive License and Supply Agreement dated as of November 30, 2009 between Protalix Ltd. and Pfizer Inc.	10-K001-3335710.16	February 26, 2010	
10.12	Employment Agreement by and between Protalix Ltd., and Tzvi Palash dated as of August 29, 2010	8-K 001-3335710.1	September 7, 2010	
10.13	License Agreement between Protalix BioTherapeutics Ltd. and Virginia Tech Intellectual Properties, Inc.	10-Q001-3335710.2	November 8, 2010	
10.14	Amended and Restated Agreement between Protalix Ltd. and Comercio e Serviços Ltda. dated June 17, 2013	10-Q001-3335710.1	May 8, 2014	
10.15	Amendment dated June 18, 2013 to the Exclusive License and Supply Agreement between Pfizer Inc. and Protalix Ltd., dated as of November 30, 2009	10-Q001-3335710.2	May 8, 2014	
10.16	Technology Transfer and Supply Agreement made as of June 18, 2013 by and between Protalix Ltd. and Fundação Oswaldo Cruz	10-Q001-3335710.3	May 8, 2014	
10.17	Employment Agreement with Moshe Manor dated September 28, 2014	8-K 001-3335710.1	September 29, 2014	
21.1	Subsidiaries	10-K001-3335721.1	February 26, 2010	
23.1	Consent of Kesselman & Kesselman, Certified Public Accountants (Isr.), A member of PricewaterhouseCoopers International Limited, independent registered public accounting firm for the Registrant			X
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002			X
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002			X
32.1	18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Certification of Chief Executive Officer			X

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

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† 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.

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 12, 2015.

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 12, 2015
/s/ Yossi Maimon Yossi Maimon	Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer)	March 12, 2015

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/s/ Shlomo Yanai Shlomo Yanai	Chairman of the Board	March 12, 2015
/s/ Amos Bar Shalev Amos Bar Shalev	Director	March 12, 2015
/s/ Zeev Bronfeld Zeev Bronfeld	Director	March 12, 2015
/s/ Yodfat Harel Buchris Yodfat Harel Buchris	Director	March 12, 2015
/s/ Aharon Schwartz Aharon Schwartz, Ph.D.	Director	March 12, 2015

**PROTALIX BIOTHERAPEUTICS, INC.**

**CONSOLIDATED FINANCIAL STATEMENTS**

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the shareholders of

**PROTALIX BIOTHERAPEUTICS, INC.**

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, changes in capital deficiency and cash flows present fairly, in all material respects, the financial position of Protalix BioTherapeutics, Inc. and its subsidiaries at December 31, 2014 and 2013, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2014, in conformity with accounting principles generally accepted in the United States of America. Also, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying "Management's Report on Internal Control over Financial Reporting" appearing under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. 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.

A company's internal control over financial report