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

# FORM 10-Q

**(Mark One)**

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

**For the quarterly period ended March 31, 2023**

**OR**

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

**For the transition period from _____ to_____**

**001-33357**
**(Commission file number)**

# PROTALIX BIOTHERAPEUTICS, INC.

**(Exact name of registrant as specified in its charter)**

| **Delaware** | **65-0643773** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |
| **2 University Plaza Suite 100 Hackensack, NJ** | **07601** |
| **(Address of principal executive offices)** | **(Zip Code)** |

**(201)-696-9345**
**(Registrant's telephone number, including area code)**

**N/A**
**(Former name, former address and former fiscal year, if changed since last report)**

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

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common stock, $0.001 par value | PLX | NYSE American |

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

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

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

| | | | |
|---|---|---|---|
| Large accelerated filer | ☐ | Accelerated filer | ☐ |
| Non-accelerated filer | ☒ | Smaller reporting company | ☒ |
| | | Emerging growth company | ☐ |

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

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

On April 30, 2023, approximately 65,414,917 shares of the Registrant's common stock, $0.001 par value, were outstanding.

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## PART I – FINANCIAL INFORMATION

**Item 1. Financial Statements**

**PROTALIX BIOTHERAPEUTICS, INC.**
**CONDENSED CONSOLIDATED BALANCE SHEETS**
(U.S. dollars in thousands)
(Unaudited)

| | March 31, 2023 | December 31, 2022 |
|---|---|---|
| **ASSETS** | | |
| **CURRENT ASSETS:** | | |
| Cash and cash equivalents | $ 33,036 | $ 17,111 |
| Short-term bank deposits | — | 5,069 |
| Accounts receivable – Trade | 1,304 | 4,586 |
| Other assets | 758 | 1,310 |
| Inventories | 20,303 | 16,804 |
| Total current assets | $ 55,401 | $ 44,880 |
| **NON-CURRENT ASSETS:** | | |
| Funds in respect of employee rights upon retirement | $ 1,252 | $ 1,267 |
| Property and equipment, net | 4,704 | 4,553 |
| Operating lease right of use assets | 5,202 | 5,087 |
| Total assets | $ 66,559 | $ 55,787 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY (NET OF CAPITAL DEFICIENCY)** | | |
| **CURRENT LIABILITIES:** | | |
| Accounts payable and accruals: | | |
| Trade | $ 5,105 | $ 5,862 |
| Other | 13,471 | 12,271 |
| Operating lease liabilities | 1,149 | 1,118 |
| Contracts liability | 11,790 | 13,178 |
| Total current liabilities | $ 31,515 | $ 32,429 |
| **LONG TERM LIABILITIES:** | | |
| Convertible notes | $ 28,267 | $ 28,187 |
| Liability for employee rights upon retirement | 1,617 | 1,642 |
| Operating lease liabilities | 4,152 | 4,169 |
| Total long term liabilities | $ 34,036 | $ 33,998 |
| Total liabilities | $ 65,551 | $ 66,427 |
| **COMMITMENTS** | | |
| **STOCKHOLDERS' EQUITY (CAPITAL DEFICIENCY)** | 1,008 | (10,640) |
| Total liabilities and stockholders' equity (net of capital deficiency) | $ 66,559 | $ 55,787 |

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

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

| | Three Months Ended | |
|---|---|---|
| | March 31, 2023 | March 31, 2022 |
| **REVENUES FROM SELLING GOODS** | $ 5,066 | $ 9,028 |
| **REVENUES FROM LICENSE AND R&D SERVICES** | 4,522 | 7,057 |
| **TOTAL REVENUE** | 9,588 | 16,085 |
| **COST OF GOODS SOLD (1)** | (3,085) | (6,034) |
| **RESEARCH AND DEVELOPMENT EXPENSES (2)** | (5,847) | (8,767) |
| **SELLING, GENERAL AND ADMINISTRATIVE EXPENSES (3)** | (3,115) | (3,154) |
| **OPERATING LOSS** | (2,459) | (1,870) |
| **FINANCIAL EXPENSES** | (649) | (618) |
| **FINANCIAL INCOME** | 172 | 202 |
| **FINANCIAL EXPENSES, NET** | (477) | (416) |
| **LOSS BEFORE TAXES ON INCOME** | (2,936) | (2,286) |
| **TAXES ON INCOME** | (195) | - |
| **NET LOSS FOR THE PERIOD** | $ (3,131) | $ (2,286) |
| **LOSS PER SHARE OF COMMON STOCK – BASIC AND DILUTED** | $ (0.05) | $ (0.05) |
| **WEIGHTED AVERAGE NUMBER OF SHARES OF COMMON STOCK USED IN COMPUTING LOSS PER SHARE – BASIC AND DILUTED** | 57,480,009 | 45,843,563 |
| **(1) Includes share-based compensation** | $ 58 | $ (6) |
| **(2) Includes share-based compensation** | $ 180 | $ 76 |
| **(3) Includes share-based compensation** | $ 308 | $ 766 |

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

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

| | Common Stock (1) | Common Stock | Additional Paid-In Capital | Accumulated Deficit | Total |
|---|---|---|---|---|---|
| | Number of Shares | Amount | | | |
| **Balance at January 1, 2022** | **45,556,647** | **$ 46** | **$ 368,852** | **$ (374,934)** | **$ (6,036)** |
| **Changes during the three-month period ended March 31, 2022:** | | | | | |
| Share-based compensation related to stock options | | | 149 | | 149 |
| Share-based compensation related to restricted stock awards | 759,482 | * | 687 | | 687 |
| Net loss for the period | | | | (2,286) | (2,286) |
| **Balance at March 31, 2022** | **46,316,129** | **$ 46** | **$ 369,688** | **$ (377,220)** | **$ (7,486)** |
| **Balance at January 1, 2023** | **53,790,167** | **$ 54** | **$ 379,167** | **$ (389,861)** | **$ (10,640)** |
| **Changes during the three-month period ended March 31, 2023:** | | | | | |
| Issuance of common stock under the Sales Agreement, net | 8,212,482 | 8 | 14,225 | | 14,233 |
| Share-based compensation related to stock options | | | 453 | | 453 |
| Share-based compensation related to restricted stock awards | | | 93 | | 93 |
| Net loss for the period | | | | (3,131) | (3,131) |
| **Balance at March 31, 2023** | **62,002,649** | **$ 62** | **$ 393,938** | **$ (392,992)** | **$ 1,008** |

*Represents an amount equal to less than $1.

(1) Common stock, $0.001 par value; Authorized – as of March 31, 2023 and 2022 – 144,000,000 and 120,000,000 shares, respectively.

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

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

| | Three Months Ended | |
|---|---|---|
| | March 31, 2023 | March 31, 2022 |
| **CASH FLOWS FROM OPERATING ACTIVITIES:** | | |
| Net loss | $ (3,131) | $ (2,286) |
| Adjustments required to reconcile net loss to net cash used in operating activities: | | |
| Share-based compensation | 546 | 836 |
| Depreciation | 280 | 270 |
| Financial income, net (mainly exchange differences) | (91) | (198) |
| Changes in accrued liability for employee rights upon retirement | 19 | 75 |
| Loss on amounts funded in respect of employee rights upon retirement | 1 | 10 |
| Amortization of debt issuance costs and debt discount | 80 | 75 |
| Changes in operating assets and liabilities: | | |
| Decrease in contracts liability (including non-current portion) | (1,388) | (2,644) |
| Decrease (increase) in accounts receivable-trade and other assets | 3,823 | (2,314) |
| Changes in operating lease right of use assets, net | 9 | (2) |
| Decrease (increase) in inventories | (3,499) | 1,360 |
| Increase (decrease) in accounts payable and accruals | 353 | (1,011) |
| Net cash used in operating activities | $ (2,998) | $ (5,829) |
| | | |
| **CASH FLOWS FROM INVESTING ACTIVITIES:** | | |
| Investment in bank deposits | | $ (16,000) |
| Proceeds from sale of short-term deposits | $ 5,000 | |
| Purchase of property and equipment | (248) | (229) |
| Amounts funded in respect of employee rights upon retirement, net | (20) | (28) |
| Net cash provided by (used in) investing activities | $ 4,732 | $ (16,257) |
| | | |
| **CASH FLOWS FROM FINANCING ACTIVITIES:** | | |
| Proceeds from issuance of common stock under the Sales Agreement, net | $ 14,233 | |
| Net cash provided by financing activities | $ 14,233 | — |
| **EFFECT OF EXCHANGE RATE CHANGES ON CASH AND CASH EQUIVALENTS** | $ (42) | $ (11) |
| **NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS** | 15,925 | (22,097) |
| **BALANCE OF CASH AND CASH EQUIVALENTS AT BEGINNING OF PERIOD** | 17,111 | 38,985 |
| **BALANCE OF CASH AND CASH EQUIVALENTS AT END OF PERIOD** | $ 33,036 | $ 16,888 |

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

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

(Continued) – 2

| | Three Months Ended | |
|---|---|---|
| | March 31, 2023 | March 31, 2022 |
| **SUPPLEMENTARY INFORMATION ON INVESTING AND FINANCING ACTIVITIES NOT INVOLVING CASH FLOWS:** | | |
| Purchase of property and equipment | $ 326 | $ 67 |
| Operating lease right of use assets obtained in exchange for new operating lease liabilities | $ 312 | $ 99 |
| **SUPPLEMENTARY DISCLOSURE ON CASH FLOWS** | | |
| Interest paid | $ 1,078 | $ 1,120 |
| Interest received | $ 78 | $ 36 |

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

**PROTALIX BIOTHERAPEUTICS, INC.**
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**
(Unaudited)

## NOTE 1 - SIGNIFICANT ACCOUNTING POLICIES

### a. General

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

The most advanced investigational drug in the Company's product pipeline is pegunigalsidase alfa, or PRX-102, a therapeutic protein candidate for the treatment of Fabry disease, a rare, genetic lysosomal disorder, which was the subject of a phase III clinical program. The PRX-102 phase III clinical program included three separate studies, which are referred to as the *BALANCE* study, the *BRIDGE* study and the *BRIGHT* study, each of which has been completed. The studies were designed to evaluate the potential for improved efficacy and better quality of life for adult patients with Fabry disease and to evaluate the safety of the Company's drug/therapy. The phase III clinical program analyzed two potential dosing regimens: 1 mg/kg every two weeks and 2 mg/kg every four weeks. In addition, the phase III clinical program included two extension studies in which subjects that participated in the Company's phase I/II clinical trials and phase III clinical trials had the opportunity to enroll and continue to be treated with PRX-102. As of March 1, 2023, sponsorship of the two open-label extension studies was transferred to the Company's development and commercialization partner for PRX-102, Chiesi Farmaceutici S.p.A. ("Chiesi").

The U.S. Food and Drug Administration (the "FDA") has indicated that the biologics license application ("BLA") for PRX-102 for the potential treatment of adult patients with Fabry disease resubmitted on November 9, 2022 by the Company, together with Chiesi, was considered a complete, class 2 response and set a PDUFA action date of May 9, 2023. The initial BLA for PRX-102 was submitted to the FDA on May 27, 2020 under the FDA's Accelerated Approval pathway, and was subsequently accepted by the FDA and granted Priority Review designation. However, in April 2021, the FDA issued a Complete Response Letter (CRL) in response to the initial BLA. In preparation for the BLA resubmission, the Company and Chiesi participated in a Type A (End of Review) meeting with the FDA on September 9, 2021. As part of the meeting minutes provided by the FDA, which included the preliminary comments and meeting discussion, the FDA, in principle, agreed that the data package proposed to the FDA for a BLA resubmission has the potential to support a traditional approval of PRX-102 for the treatment of Fabry disease. The data package in the BLA resubmission, given the change in the regulatory landscape in the United States, included the final two-year analyses of the Company's phase III *BALANCE* clinical trial of PRX-102, which was completed in July 2022, and long-term data from the Company's open-label extension study of PRX-102 in adult patients treated with a 2 mg/kg every four weeks dosage of PRX-102.

On February 7, 2022, the Company, together with Chiesi, submitted a Marketing Authorization Application ("MAA") for PRX-102 to the European Medicines Agency ("EMA") which was subsequently validated by the EMA. The submission was made after the October 8, 2021 meeting the Company held, together with Chiesi, with the Rapporteur and Co-Rapporteur of the EMA regarding PRX-102.

The MAA submission included a comprehensive set of preclinical, clinical and manufacturing data compiled from the Company's completed and ongoing clinical studies evaluating PRX-102 as a potential alternative treatment for adult patients with Fabry disease, including data from the Company's completed 12–month switch–over phase III *BRIGHT* clinical trial in adult patients with Fabry disease treated with a 2 mg/kg every four weeks dosage to support an additional potential treatment regimen for Fabry patients. As part of the EMA review process, Chiesi and the Company responded to the Day 120 list of questions in September 2022 (following a 3-month clock-stop period) and the list of outstanding issues of Day 180 in December 2022. An essential portion of the Day 120 response included the submission of the final analysis of the two-year *BALANCE* study (the final Clinical Study Report), and an interim analysis of the

**PROTALIX BIOTHERAPEUTICS, INC.**
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**
(Unaudited)

Company's long-term, open-label extension study of PRX-102 in adult patients with Fabry disease treated with the 2 mg/kg every four weeks dosage.

On February 24, 2023, the Company, together with Chiesi, announced that the EMA's Committee for Medicinal Products for Human Use (the "CHMP") adopted a positive opinion, recommending marketing authorization for PRX-102. The CHMP opinion was referred for final action to the European Commission (the "EC"). A final EC decision on the MAA is expected in the beginning of May 2023.

In addition to PRX-102, the Company's product pipeline currently includes, among other candidates:

(1) PRX-115, the Company's plant cell-expressed recombinant PEGylated uricase (urate oxidase) – a chemically modified enzyme to treat severe gout; and

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

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

On July 2, 2021, the Company entered into an At The Market Offering Agreement (the "2021 Sales Agreement") with H.C. Wainwright & Co., LLC, as the Company's sales agent (the "Agent") which was amended on May 2, 2022. Pursuant to the terms of the 2021 Sales Agreement, the Company was able to sell, from time to time through the Agent, shares of its common stock, par value $0.001 per share (the "Common Stock"), having an aggregate offering price of up to $20.0 million (the "ATM Shares"). Upon execution of the 2021 Sales Agreement, the Company terminated the ATM Equity Offering$^{SM}$ Sales Agreement it had entered into on October 1, 2020 with BofA Securities, Inc. ("BofA Securities"). During the term of the sales agreement with BofA Securities, the Company sold a total of 3,296,123 shares of Common Stock for total gross proceeds of approximately $13.8 million.

As of March 31, 2023, the Company sold a total of 13,980,060 ATM Shares for total gross proceeds of approximately $20.0 million under the 2021 Sales Agreement, thereby completing the ATM program under said agreement.

On February 27, 2023, the Company entered into an At The Market Offering Agreement (the "2023 Sales Agreement") with the Agent. Pursuant to the terms of the 2023 Sales Agreement, the Company may sell, from time to time through the Agent, ATM Shares having an aggregate offering price of up to $20.0 million. As of March 31, 2023, shares of Common Stock for total gross proceeds of approximately $16.5 million remain available to be sold under the 2023 Sales Agreement.

On October 19, 2017, Protalix Ltd. and Chiesi entered into an Exclusive License and Supply Agreement (the "Chiesi Ex-US Agreement") pursuant to which Protalix Ltd. granted to Chiesi an exclusive license for all markets outside of the United States to commercialize pegunigalsidase alfa. On July 23, 2018, Protalix Ltd. entered into an Exclusive License and Supply Agreement with Chiesi (the "Chiesi US Agreement") with respect to the commercialization of pegunigalsidase alfa in the United States.

Under each of the Chiesi Ex-US Agreement and the Chiesi US Agreement (collectively, the "Chiesi Agreements"), Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of each agreement. In addition, under the Chiesi Ex-US Agreement, Protalix Ltd. is entitled to additional payments of up to $25.0 million in pegunigalsidase alfa development costs and to receive additional payments of up to $320.0 million, in the aggregate, in regulatory and commercial milestone payments. Under the Chiesi US Agreement, Protalix Ltd. is entitled to payments of up to a maximum of $20.0 million to cover development costs for pegunigalsidase alfa and to receive additional payments of up to a maximum of $760.0 million, in the aggregate, in regulatory and commercial milestone payments. To date, Protalix Ltd. has received the complete amount of development costs to which it is entitled under the Chiesi Agreements.

**PROTALIX BIOTHERAPEUTICS, INC.**
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**
(Unaudited)

Under the terms of both of the Chiesi Agreements, Protalix Ltd. will manufacture all of the pegunigalsidase alfa needed under the agreements, subject to certain exceptions, and Chiesi will purchase pegunigalsidase alfa from Protalix, subject to certain terms and conditions. Under the Chiesi Ex-US Agreement, Chiesi is required to make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales outside of the United States, as consideration for product supply. Under the Chiesi US Agreement, Chiesi is required to make tiered payments of 15% to 40% of its net sales, depending on the amount of annual sales in the United States, as consideration for product supply.

On May 13, 2021, the Company signed a binding term sheet with Chiesi pursuant to which the Company and Chiesi amended the Chiesi Agreements in order to provide the Company with near-term capital. Chiesi agreed to make a $10.0 million payment to the Company before the end of the second quarter of 2021 in exchange for a $25.0 million reduction in a longer term regulatory milestone payment provided in the Chiesi EX-US Agreement. All other regulatory and commercial milestone payments remain unchanged. The Company received the payment in June 2021. The Company also agreed to negotiate certain manufacturing related matters.

Since its approval by the FDA, taliglucerase alfa has been marketed by Pfizer Inc. (“Pfizer”) in accordance with the exclusive license and supply agreement entered into between Protalix Ltd. and Pfizer, which is referred to herein as the Pfizer Agreement. In October 2015, Protalix Ltd. and Pfizer entered into an amended exclusive license and supply agreement, which is referred to herein as the Amended Pfizer Agreement, pursuant to which the Company sold to Pfizer its share in the collaboration created under the Pfizer Agreement for the commercialization of Elelyso. As part of the sale, the Company agreed to transfer its rights to Elelyso in Israel to Pfizer while gaining full rights to it in Brazil. Under the Amended Pfizer Agreement, Pfizer is entitled to all of the revenues, and is responsible for 100% of expenses globally for Elelyso, excluding Brazil where the Company is responsible for all expenses and retains all revenues.

On June 18, 2013, the Company entered into a Supply and Technology Transfer Agreement (the “Brazil Agreement”) with Fundação Oswaldo Cruz (“Fiocruz”), an arm of the Brazilian Ministry of Health (the “Brazilian MoH”), for taliglucerase alfa. Fiocruz’s purchases of BioManguinhos alfataliglicerase to date have been significantly below certain agreed-upon purchase milestones and, accordingly, the Company has the right to terminate the Brazil Agreement. Notwithstanding the termination right, the Company is, at this time, continuing to supply BioManguinhos alfataliglicerase to Fiocruz and patients continue to be treated with BioManguinhos alfataliglicerase in Brazil.

The novel coronavirus disease (“COVID-19”), which was declared by the World Health Organization to be a global pandemic on March 11, 2020, has had numerous adverse effects on the global economy. To date, the Company’s clinical trials have not been adversely affected by COVID-19, although certain practices the Company adopted during the earlier stages of the pandemic in its offices and facilities in an effort to promote social distancing resulted in minor delays in the performance of administrative activities outside of the clinical programs.

The Company expects to continue to incur significant expenditures in the near future due to research and developments efforts with respect to the product candidates. Under the terms of the Company’s outstanding 7.50% Senior Secured Convertible Notes due 2024 (the “2024 Notes”), the Company is required to comply with certain financial covenants, including the maintenance of a minimum cash balance of at least $7.5 million. As of March 31, 2023, the Company is in compliance with all such covenants. The Company believes that its cash and cash equivalents as of March 31, 2023, together with additional funds raised from the sale of ATM Shares under the 2023 Sales Agreement subsequent to March 31, 2023 are sufficient to satisfy the Company’s capital needs for at least 12 months from the date that these financial statements are issued.

**b. Basis of presentation**

The accompanying unaudited condensed consolidated financial statements of the Company have been prepared in accordance with generally accepted accounting principles in the United States (“GAAP”) for interim financial information. Accordingly, they do not include all of the information and notes required by GAAP for annual financial statements. In the opinion of management, all adjustments (of a normal recurring nature) considered necessary for a fair statement of the results for the interim periods presented have been included. Operating results for the interim period are not necessarily indicative of the results that may be expected for the full year.

**PROTALIX BIOTHERAPEUTICS, INC.**
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**
(Unaudited)

These unaudited condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements in the Annual Report on Form 10-K for the year ended December 31, 2022, filed by the Company with the U.S. Securities and Exchange Commission (the "Commission"). The comparative balance sheet at December 31, 2022 has been derived from the audited financial statements at that date. There have been no material changes in our significant accounting policies as described in our consolidated financial statements for the year ended December 31, 2022.

**c. Loss per share**

Basic and diluted loss per share ("LPS") are computed by dividing net loss by the weighted average number of shares of Common Stock attributable to common stockholders outstanding for each period. The calculation of diluted LPS does not include 36,292,208 shares of Common Stock underlying outstanding options and shares of Common Stock issuable upon conversion of the outstanding 2024 Notes and the exercise of outstanding warrants for the three months ended March 31, 2023, and 33,004,217 shares of Common Stock underlying outstanding options and shares of Common Stock issuable upon conversion of the Company's then outstanding 2024 Notes and the exercise of outstanding warrants for the three months ended March 31, 2022 because their effect would be anti-dilutive.

**d. Revenue recognition**

The Company accounts for revenue pursuant to Accounting Standards Codification, Topic 606, Revenue from Contracts with Customers ("ASC 606"). Under ASC 606, a contract with a customer exists only when: the parties to the contract have approved it and are committed to perform their respective obligations, the Company can identify each party's rights regarding the distinct goods or services to be transferred ("performance obligations"), the Company can determine the transaction price for the goods or services to be transferred, the contract has commercial substance and it is probable that the Company will collect the consideration to which it will be entitled in exchange for the goods or services that will be transferred to the customer.

Revenues are recorded in the amount of consideration to which the Company expects to be entitled in exchange for performance obligations upon transfer of control to the customer.

1. Revenues from selling products

   The Company recognizes revenues from selling goods at a point in time when control over the product is transferred to customers (upon delivery).

2. Revenues from Chiesi Agreements

   The Company has identified two performance obligations in the Chiesi Agreements as follows: (i) the license and research and development services and (ii) the contingent performance obligation regarding future manufacturing.

   The Company determined that the license together with the research and development services should be combined into single performance obligation since Chiesi cannot benefit from the license without the research and development services. The research and development services are highly specialized and are dependent on the supply of the drug.

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

**PROTALIX BIOTHERAPEUTICS, INC.**
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**
(Unaudited)

The transaction price was comprised of fixed consideration and variable consideration (capped research and development reimbursements). Under ASC 606, the consideration to which the Company would be entitled upon the achievement of contractual milestones, which are contingent upon the occurrence of future events, are a form of variable consideration. The Company estimates variable consideration using the most likely method. Amounts included in the transaction price are recognized only when it is probable that a significant reversal of cumulative revenues will not occur. Prior to recognizing revenue from variable consideration, the Company uses significant judgment to determine the probability of significant reversal of such revenue.

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

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

3. Revenue from R&D services

Revenue from the research and development services is recognized over time using the cost-to-cost method since the customer benefits from the research and development services as the entity performs the service.

## NOTE 2 - INVENTORIES

Inventories at March 31, 2023 and December 31, 2022 consisted of the following:

| (*U.S. dollars in thousands*) | March 31, 2023 | December 31, 2022 |
|---|---|---|
| Raw materials | $ 4,308 | $ 3,508 |
| Work in progress | 1,533 | 2,678 |
| Finished goods | 14,462 | 10,618 |
| Total inventory | $ 20,303 | $ 16,804 |

## NOTE 3 – FAIR VALUE MEASUREMENT

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

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

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

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

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

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

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

**PROTALIX BIOTHERAPEUTICS, INC.**
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**
(Unaudited)

Based on a Level 3 measurement, as of March 31, 2023, the fair value of the $28.75 million aggregate principal amount of the Company's outstanding 2024 Notes is approximately $41.4 million. The value of these notes was estimated by implementing the binomial model. The liability component was valued based on the Income Approach. The following parameters were used:

| | 2024 Notes |
|---|---|
| Stock price (USD) | 2.10 |
| Expected term | 1.42 |
| Risk free rate | 4.19 % |
| Volatility | 62.47 % |
| Yield | 12.60 % |

**NOTE 4 – REVENUES**

The following table summarizes the Company's disaggregation of revenues:

| (*U.S. dollars in thousands*) | Three Months Ended March 31, 2023 | 2022 |
|---|---|---|
| Pfizer | $ 2,266 | $ 3,356 |
| Brazil | $ 2,800 | $ 5,454 |
| Chiesi | $ — | $ 218 |
| Total revenues from selling goods | $ 5,066 | $ 9,028 |
| Revenues from license and R&D services | $ 4,522 | $ 7,057 |

**NOTE 5 – STOCK TRANSACTIONS**

**At-the-Market (ATM) Offering**

During the three months ended March 31, 2023, the Company sold, in the aggregate, 8,212,482 shares of Common Stock under the 2023 Sales Agreement and the 2021 Sales Agreement. The Company generated aggregate gross proceeds equal to approximately $14.9 million in connection with such sales.

**NOTE 6 – SUBSEQUENT EVENTS**

During April 2023, the Company sold, in the aggregate, 3,412,268 shares of Common Stock under the 2023 Sales Agreement. The Company generated aggregate gross proceeds equal to approximately $7.9 million in connection with such sales.

**Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations**

**CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS AND RISK FACTORS SUMMARY**

*You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the consolidated financial statements and the related notes included elsewhere in this Form 10-Q and in our Annual Report on Form 10-K for the year ended December 31, 2022. 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 within the meanings of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, including statements regarding expectations, beliefs, intentions or strategies for the future. When used in this report, the terms "anticipate," "believe," "estimate," "expect," "can," "continue," "could," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" and words or phrases of similar import, as they relate to our company 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 as a result of several factors.*

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

- the risk that the FDA might not grant marketing approval for PRX-102, by the Prescription Drug User Fee Act (PDUFA) action date or at all, and other risks related to the timing, progress and likelihood of final approval by the FDA of the resubmitted PRX-102 BLA;

- risks related to the timing, progress and likelihood of approval by the EMA of the MAA for PRX-102, and of approvals by other applicable health regulatory authorities;

- the risk that a marketing approval of PRX-102 by either the FDA or the EMA will be conditioned on significant limitations on its use;

- whether, if approved by the FDA, EMA and other applicable health regulatory authorities, the use of PRX-102 will be commercially successful;

- the likelihood that the FDA, EMA or other applicable health regulatory authorities will approve an alternative dosing regimen;

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

- the risk that the FDA, EMA, or other foreign regulatory authorities may not accept or approve a marketing application we file for any of our product candidates, and other risks relating to the review process;

- risks associated with the novel coronavirus disease, or COVID-19, outbreak and variants, which may adversely impact our business;

- risks related to any transactions we may effect in the public or private equity markets to raise capital to finance future research and development activities, general and administrative expenses and working capital;

- risks relating to our evaluation and pursuit of strategic alternatives;

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

- risks relating to our ability to manage our relationship with our collaborators, distributors or partners, including, but not limited to, Pfizer and Chiesi;

- risks related to the amount and sufficiency of our cash and cash equivalents;

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

- risks relating to changes to interim, topline or preliminary data from clinical trials that we announce or publish;

- risk of significant lawsuits, including stockholder litigation, which is common in the life sciences sector;

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

- delays in our preparation and filing of applications for regulatory approval; the inherent risks and uncertainties in developing drug platforms and products of the type we are developing;

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

- risks related to our supply of drug product to Pfizer;

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

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

- potential product liability risks, and risks of securing adequate levels of related insurance coverage;

- the possibility of infringing a third-party's patents or other intellectual property rights and the uncertainty of obtaining patents covering our products and processes and successfully enforcing our intellectual property rights against third-parties;

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

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

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

**Recent Company Developments**

- On March 21, 2023, the first patient was dosed in our phase I First in Human (FIH) clinical trial of PRX-115.

- On February 24, 2023, we, together with Chiesi, announced that the CHMP has adopted a positive opinion, recommending marketing authorization for PRX-102. The CHMP opinion was referred for final action to the EC. A final EC decision on the MAA is expected in the beginning of May 2023.

- On February 21, 2023, we announced our participation in the 19th Annual WORLD*Symposium*™ 2023, which took place on February 22-26, 2023 at the Hilton Orlando in Orlando, Florida. We hosted an informational booth at the symposium.

In light of recent developments relating to the COVID-19 pandemic and the focus of healthcare providers and hospitals on fighting the virus and its variants, and consistent with the FDA's updated industry guidance for conducting clinical trials issued on March 18, 2020, we and our contract research organizations have made certain adjustments to the operation of our clinical trials in an effort to ensure the monitoring and safety of patients and minimize risk to trial integrity during the pandemic and generally, and we may need to make adjustments again in the future.

We are in close contact with our principal investigators, clinical sites and clinical research organizations, which are primarily located in the United States and Europe, and to date, the COVID-19 pandemic has had a minimal effect on the performance of the phase III clinical trials of PRX-102 as many of the patients were already treated in home care settings. We were able to complete all three of the clinical trials.

***Delisting from Tel Aviv Stock Exchange***

On December 21, 2022, we announced that that we have decided that it is our company's best interest to voluntarily delist our common stock from the Tel Aviv Stock Exchange, or the TASE. The delisting took effect on March 22, 2023, and the last trading day on the TASE was March 20, 2023.

**ProCellEx: Our Proprietary Protein Expression System**

ProCellEx is our proprietary platform used to produce and manufacture recombinant proteins through plant cell-based expressions in suspension. ProCellEx consists of a comprehensive set of proprietary technologies and capabilities, including the use of advanced genetic engineering and plant cell culture technology, enabling us to produce complex, proprietary, and biologically equivalent proteins for a variety of human diseases. Our protein expression system facilitates the creation and selection of high-expressing, genetically-stable cell lines capable of expressing recombinant proteins.

Our ProCellEx technology allows for many unique advantages, including: biologic optimization; an ability to handle complex protein expressions; flexible manufacturing with improvements through efficiencies, enhancements and/or rapid horizontal scale-ups; a simplified production process; elimination of the risk of viral contaminations from mammalian components; and intellectual property advantages.

We are the first and only company to gain FDA approval of a protein produced through plant cell-based expression. Our ProCellEx platform uses flexible polyethylene disposable bioreactors and is optimized for plant cell cultures. As opposed to the large stainless-steel bioreactors commonly used for recombinant protein production, our ProCellEx bioreactors are easy to use and maintain and allow for the major advantage of rapid horizontal scale-up.

**Plant Cell Production Advantages**

**Large-Scale Plant Cell Production Advantages**

- Rapid product roll-out and development
- No risk of viral contamination from mammalian components
- Manufacturing maintained at room temperature
- Highly tolerant of small changes in production conditions, including Ph and temperature
- Easy to use and maintain, with no requirement for complicated monitors
- Maintain production parameter constant → high reproducibility
- Independent, separately controlled, disposable bioreactors - no "cross talking"
- Rapid and flexible horizontal scale-up in accordance with changing production needs

**Mammalian Cell Expression**

Chinese Hamster Ovary (CHO) cell lines

- High set-up costs involving large bioreactors
- Cell cultures require a complex medium; small changes in composition may affect product characteristics
- Require highly controlled growth conditions in the bioreactor (e.g., Ph., temp and $CO_2$)
- Susceptibility to viral contaminations

**Bacteria and Yeast Cell Expression**

Bacteria or yeast cell lines

- Limited to non-glycosylated simple proteins
- Cannot produce antibodies, enzymes, and other complex proteins

**ProCellEx®: Protalix's Differentiated Plant Cell Protein Expression Platform**

**Unique Genetic Engineering Tools**

Generates **improved tobacco plant cell lines** expressing plant unique expression cassettes designed to produce therapeutic proteins with **optimized pharmacokinetic and pharmacodynamic profiles**

**Customized Chemical Modifications**

Produces complex glycosylated proteins with potentially improved biologic attributes, including **reduced immunogenicity** and **enhanced protein stability/activity**

**Intellectual Property Advantages**

Proprietary manufacturing processes and development of 2nd generation products, related to Composition of Matter protection and FTO (Freedom-to-Operate)


**Optimized for Complexity**

Ability to express proteins that are difficult to express in other cell-based systems

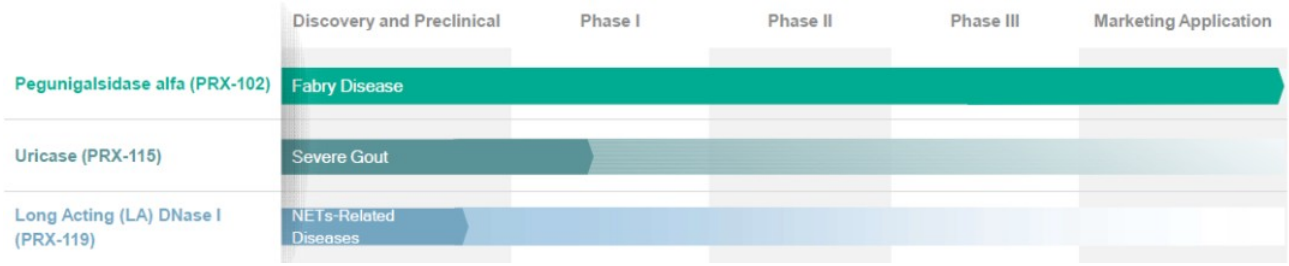
**Streamlined Production Process**

Simplified maintenance with **high batch-to-batch reproducibility** and **no risk of viral contamination**

**Poised for Flexible Scale-Up**

GMP-compliant infrastructure with modular capabilities allows for **rapid horizontal scale-up** to maintain production volume

**Product Pipeline**




***Pegunigalsidase Alfa (PRX-102) for the Treatment of Fabry Disease***

PRX-102, our lead product candidate, is a late-stage clinical asset in development for the treatment of Fabry disease. We expect PRX-102 to be the primary subject of our development efforts in the short-term. It is our proprietary, investigational, plant cell culture expressed enzyme, and a chemically modified stabilized version of, the recombinant α-Galactosidase-A protein, a lysosomal enzyme, under development for the treatment of Fabry disease. Fabry disease is a serious life-threatening rare genetic disorder. Fabry patients lack or have low levels of α-galactosidase-A resulting in the progressive accumulation of abnormal deposits of a fatty substance called globotriaosylceramide, or $Gb_3$, in blood vessel walls throughout their body. The ultimate consequences of $Gb_3$ deposition range from episodes of pain and impaired peripheral sensation to end-organ failure, particularly of the kidneys, but also of the heart and the cerebrovascular system. Fabry disease occurs in one person per 40,000 to 60,000 males.

The global market for Fabry disease, that includes Sanofi's Fabrazyme®, Shire's (acquired by Takeda Pharmaceutical Company Limited) Replagal®, and Amicus Therapeutics' Galafold®, among others, was $2.2 billion in 2022, is forecasted to be approximately $2.3 billion in 2023 and is forecasted to grow at a CAGR of approximately 11.9% from 2022-2028.

Our phase III clinical program included three separate clinical trials which are referred to as the *BALANCE* study, the *BRIDGE* study and the *BRIGHT* study, all of which have been completed. In addition, the phase III clinical program included two extension studies in which subjects that participated in our phase I/II clinical trials and our phase III clinical trials were given the opportunity to enroll and continue to be treated with PRX-102. As of March 1, 2023, sponsorship of the two open-label extension studies was transferred to Chiesi, and Chiesi is now administering the extension studies.

The FDA has indicated that the BLA for PRX-102 for the potential treatment of adult patients with Fabry disease that we, together with Chiesi, resubmitted on November 9, 2022 was considered a complete, class 2 response and set a PDUFA action date of May 9, 2023. The initial BLA for PRX-102 was submitted to the FDA on May 27, 2020 under the FDA's Accelerated Approval pathway, and was subsequently accepted by the FDA and granted Priority Review designation. However, in April 2021, the FDA issued the CRL in response to the initial BLA. In preparation for the BLA resubmission, the Company and Chiesi participated in a Type A (End of Review) meeting with the FDA on September 9, 2021. As part of the meeting minutes provided by the FDA, which included the preliminary comments and meeting discussion, the FDA, in principle, agreed that the data package proposed to the FDA for a BLA resubmission has the potential to support a traditional approval of PRX-102 for the treatment of Fabry disease. The data package in the BLA resubmission, given the change in the regulatory landscape in the United States, includes the final two-year analyses of our *BALANCE* study and long-term data from our open-label extension study of PRX-102 in adult patients treated with a 2 mg/kg every four weeks dosage of PRX-102.

On February 7, 2022, we, together with Chiesi, submitted an MAA for PRX-102 to the EMA which was subsequently validated by the EMA. The submission was made after the October 8, 2021 meeting we held, together with Chiesi, with the Rapporteur and Co-Rapporteur of the EMA regarding PRX-102.

The MAA submission includes a comprehensive set of preclinical, clinical and manufacturing data compiled from our completed and ongoing clinical studies evaluating PRX-102 as a potential alternative treatment for adult patients with Fabry disease, including data from our completed 12–month switch–over phase III *BRIGHT* clinical trial in adult patients with Fabry disease treated with a 2 mg/kg every four weeks dosage to support an additional potential treatment regimen for Fabry patients. As part of the EMA review process, we and Chiesi responded to the Day 120 list of questions in September 2022 (following a 3-month clock-stop period) and to the list of outstanding issues of Day 180 in December 2022. An essential portion of the Day 120 response included the submission of the final analysis of the two-year *BALANCE* study (the final Clinical Study Report), and an interim analysis of our long-term, open-label extension study of PRX-102 in adult patients with Fabry disease treated with the 2 mg/kg every four weeks dosage. The EMA's approval of PRX-102 at this time does not include the 2 mg/kg every four weeks dosage.

On February 24, 2023, we, together with Chiesi, announced that CHMP adopted a positive opinion, recommending marketing authorization for PRX-102. The CHMP opinion was referred for final action to the EC. A final EC decision on the MAA is expected in the beginning of May 2023.

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

Chiesi, together with Protalix, participated in an Oral Explanation at a meeting of the EMA's Committee for Orphan Medicinal Products (COMP) held on March 21, 2023, as part of the Orphan Drug Designation maintenance process. Following the meeting, Chiesi formally withdrew the application for Orphan Drug Designation for PRX-102. The EC first granted Orphan Drug Designation for PRX-102 for the treatment of Fabry disease in December 2017.

***Key Trials and Design***

Our clinical development program is designed to show that PRX-102 has a potential clinical benefit in all adult Fabry patient populations when compared to currently marketed Fabry disease enzymes, agalsidase beta (Fabrazyme®; marketed by Sanofi (acquired Genzyme)) and agalsidase alfa (Replagal®; marketed by Takeda Pharmaceutical Company Limited (acquired Shire Plc)). In preclinical studies, PRX-102 showed significantly longer half-life due to higher enzyme stability, enhanced activity in Fabry disease affected organs leading to reduction of the accumulated substrate and reduced immunogenicity, which together can potentially lead to improved efficacy through increased substrate clearance and significantly lower formation of anti-drug antibodies, or ADAs. Providing a meaningful improvement in the health and quality of life for Fabry patients being treated with PRX-102 represents a significant potential market opportunity.

Our phase III clinical program of PRX-102 for the treatment of Fabry disease includes three individual studies; the *BALANCE* study, the *BRIDGE* study and the *BRIGHT* study, all of which have been completed. In 2016, we completed a phase I/II clinical trial of PRX-102, which was a dose range finding study in ERT-naïve adult Fabry patients. In the phase III clinical program overall, two potential dosing regimens for PRX-102 were analyzed; 1 mg/kg every two weeks, with the potential for improved efficacy and safety offering a potential alternative to existing enzyme replacement therapies, and 2 mg/kg every four weeks, which has the potential to lower treatment burden versus existing treatments and potentially provide a better quality of life for a subset of adult Fabry patients.

Patients who completed the *BALANCE*, *BRIDGE* and *BRIGHT* studies, and the extension of the phase I/II study, were offered the opportunity to continue PRX-102 treatment in one of two long-term open-label extension studies. Currently, 126 subjects who participated in our PRX-102 clinical program have opted, with the advice of the treating physician, to continue PRX-102 treatment in one of our long-term, open label, extension studies. Such extension studies include 97 patients in the 1 mg/kg every two weeks extension study (PB-102-F60) with a total cumulative exposure of approximately 400 patient years (10 subjects who completed an extension study from the phase I/II study, 18 subjects who completed the *BRIDGE* study; 69 subjects who completed the *BALANCE* study), and 29 subjects who completed the *BRIGHT* study, in the 2 mg/kg every four weeks extension study (PB-102-F51) with a total cumulative exposure of approximately 110 patient years. Two of such subjects are being treated with 1 mg/kg every two weeks. As of March 1, 2023, sponsorship of the two extension studies was transferred to Chiesi, and Chiesi is now administering the open-label extension studies.

In February 2020, we, together with Chiesi, announced an agreement with the FDA for the Initial Pediatric Study Plan (iPSP) for PRX-102. The joint announcement was made after completion of discussions with the FDA and receipt of confirmation from the FDA in an official "Agreement Letter" which outlines an agreed-upon approach to evaluate the safety and efficacy of PRX-102 in pediatric Fabry patients in a clinical trial to be performed by Chiesi with our collaborative efforts.

***Phase III BALANCE Study***

The pivotal *BALANCE* study was a 24-month, randomized, double blind, active control study of PRX-102 in adult Fabry patients with deteriorating renal function that was designed to evaluate the safety and efficacy of 1 mg/kg of PRX-102 administered every two weeks compared to agalsidase beta. Topline results from the completed study were announced in April 2022 and the Clinical Study Report for the *BALANCE* study was completed in July 2022. The final analysis confirmed the positive topline results and favorable tolerability profile. A total of 78 patients who were previously treated with agalsidase beta for at least one year with an estimated glomerular filtration rate (eGFR) slope at screening worse than -2 mL/min/1.73m$^2$/year were enrolled in the study. Patients were randomized on a 2:1 ratio for switching to PRX-102 or continuing on agalsidase beta. A total of 77 patients were treated; 52 with PRX-102 and 25 with agalsidase beta. Approximately 40% of the enrolled patients were female.

The primary endpoint of the *BALANCE* study is the comparison in the annualized rate of decline of estimated Glomerular Filtration Rate, or eGFR, slope between the agalsidase beta and PRX-102 treatment arms. eGFR is considered a reliable and accepted test to

measure kidney function and stage of kidney disease. Additional parameters evaluated include: cardiac assessment, Lyso-$Gb_3$ (a biomarker for monitoring Fabry patients during therapy), pain, quality of life, immunogenicity, Fabry Clinical Events, pharmacokinetics and other parameters.

Given the changed regulatory landscape in the United States with the full approval of agalsidase beta in March 2021 based on clinical endpoints, we changed the primary analysis of the *BALANCE* study from superiority to non-inferiority, as demonstrating superiority is no longer required under FDA guidelines. As part of the September 2021 Type A End of Review meeting, the FDA, in principle, agreed that the proposed analysis of the *BALANCE* study demonstrating non-inferiority to agalsidase beta to be included in the data package for the PRX-102 BLA resubmission has the potential to support the approval of PRX-102 for the treatment of Fabry disease. The primary endpoint of the *BALANCE* study compared the eGFR annualized changes (slope) between the two treatment arms in the intent-to-treat (ITT) analysis set (77 patients). The study met its pre-specified primary endpoint and demonstrated that PRX-102 was statistically non-inferior to agalsidase beta.

The median (95% confidence interval) of the eGFR slope in the PRX-102 arm was -2.514 mL/min/1.73$m^2$/year (-3.788, -1.240) and -2.155 mL/min/1.73$m^2$/year (-3.805, -0.505) in the agalsidase beta arm, demonstrating a large overlap in the confidence intervals of the two arms. The difference in medians (95% confidence interval) is -0.359 mL/min/1.73$m^2$/year (-2.444, 1.726). The prespecified non-inferiority margin was met. The final results of the per-protocol analysis set (72 patients) are consistent with the ITT results, with an even smaller difference in medians (95% confidence interval); -0.118 mL/min/1.73$m^2$/year (-2.450, 2.213). Additional sensitivity and supportive analyses investigated mean eGFR slopes using other statistical models. These models yielded results similar to the primary analysis and confirming non-inferiority of PRX-102 to agalsidase beta. These results supported the robustness of the methodology used for comparisons of treatment effects in the *BALANCE* study.

The study population (ITT analysis set) was composed of 47 males (61.0%) and 30 females (39.0%), with a mean (range) age of 44.3 (18-60) years. The mean duration of prior treatment with agalsidase beta was approximately six years. At baseline, mean (SD) eGFR was 73.69 ml/min/1.73$m^2$ (20.32) and median eGFR was 74.51 ml/min/1.73$m^2$; mean (SD) eGFR slope was -8.10 mL/min/1.73$m^2$/year (5.92) and median eGFR slope was -7.25 ml/min/1.73$m^2$/year.

A consistent efficacy response was also observed across biomarkers and functional systems relevant to Fabry disease, as demonstrated via secondary endpoints, where in some cases the trend was in favor of PRX-102 and in some in favor of agalsidase beta, but the actual difference between the two arms is always clinically small, supporting the comparability of the two treatments.

Key secondary endpoints included Urine protein creatinine ratio (UPCR) as indicator of proteinuria, plasma levels of lyso –$Gb_3$, imaging marker of cardiac remodeling (Left Ventricular Mass Index, LVMI, by cardiac MRI), disease severity (by Mainz Severity Score Index, MSSI), pain severity (Short Form Brief Pain Inventory, BPI) and quality of life (EQ-5D-5L). Both treatments showed either a stabilization of clinical parameters (e.g., for eGFR, eGFR slope and UPCR) or prevention of further progression of Fabry disease (e.g., LVMI, MSSI).

- *Secondary measures of kidney function*. In addition to eGFR levels and slope, the proportion of patients categorized as having severe proteinuria (UPCR ≥ 1 gr/gr) in the PRX-102 arm remained stable during the study (at baseline, 7/52 [13.5%] and 6/45 [13.3%] 24-month), while in the agalsidase beta arm, the proportion increased slightly with 3/25 (12.0%) and 4/24 (16.7%), respectively. Mean (SE) UPCR data (post-hoc analysis) for the entire study population remained stable throughout the study with a slight advantage for PRX-102 at 24-months compared to agalsidase beta (Table 1).

- *Biomarkers of Fabry disease*. Mean (SE) and median (range) plasma lyso-$Gb_3$ change from baseline to 24 months of treatment in the PRX-102 arm were 3.30 (1.38) and 1.15 (-32.2 to 32.7) nM for PRX-102, and -8.74 (4.85) and -1.50 (-102.3 to 2.4) nM for agalsidase beta. As expected, a gender difference was noted, with female Fabry patients exhibiting lower values at baseline and no remarkable changes during the study. Overall, the absolute changes of the Fabry biomarkers were minor in both treatment arms and were considered not clinically significant since there was no indication of $Gb_3$ re-accumulation nor of disease progression.

- *Measures of cardiac disease*. LVMi was centrally evaluated based on cardiac MRI. An increase in LVMi is indicative of progressing cardiomyopathy, hence preventing an increase in LVMI represents a therapeutic goal in Fabry patients. In the *BALANCE* study, the change from baseline in both treatment arms was analyzed by absence/presence of hypertrophy at baseline (defined as a LVMI above 91 g/$m^2$ for males and LVMI above 77 g/$m^2$ for females at baseline) and by gender (Kawel-Boehm 2015). Similar results were achieved in the two treatment arms after 24 months, with a slight reduction in the mean (SE) LVMi values in the PRX-102 arm -4.238 (5.731) and a small increase in the agalsidase beta arm 2.417 (9.620) for patients with hypertrophy at baseline. Small differences were observed also in those patients without hypertrophy at baseline in both treatment arms.

- *Measures of systemic disease burden (MSSI).* Further evidence of the stabilization of the disease is provided by the MSSI overall scores, which remained stable throughout the *BALANCE* study in both arms, with the baseline score in both groups at the low end of the moderate range (means of 23.18 points in the PRX-102 arm and 25.16 points in the agalsidase beta arm), that slightly decreased (improvement by -2.1 points) in the PRX-102 arm and slightly increased in the agalsidase beta arm (+2.0 points). In this case, the CI of the difference in mean changes did not contain 0, suggesting a difference between the two arms in favor of PRX-102.

- *Patient reported outcomes.* With regards to the patient-reported outcomes (BPI and EQ-5D-5L), the two treatments showed very similar results, with the majority of patients reporting an improvement or no change in both groups, for each domain.

For an overview of primary and secondary endpoints collected in the *BALANCE* study, please refer to the Table 1 below.

**Table 1: Summary Table of Comparison of Treatment Benefit Data in the *BALANCE* Study, (Mean (SE) [median]), Efficacy Population**

| **Parameter** | | **PRX-102 (N = 52)** | | **Agalsidase beta (N = 25)** | |
|---|---|---|---|---|---|
| eGFR ($ml/min/1.73m^2$) | | **n** | | **n** | |
| | Baseline | 52 | 73.46 (2.80) [73.45] | 25 | 74.16 (4.19) [74.85] |
| | Month 24 | 47 | 70.53 (3.19) [69.35] | 24 | 72.05 (4.69) [74.48] |
| | Change from Baseline | 47 | -3.60 (1.58) [-2.39] | 24 | -1.97 (1.51) [-3.20] |
| eGFR slope ($ml/min/1.73m^2/yr$) | Baseline | 52 | -8.03 (0.92) [-6.70]<br>Range: -30.5; 6.3 | 25 | -8.25 (0.85) [-7.84]<br>Range: -20.3; -2.8 |
| | Month 24 | 51 | -2.38 (1.25) [-2.51]<br>Q1; Q3: -4.8; 0.8 | 25 | -2.31 (0.71) [-2.16]<br>Q1; Q3: -4.6; -0.5 |
| Reaching kidney therapeutic goal[a] | Month 24 | 52 | 41 patients (80.4%) | 25 | 20 patients (80.0%) |
| UPCR | Baseline | 52 | 0.441 (0.084) | 25 | 0.284 (0.097) |
| | Month 24 | 45 | 0.480 (0.118) | 24 | 0.489 (0.162) |
| | Change from Baseline | 45 | 0.088 (0.067) | 24 | 0.197 (0.085) |
| Plasma lyso-$Gb_3$ (nM) | Baseline | 52 | 26.22 (3.78) [15.20] | 25 | 32.14 (7.08) [17.60] |
| | Month 24 | 46 | 29.22 (4.48) [18.80] | 22 | 19.65 (3.60) [15.30] |
| | Change from Baseline | 46 | 3.30 (1.38) [1.15] | 22 | -8.74 (4.85) [-1.50] |
| LVMI ($g/m^2$) | Baseline | 40 | 75.97 (5.13) | 22 | 82.22 (6.34) |
| | Month 24 | 35 | 71.56 (5.20) | 20 | 82.43 (8.39) |
| | Change from Baseline | 28 | -0.64 (2.69) | 19 | 0.29 (3.73) |
| MSSI (overall score)[a] | Baseline | 49 | 23.18 (1.42) | 25 | 25.16 (2.14) |
| | Month 24 | 46 | 22.11 (1.80) | 23 | 27.09 (2.30) |
| | Change from Baseline | 44 | -2.07 (0.77) | 23 | 2.04 (1.10) |
| BPI (score for pain at its worst)[b] | Baseline | 52 | 3.5 (0.4) | 25 | 2.6 (0.6) |
| | Month 24 | 45 | 3.3 (0.5) | 22 | 3.0 (0.7) |
| | Change from Baseline | 45 | -0.1 (0.5) | 22 | 0.6 (0.6) |

BPI=brief pain inventory; eGFR=estimated glomerular filtration rate; lyso-$Gb_3$=globotriaosylsphingosine; LVMI=Left Ventricular Mass Index; MSSI=Mainz Severity Score Index; UPCR=Urine Protein Creatinine Ratio.

[a] Wanner 2018; [b] Higher scores indicate higher symptom severity.

Forty-seven (90.4%) patients in the PRX-102 arm experienced at least one treatment-emergent adverse event (TEAE) compared to 24 (96.0%) in the agalsidase beta arm. The number of events adjusted to 100 years of exposure is 572.36 events for the PRX-102 arm and 816.85 events for the agalsidase beta arm.

Treatment-related adverse events were reported for 21 (40.4%) patients in the PRX-102 arm compared to 11 (44.0%) in the agalsidase beta arm. The number of treatment-related events adjusted to 100 years of exposure is 42.85 events for the PRX-102 arm and 152.91 events for the agalsidase beta arm.

Usage of infusion pre-medication was tapered down during the study, if possible, for all patients. At baseline, 21 (40.4%) patients in the PRX-102 arm used infusion premedication compared to 16 (64.0%) in the agalsidase beta arm. At the end of the study, only three out of 47 (6.4%) patients in the PRX-102 arm used infusion premedication compared to three out of 24 (12.5%) in the agalsidase beta arm. Even with this reduction in use of premedication, there were fewer reported infusion-related reactions with PRX-102: 11 (21.2%) patients in the PRX-102 arm experienced a total of 13 events compared to six (24.0%) patients experiencing a total of 51 events in the agalsidase beta arm. The number of infusion-related reactions adjusted to 100 infusions is 0.5 for the PRX-102 arm and 3.9 for the agalsidase beta arm.

Assessment of immunogenicity, that is, the existence and development of anti PRX-102 antibodies or anti-agalsidase beta antibodies, in the study indicated that for the PRX-102 arm, 18 (34.6%) patients were ADA positive at baseline, of which 17 (94.4%) had neutralizing antibody activity. For the agalsidase beta arm, eight (32.0%) patients were ADA positive at baseline, of which seven (87.5%) had neutralizing antibody activity. Only a small number of patients showed treatment-emergent ADA. At the end of the two-year study, 11 (23.4%) patients who received PRX-102 were ADA positive, of which seven (63.6%) had neutralizing antibody activity, while in the agalsidase beta arm six (26.1%) were ADA-positive and all six (100%) had neutralizing antibody activity. There was little change in the percentage of patients who were ADA positive, with a trend of reduction observed in the PRX-102 arm and stability in the agalsidase beta arm. The proportion of patients with neutralizing ADA decreased in the PRX-102 arm while it remained stable in the agalsidase beta arm.

Out of the 78 randomized patients, six patients discontinued the study: out of the five (9.4%) from the PRX-102 arm, one patient withdrew consent prior to the first infusion, two discontinued due to personal reasons, and two due to adverse events (one due to an unrelated adverse event and one due to a treatment related adverse event); one (4%) patient from the agalsidase beta arm discontinued for personal reasons. There were no deaths in this study.

Considering that in the trial, patients in the PRX-102 arm were exposed for the first time to the novel enzyme, tolerability data appear favorable for PRX-102 and in line with what was observed in the previous clinical studies of PRX-102.

Of the patients who completed the trial from both the PRX-102 and agalsidase beta treatment arms, 69 have opted, with the advice of the treating physician, to receive PRX-102 1 mg/kg every two weeks in the long-term open-label extension study which is now sponsored by Chiesi.

The results of the direct, blinded comparison of PRX-102 to agalsidase beta, for the primary efficacy renal endpoints (i.e., eGFR change, eGFR slope) and for the main secondary endpoints (e.g., urine protein to creatinine ratio [UPCR] LVMI, MSSI, BPI) strongly suggest comparability in treatment effects between the two treatments.

At the same time a potentially favorable safety profile was identified based on lower rates of IRR, lower ADA positivity, and less premedication use in the PRX-102 arm compared to agalsidase beta. Overall, a positive benefit-risk balance was confirmed.

***Phase III BRIDGE Study***

The *BRIDGE* study was a 12-month open-label, single arm switch-over study evaluating the safety and efficacy of pegunigalsidase alfa, 1 mg/kg infused every two weeks, in up to 22 Fabry patients previously treated with agalsidase alfa for at least two years and on a stable dose for at least six months. The trial was completed in December 2019. Patients were screened and evaluated over three months while continuing agalsidase alfa treatment.

Final results of the data generated in the *BRIDGE* study showed substantial improvement in renal function as measured by mean annualized eGFR slope in both male and female patients. Twenty of 22 patients completed the 12-month treatment duration. Eighteen of the patients who completed the study opted to roll over to a long-term extension study and continue to be treated with PRX-102. In the study, the mean annualized eGFR slope of the study participants improved from -5.90 mL/min/1.73m$^2$/year while on agalsidase alfa to -1.19 mL/min/1.73m$^2$/year on PRX-102 in all patients. Male patients improved from -6.36 mL/min/1.73m$^2$/year to -1.73 mL/min/1.73m$^2$/year and female patients improved from -5.03 mL/min/1.73m$^2$/year to -0.21 mL/min/1.73m$^2$/year. Following the switch to PRX-102, there was a decrease in patients with progressing or fast progressing kidney disease which is consistent with the therapeutic goals for Fabry disease, as identified by Christoph Wanner, et. al., in 2019, and most patients achieved a stable status post-switch.

PRX-102 was well-tolerated in the *BRIDGE* study, with all adverse events being transient in nature without sequelae. Of the 22 patients enrolled in the *BRIDGE* study, the majority of TEAEs were mild or moderate in severity, with two patients (9.1%) withdrawing from the therapy due to hypersensitivity reaction that was resolved. The most common moderate TEAEs were nasopharyngitis, headache and dyspnea.

An immunogenicity assessment indicated that four out of 20 patients (20%) developed persistent ADAs over the course of the study, of which two had neutralizing activity.

Baseline characteristics of the 20 patients who completed the study, ranging from ages 28 to 60 years, were as follows: mean eGFR 75.87 mL/min/1.73m$^2$ in males, and 86.14 mL/min/1.73m$^2$ in females and plasma lyso-$Gb_3$ were 51.81 nM and 13.81 nM in males and females, respectively. While lyso-$Gb_3$ levels remain slightly high, particularly within the male cohort, continuous reduction in lyso-$Gb_3$ levels was observed of 19.55 nM (32.35%) in males and 4.57 nM (29.81%) in females.

Of the patients who completed the trial, 18 have opted, with the advice of the treating physician, to continue receiving PRX-102 1 mg/kg every two weeks in a long-term open-label extension study which now sponsored by Chiesi.

***Phase III BRIGHT Study***

The *BRIGHT* study was a multicenter, multinational open-label, switch-over study designed to evaluate the safety, efficacy and pharmacokinetics of treatment with 2 mg/kg of PRX-102 administered every four weeks for 52 weeks (a total of 14 infusions). The trial, which was completed in June 2020, enrolled 30 adult patients (24 males and 6 females) with mean (SD) age of 40.5 (11.3) years, ranging from 19 to 58 years previously treated with a commercially available ERT (agalsidase beta or agalsidase alfa), for at least three years and on a stable dose administered every two weeks. To determine eligibility for participation in the study, candidates were screened to identify and select Fabry patients with clinically stable kidney disease. The most common Fabry disease symptoms at baseline were acroparesthesia, heat intolerance, angiokeratomas and hypohydrosis. Patients who matched the criteria were enrolled in the study and switched from their current treatment of IV infusions every two weeks to 2 mg/kg of PRX-102 every four weeks for 12 months. Patients participating in the study were evaluated, among other disease parameters, to determine if their kidney disease had not further deteriorated while being treated with the four-week dosing regimen as measured by eGFR and for lyso-$Gb_3$ levels as a Fabry biomarker, as well as other parameters. In addition, participating patients were evaluated to assess the safety and tolerability of PRX-102.

We announced final results from the *BRIGHT* study in March 2022. The results indicate that 2 mg/kg of PRX-102 administered by intravenous infusion every four weeks was well tolerated, and Fabry disease assessed by eGFR slope and plasma lyso-$Gb_3$ was stable throughout PRX-102 treatment in adult Fabry patients. None of the patients without ADAs at screening developed treatment-induced ADAs following the switch to PRX-102 treatment.

All 30 patients received at least one dose of PRX-102, and 29 patients completed the one-year study. Of these 29 patients, 28 received the intended regimen of 2 mg/kg every four weeks throughout the entire study, while one patient was switched to 1 mg/kg PRX-102 every two weeks per protocol at the 11th infusion. One patient withdrew from the study after the first infusion due to a traffic accident.

First infusions of PRX-102 were administered under controlled conditions at the investigation site. Based on the protocol-specified criteria, patients were able to receive their PRX-102 infusions at a home care setup once the applicable Investigator and Sponsor Medical Monitor agreed that it was safe to do so. Safety and efficacy exploratory endpoints were assessed throughout the 52-week study.

Overall, 33 of 183 total TEAEs reported in nine (30.0%) of the patients were considered treatment related; all were mild or moderate in severity and the majority were resolved at the end of the study. There were no serious or severe treatment-related TEAEs and no TEAEs led to death or study withdrawal. Of the treatment-related TEAEs, 27 were infusion-related reactions (IRRs) and the remainder were single events of diarrhea, erythema, fatigue, influenza-like illness, increases urine protein/creatinine ratio, and urine positive for white blood cells. The 27 IRRs were reported in five (16.7%) patients, all male. All IRRs occurred during the infusion or within two hours post-infusion; no events were recorded between two and 24 hours post-infusion.

Study outcome measures show that plasma lyso-$Gb_3$ concentrations remained stable during the study with a mean change (±SE) of 3.01 nM (0.94) from baseline (19.36 nM ±3.35) to Week 52 (22.23 ±3.60 nM). Mean absolute eGFR values were stable during the 52-week treatment period, with a mean change from baseline of -1.27 mL/min/1.73m$^2$ (1.39). Mean (SE) eGFR slope, at the end of the study, for the overall population, was -2.92 (1.05) mL/min/1.73m$^2$/year indicating stability.

The study suggests that Fabry patients who are currently receiving ERT every two weeks may be successfully transitioned to PRX-102 2 mg/kg every four weeks as an effective and tolerable alternative treatment option. Additional long term data is being collected as part of the ongoing long term extension study of the 2 mg/kg PRX-102 every four weeks dose.

Following a survey of participants using the Quality of Life EQ-5D-5L questionnaire, responses indicate that patient perception of their own health remained high and stable throughout the 52-week study duration, with overall health mean (SE) scores of 78.3 (3.1) and 82.1 (2.9) at baseline and Week 52, respectively, in a 0 to 100 scale. Using the short-form Brief Pain Inventory, or questionnaire,

approximately 75% of study participants had an improvement or no change in average pain severity at Week 52 (compared to baseline). The short-form BPI interference items also remained stable during the study. Pain-related results indicate that there was no increase and/or relapse in pain. No Fabry clinical events were reported during the study.

***Open-Label Extension Studies***

Our PRX-102 clinical program included two open-label extension studies; one of the 1 mg/kg PRX-102 every two weeks dosage, which we refer to as the F60 Study and the second of the 2 mg/kg PRX-102 every four weeks dosage, which we refer to as the F51 Study. Patients who completed the *BALANCE* Study, the *BRIDGE* Study and our phase I/II extension study were given the opportunity to enroll in the F60 Study and patients who completed the *BRIGHT* Study were given the opportunity to enroll in the F51 Study. Overall, 97 patients enrolled in the F60 Study; 69 patients from the *BALANCE* Study, 18 patients from the *BRIDGE* Study and 10 patients from the phase I/II study. In addition, 29 patients enrolled in the F51 Study. As of April 30, 2023, 88 patients are actively participating in the F60 Study and 28 patients are actively participating in the F51 Study. Sponsorship of both the F60 Study and the F51 Study were transferred to Chiesi as of February 28, 2023.

***COVID-19 Impact on PRX-102 Clinical Trials***

To date, the COVID-19 pandemic has had a minimal effect on the performance of the phase III clinical trials of PRX-102 as many of the patients were already treated in home care settings. We were able to complete all three studies. In a minimal amount of cases, patients who completed a trial were not able to be transferred into an extension study due to the pandemic restrictions, and, accordingly, the main trial was prolonged for the patients to permit the continuation of treatment.

***Phase I/II Study***

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

The adult symptomatic, ERT-naïve Fabry disease patients enrolled in the phase I/II study were evaluated for $Gb_3$ levels in kidney biopsies and for plasma Lyso-$Gb_3$ concentration by the quantitative BLISS methodology. Biopsies were available from 14 patients. The outcome of ≥ 50% reduction in the average number of $Gb_3$ inclusions per kidney PTC from baseline to Month 6 was demonstrated in 11 of 14 (78.6%) of the patients treated with PRX-102. The overall results demonstrate that PRX-102 reaches the affected tissue and reduces kidney $Gb_3$ inclusions burden and Lyso-$Gb_3$ in the circulation. A high correlation was found between the two Fabry disease biomarkers, reduction of kidney $Gb_3$ inclusions and the reduction of plasma Lyso-$Gb_3$ over six months of treatment.

Data was recorded at 24 months from 11 patients who completed 12 months of the long-term open-label extension trial that succeeded the phase I/II study. Patients who did not continue in the extension trial included: female patients who became or planned to become pregnant and therefore were unable to continue in accordance with the study protocol; and patients who relocated to a location where treatment was not available under the clinical study.

Results show that Lyso-$Gb_3$ levels decreased approximately 90% from baseline. Renal function remained stable with mean eGFR levels of 108.02 and 107.20 at baseline and 24 months, respectively, with a modest annual eGFR slope of -2.1. An improvement across all the gastrointestinal symptoms evaluated, including severity and frequency of abdominal pain and frequency of diarrhea, was noted. Cardiac parameters, including LVM, LVMI and EF, remained stable with no cardiac fibrosis development detected. In conclusion, an improvement of over 40% in disease severity was shown as measured by the Mainz Severity Score Index, or MSSI, a score compiling the different elements of the disease severity including neurological, renal and cardiovascular parameters. In addition, an improvement was noted in each of the individual parameters of the MSSI.

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

***Commercialization Agreements with Chiesi Farmaceutici***

We have entered into two exclusive global licensing and supply agreements for PRX-102 for the treatment of Fabry disease with Chiesi. The agreements have significant revenue potential for Protalix. Under the agreements, Protalix Ltd. has received $50.0 million in upfront payments and development cost reimbursements of $45.0 million, and is entitled to approximately $1.0 billion in potential milestone payments and tiered royalties of 15% - 35% (ex-US) and 15% - 40% (US).

On October 19, 2017, Protalix Ltd. and Chiesi entered into the Chiesi Ex-US Agreement pursuant to which Chiesi was granted an exclusive license for all markets outside of the United States to commercialize PRX-102. Under the Chiesi Ex-US Agreement, Chiesi made an upfront payment to Protalix Ltd. of $25.0 million in connection with the execution of the agreement, and Protalix Ltd. was entitled to additional payments of up to $25.0 million in development costs in the aggregate, capped at $10.0 million per year. Protalix Ltd. is also eligible to receive additional payments of up to a maximum of $320.0 million in regulatory and commercial milestone payments. Protalix Ltd. agreed to manufacture all of the PRX-102 needed for all purposes under the agreement, subject to certain exceptions, and Chiesi will purchase PRX-102 from Protalix Ltd., subject to certain terms and conditions. Chiesi is required to make tiered payments of 15% to 35% of its net sales, depending on the amount of annual sales, as consideration for the supply of PRX-102.

On July 23, 2018, Protalix Ltd. entered into the Chiesi US Agreement with respect to the development and commercialization of PRX-102 in the United States. Protalix Ltd. received an upfront, non-refundable, non-creditable payment of $25.0 million from Chiesi and was entitled to additional payments of up to a maximum of $20.0 million to cover development costs for PRX-102, capped at $7.5 million per year. Protalix Ltd. is also eligible to receive additional payments of up to a maximum of $760.0 million, in the aggregate, in regulatory and commercial milestone payments. Chiesi agreed to make tiered payments of 15% to 40% of its net sales under the Chiesi US Agreement to Protalix Ltd., depending on the amount of annual sales, subject to certain terms and conditions, as consideration for product supply.

On May 13, 2021, we signed a binding term sheet with Chiesi amending the Chiesi Agreements in order to provide our company with near-term capital. Chiesi agreed to make a $10.0 million payment to us before the end of the second quarter of 2021 in exchange for a $25.0 million reduction in a longer term regulatory milestone payment provided in the Chiesi EX-US Agreement. All other regulatory and commercial milestone payments remain unchanged. We received the payment in June 2021. We also agreed to negotiate certain manufacturing related matters.

On August 29, 2022, we entered into the F/F Agreement and the Letter Agreement. Under the F/F Agreement, we agreed to supply Chiesi with drug substance for PRX-102 and, following relevant technology and technical information transfer activities, Chiesi has agreed, among other things, to provide us with commercial fill/finish services for PRX-102, including to support the anticipated global launch of PRX-102. The F/F Agreement will expire December 31, 2025, unless terminated earlier in accordance with its terms and may be extended by mutual agreement in writing for an additional period of seven years. The Letter Agreement changed the obligations of both us and Chiesi under the License Agreements with respect to, among other things, the evaluation, selection and establishment of an initial alternate source of commercial fill/finish services for PRX-102. In addition, the Letter Agreement amended certain provisions of the License Agreements to reflect the appointment of Chiesi as a supplier to our company of commercial fill/finish services and the potential establishment of an initial alternate source of commercial fill/finish services.

As of March 1, 2023, sponsorship of the two extension studies was transferred to Chiesi, and Chiesi is now administering the extension studies.

***Elelyso® for the Treatment of Gaucher Disease***

Elelyso (taliglucerase alfa), our first commercial product, was approved by the FDA in 2012 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. In August 2014, the FDA approved Elelyso for injection for pediatric patients. Elelyso is the first plant cell derived recombinant protein to be approved by the FDA for the treatment of Gaucher disease and is now approved in over 20 markets.

Gaucher disease, also known as glucocerebrosidase, or GCD, deficiency, is a rare genetic autosomal recessive disorder and one of the most common Lysosomal Storage Disorders, or LSDs, in the world. It is one of a group of disorders that affect specific enzymes that normally break down fatty substances for reuse in the cells. If the enzymes are missing or do not work properly, the substances can build up and become toxic. Gaucher disease occurs when a lipid called glucosylceramide accumulates in the cells of the bone marrow, lungs, spleen and liver, and sometimes the brain. Gaucher disease symptoms can include fatigue, anemia, easy bruising and bleeding, severe bone pain and easily broken bones, and distended stomach due to an enlarged spleen and thrombocytopenia. Epidemiology of Gaucher disease varies; recent literature provides that prevalence of Gaucher disease ranges from 0.70 to 1.75 per 100,000 in the

general population. In people of Ashkenazi Jewish heritage, estimates of occurrence vary from approximately 1 in 400 to 1 in 850 people.

The global market for Gaucher disease, that includes Sanofi's Cerezyme®, Shire's (acquired by Takeda Pharmaceutical Company Limited) Vpriv®, and Sanofi's Cerdelga®, among others, was $1.6 billion in 2022, is forecasted to be approximately $1.6 billion in 2023 and is forecasted to grow at a CAGR of approximately 3% from 2022-2028.

***Commercialization Agreements for Elelyso***

We have licensed to Pfizer the global rights to Elelyso in all markets excluding Brazil. Pfizer retains 100% of revenue and reimburses 100% of direct costs. We manufacture drug substance for Pfizer, subject to certain terms and conditions.

For the first 10-year period after the execution of our Amended Pfizer Agreement, we have agreed to sell drug substance to Pfizer for the production of Elelyso, and Pfizer maintains the right to extend the supply period for up to two additional 30-month periods subject to certain terms and conditions. In a subsequent amendment, we agreed that after the completion of the first 10-year supply period, the supply term would automatically extend for a five-year period.

We maintain distribution rights to Elelyso in Brazil through a supply and technology transfer agreement with Fiocruz, an arm of the Brazilian MoH.

***Uricase (PRX-115)***

PRX-115 is our plant cell-expressed recombinant PEGylated uricase (urate oxidase) – a chemically modified enzyme under development for the potential treatment of severe gout. We use ProCellEx to express an optimized recombinant uricase enzyme under development for the potential treatment of severe gout which we are designing to lower uric acid levels while having low immunogenicity and increased half-life in the circulation. Pre-clinical data demonstrates stable PK profile and long half-life, low immunogenic risk and high specific activity which supports the potential of PRX-115 to be a safe and effective treatment for severe gout. Results from the one-month multiple dosing toxicity studies in two species demonstrate that PRX-115 is well tolerated.

On March 21, 2023, the first patient was dosed in our phase I First in Human (FIH) clinical trial of PRX-115, a double-blind, placebo-controlled trial designed to evaluate the safety, pharmacokinetics, pharmacodynamics (reduction of uric acid) and immunogenicity of PRX-115 in patients with elevated uric acid levels (>6.0 mg/dL). The trial is a single ascending dose (SAD) study with up to seven cohorts, and patients are to be randomized 3:1 to receive a single intravenous (IV) dose of PRX-115 or a placebo. The study is being conducted at New Zealand Clinical Research (NZCR) under the New Zealand Medicines and Medical Devices Safety Authority (MedSafe) and the Health and Disability Ethics Committee (HDEC) guidelines, and is expected to enroll approximately 56 patients with no previous exposure to PEGylated uricase.

Gout is the most common inflammatory arthritis in the United States, affecting an estimated 9.2 million adults. Gout is caused by factors that elevate serum uric acid, or sUA, levels, which may include diet or genetic predisposition and environmental factors leading to hyperuricemia and tissue deposition of monosodium urate crystals, tophi, in joints and soft tissues, causing acute and chronic inflammation, and is characterized by recurrent flares. Gout flares lead to substantial morbidity by causing severe pain, reduced quality of life, decreased physical function, increased healthcare costs, and lost economic productivity. Furthermore, gout is strongly associated with metabolic syndrome, and may contribute to myocardial infarction, type 2 diabetes mellitus, chronic kidney disease, or CKD, and premature mortality.

Severe gout is generally described as a state of gout in which there is a presence of monosodium urate crystals with any of the following: frequent recurrent gout flares, chronic gouty arthritis, subcutaneous tophi or disease elements of gout seen via imaging. It is estimated that approximately 2% of the gout patient population is considered to have chronic refractory disease, and we believe the incidence of severe gout is higher.

Currently available urate-lowering therapies, or ULTs, can be effective in treating gout. However, we believe that new effective, safe therapies are needed to treat severe gout and chronic refractory gout regardless of treatment history. One treatment option may be a therapeutic use of the uricase enzyme which converts uric acid to allantoin, which is easily eliminated through urine. The uricase enzyme does not exist naturally in humans. To date, two variants of recombinant uricases are approved for marketing: (i) Krystexxa® (pegloticase) for treatment of chronic gout refractory to conventional therapy (gout patients who have contraindication/failure of other lowering uric acid treatments) and (ii) Elitek®, indicated for the treatment of tumor lysis syndrome but not gout. Both have a black box warning for anaphylaxis and other major side-effects. In particular, 89% of patients treated with Krystexxa developed an immunogenic response associated with a failure to maintain normalization of serum uric acid levels over a 6-month therapy cycle. In addition, a recent phase IV study demonstrates that co-treatment with Krystexxa and methotrexate prolongs efficacy and increases

tolerability in patients with refractory gout. Krystexxa is no longer marketed in the European Union. The EC withdrew the marketing authorization for Krystexxa in 2016 at the request of the marketing authorization holder which notified the EC of its decision not to market the product in the European Union for commercial reasons.

***PRX-119***

PRX-119 is our plant cell-expressed PEGylated recombinant human DNase I product candidate being designed to elongate half-life in the circulation for NETs-related diseases. NETs, Neutrophil extracellular traps, are web-like structures, released by activated neutrophils that trap and kill a variety of microorganisms. NETs are composed of DNA, histones, antimicrobial and pro-inflammatory proteins. Excessive formation or ineffective clearance of NETs can cause different pathological effects. NETs formation has been observed in various autoimmune, inflammatory and fibrotic conditions, diverse forms of thrombosis, cancer and metastasis. According to scientific literature, animal studies have demonstrated that DNase treatment reduces NETs toxicity. Our proprietary modified DNase I design for long and customized systemically circulating in the bloodstream, may potentially enable effective treatment of acute and chronic conditions.

***Intellectual Property***

A key element of our overall strategy is to establish a broad portfolio of patents to protect our proprietary technology, proprietary product and product candidates and their methods of use. As of March 31, 2023, we hold a broad portfolio of over 80 patents in Europe, the United States, Israel and additional countries worldwide, as well as over 30 pending patent applications.

***Scientific Presentations***

We hosted an informational booth at the 19th Annual WORLD*Symposium*™ 2023, which took place February 22-26, 2023 at the Hilton Orlando in Orlando, Florida. Chiesi also participated in the symposium, hosting, among other events, the following presentations:

“First results of a head-to-head trial of pegunigalsidase alfa vs. agalsidase beta in Fabry disease: 2-year results of the phase 3 randomized, double-blind, BALANCE study,” an abstract (lead author Eric Wallace, M.D., Co-Director of the University of Alabama at Birmingham Fabry Disease Clinic, a principal investigator in our phase III clinical trials of PRX-102) presented by David G. Warnock, M.D., University of Alabama at Birmingham.

“Long-term safety and efficacy of pegunigalsidase alfa administered every 4 weeks in patients with Fabry disease: two-year interim results from the ongoing phase 3 BRIGHT51 open-label extension study,” an abstract presented by John Bernat, M.D., Ph.D., Medical Director of the Iowa Lysosomal Storage Disorders Center, a principal investigator in our phase III clinical trials of PRX-102.

Both of the abstracts were also available during the symposium as poster presentations. Copies of presentations are available on our website under the Presentation tab in the Investors section.

***Research & Development***

We continuously work on the further development of our ProCellEx plant cell expression technology and bioreactor system. In addition, we are working on the development of new products, each in different initial stages of development, for specific products for which there are unmet needs in terms of efficacy and safety. Our development strategy focuses on the utilization of different modification approaches and development improvements, customized for each protein product, in all stages of expression and development.

**Critical Accounting Policies**

Our significant accounting policies are more fully described in Note 1 to our consolidated financial statements appearing in this Quarterly Report. There have been no material changes to our critical accounting policies since we filed our Annual Report on Form 10-K for the year ended December 31, 2022.

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.

**Results of Operations**

***Three months ended March 31, 2023 compared to the three months ended March 31, 2022***

*Revenues from Selling Goods*

We recorded revenues from selling goods of $5.1 million during the three months ended March 31, 2023, a decrease of $3.9 million, or 43%, compared to revenues of $9.0 million for the three months ended March 31, 2022. The decrease resulted primarily from a decrease of $2.7 million in sales to Brazil and a decrease of $1.1 million in sales to Pfizer, both resulting from timing differences.

*Revenues from License and R&D Services*

We recorded revenues from license and R&D services of $4.5 million for the three months ended March 31, 2023, a decrease of $2.6 million, or 37%, compared to revenues of $7.1 million for the three months ended March 31, 2022. Revenues from license and R&D services are comprised primarily of revenues we recognized in connection with the Chiesi Agreements.

*Cost of Goods Sold*

Cost of goods sold was $3.1 million for the three months ended March 31, 2023, a decrease of $2.9 million, or 48%, from cost of goods sold of $6.0 million for the three months ended March 31, 2022. The decrease in cost of goods sold was primarily the result of the decrease in sales of goods.

*Research and Development Expenses*

For the three months ended March 31, 2023, our total research and development expenses were approximately $5.8 million comprised of approximately $3.5 million in subcontractor-related expenses, approximately $1.5 million of salary and related expenses, approximately $0.1 million of materials-related expenses and approximately $0.7 million of other expenses. For the three months ended March 31, 2022, our total research and development expenses were approximately $8.8 million comprised of approximately $5.8 million in subcontractor-related expenses, approximately $2.0 million of salary and related expenses, approximately $0.2 million of materials-related expenses and approximately $0.8 million of other expenses.

Total decrease in research and developments expenses was $3.0 million, or 34%, for the three months ended March 31, 2023 compared to the three months ended March 31, 2022. The decrease in research and development expenses primarily resulted from the completion of our Fabry clinical program and of a substantial portion of the regulatory processes related to the BLA and MAA submissions for PRX-102.

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

*Selling, General and Administrative Expenses*

Selling, general and administrative expenses were $3.1 million for the three months ended March 31, 2023, a decrease of $0.1 million, or 3%, compared to $3.2 million for the three months ended March 31, 2022. A decrease of approximately $0.4 million in salary and related expenses was partially offset by an increase of $0.3 million in professional fees.

*Financial Expenses, Net*

Financial expenses, net were $0.5 million for the three months ended March 31, 2023, compared to financial expenses, net of $0.4 million for the three months ended March 31, 2022.

*Income taxes*

Section 174 of the Tax Cuts and Jobs Act, which was enacted in December 2017, eliminated the option to immediately deduct research and development expenses in the year incurred. The amended provision under Section 174 requires us to capitalize and amortize these expenditures over fifteen years (for out of U.S.-based research and development). In the three months ended March 31, 2023, we recorded income taxes of approximately $0.2 million.

**Liquidity and Capital Resources**

Our sources of liquidity includes our cash and cash equivalents balance. At March 31, 2023, we had $33.0 million in cash and cash equivalents. We have primarily financed our operations through equity and debt financings, business collaborations, and grants funding.

During the year ended December 31, 2022, we raised gross proceeds equal to approximately $8.7 million from the sale of 7,473,038 shares of our common stock under our ATM program. During the three months ended March 31, 2023, we raised gross proceeds equal to approximately $14.9 million from sales of common stock under our ATM program through the sale of 8,212,482 shares of our common stock.

On August 25, 2021, we completed exchanges, or the Exchanges, of a substantial majority of our then outstanding 7.50% Senior Secured Convertible Notes due 2021, or the 2021 Notes, with institutional note holders of a substantial majority of the 2021 Notes. The Exchanges involved the exchange of an aggregate of $54.65 million principal amount of our 2021 Notes for an aggregate of $28.75 million principal amount of newly issued 7.50% Senior Secured Convertible Notes due 2024, or the 2024 Notes, $25.90 million in cash, and approximately $1.1 million in cash representing accrued and unpaid interest through the closing date. The initial conversion rate for the 2024 Notes is 563.2216 shares of our common stock for each $1,000 principal amount of 2024 Notes (equivalent to an initial conversion price of approximately $1.7755 per share of common Stock, subject to adjustment in certain circumstances. This initial conversion price represents a premium of approximately 32.5% relative to the closing price of the common stock on the NYSE American on August 13, 2021. After giving effect to the Exchanges, $3.27 million aggregate principal amount of the 2021 Notes remained outstanding. On November 15, 2021, all of the then outstanding 2021 Notes matured and were paid in full.

The 2024 Notes were issued pursuant to the Indenture dated as of August 24, 2021 between us, the guarantors party thereto, The Bank of New York Mellon Trust Company, N.A., as trustee and Wilmington Savings Fund Society, FSB, as collateral agent, or the 2024 Indenture. Interest on the Notes are payable semi-annually at a rate of 7.50% per annum. The 2024 Notes will mature on September 1, 2024, unless earlier purchased, converted, exchanged or redeemed, and are guaranteed by our subsidiaries. The 2024 Notes are secured by perfected liens on all of our assets, including those of our subsidiaries. Under the terms of the 2024 Indenture, we are required to comply with certain covenants, including the requirement to maintain a minimum cash balance of at least $7.5 million. Failure to comply with such covenants may result in an event of default under the 2024 Indenture and, accordingly, may result in the acceleration of the payment of the notes or in additional interest payments. As of March 31, 2023, we were in compliance with all covenants.

We believe that our cash and cash equivalents as of March 31, 2023, together with additional funds raised from the sale of shares under our ATM program subsequent to March 31, 2023 are sufficient to satisfy our capital needs for at least 12 months from the date that these financial statements are issued.

*Cash Flows*

Net cash used in operations was $3.0 million for the three months ended March 31, 2023. The net loss for the three months ended March 31, 2023 of $3.1 million was increased by a $1.4 million decrease in contracts liability and a $3.5 million increase in inventories and was partially offset by a $3.8 million decrease in accounts receivable-trade and other assets and $0.5 million in share-based compensation. Net cash provided by investing activities for the three months ended March 31, 2023 was $4.7 million and consisted primarily of proceeds from sale of short-term deposits. Net cash provided by financing activities was $14.2 million resulting primarily from the sale of common stock under our ATM program.

Net cash used in operations was $5.8 million for the three months ended March 31, 2022. The net loss for the three months ended March 31, 2022 of $2.3 million was increased by a $2.6 million decrease in contracts liability, a $2.3 million increase in accounts receivable and other assets and $1.0 million decrease in account payable and accruals, and was partially offset by a $1.4 million decrease in inventories and a $0.8 million in share-based compensation. Net cash used in investing activities for the three months ended March 31, 2022 was $16.3 million and consisted primarily of investment in bank deposits.

*Future Funding Requirements*

As a result of our significant research and development expenditures and the lack of significant revenue from sales of taliglucerase alfa, we have generated operating losses from our continuing operations since our inception. Our outstanding 2024 Notes are secured by a perfected lien on all of our assets. Under the terms of the 2024 Indenture, we are required to comply with certain covenants, including the requirement to maintain a minimum cash balance of at least $7.5 million. Failure to comply with such covenants may result in an event of default under the 2024 Indenture and, accordingly, may result in the acceleration of the payment of the notes or in additional interest payments. As of March 31, 2023, we were in compliance with all covenants.

We expect to continue to incur significant expenditures in the near future as we increase our research and developments efforts with respect to our product candidates. We cannot anticipate the costs or the timing of the occurrence of such costs. To the extent we need to obtain additional financing, it may be more difficult for us to do so given the volatility of the price of our common stock. Our material cash needs for the next 24 months will include, among other expenses, (i) costs of preclinical and clinical trials, (ii) employee salaries, (iii) payments for rent and operation of our manufacturing facilities, (iv) fees to our consultants and legal advisors, patent advisors and fees for service providers in connection with our research and development efforts and (v) payments of principal and interest on our outstanding 2024 Notes. We believe that the funds currently available to us are sufficient to satisfy our capital needs for at least 12 months.

As discussed above, we may be required to raise additional capital to develop our product candidates and continue research and development activities. Our ability to raise capital, and the amounts of necessary capital, will depend on many other factors, including:

- the duration and cost of discovery and preclinical development and laboratory testing and clinical trials for our product candidates;
- our progress in commercializing BioManguinhos alfataliglicerase in Brazil;
- 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; and
- the costs associated with any litigation claims.

We expect to finance our future cash needs through corporate collaborations, licensing or similar arrangements, public or private equity offerings and/or debt financings. We currently do not have any commitments for future external funding, except with respect to the development-related payments and milestone payments that may become payable under the Chiesi Agreements. As of March 31, 2023, shares of our common stock for total gross proceeds of approximately $16.5 million remain available to be sold under our 2023 Sales Agreement. During April 2023, we sold, in the aggregate, 3,412,268 shares of Common Stock under the 2023 Sales Agreement generating gross proceeds equal to approximately $7.9 million.

**Effects of Currency Fluctuations**

Currency fluctuations could affect us through increased or decreased acquisition costs for certain goods and services and salaries expenses. We do not believe currency fluctuations have had a material effect on our results of operations during the three months ended March 31, 2023.

**Off-Balance Sheet Arrangements**

We have no off-balance sheet arrangements as of each of March 31, 2023 and December 31, 2022.

**Item 3. 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 U.S. dollar. Most of our revenues and more than 50% of our expenses and capital expenditures are and were 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 43% of our costs, including salaries, expenses and office expenses, are incurred in NIS. Inflation in Israel may have the effect of increasing the U.S. dollar cost of our operations in Israel. If the U.S. dollar declines in value in relation to the NIS, it will

become more expensive for us to fund our operations in Israel. A revaluation of 1% of the NIS will affect our loss before tax by less than 1%. The exchange rate of the U.S. dollar to the NIS, based on exchange rates published by the Bank of Israel, was as follows:

| | March 31, | | December 31, |
|---|---|---|---|
| | 2023 | 2022 | 2022 |
| Average rate for period | 3.536 | 3.197 | 3.360 |
| Rate at period-end | 3.615 | 3.176 | 3.519 |

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.

**Item 4. 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 Quarterly Report on Form 10-Q. The 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 Quarterly Report on Form 10-Q, 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.

Based on the evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the end of the period covered by this Quarterly Report on Form 10-Q, 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 relating to our company and our consolidated subsidiary is made known to management, including the Chief Executive Officer and Chief Financial Officer, particularly during the period when our periodic reports are being prepared.

**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.

**Changes in Internal Control over Financial Reporting**

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 quarter ended March 31, 2023 that have materially affected, or that are reasonably likely to materially affect, our internal control over financial reporting.

## PART II – OTHER INFORMATION

### Item 1. Legal Proceedings

We are not involved in any material legal proceedings.

### Item 1A. Risk Factors

There have been no material changes to the risk factors previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2022.

### Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

### Item 3. Defaults Upon Senior Securities

None.

### Item 4. Mine Safety Disclosure

Not applicable.

### Item 5. Other Information

None.

### Item 6. Exhibits

| Exhibit Number | Exhibit Description | Incorporated by Reference | | | | Filed or Furnished Herewith |
|---|---|---|---|---|---|---|
| | | Form | File Number | Exhibit | Date | |
| 1.1 | At the Market Offering Agreement, dated February 27, 2023, between the Company and H.C. Wainwright & Co., LLC | 8-K | 001-33357 | 1.1 | February 27, 2023 | |
| 3.1 | Certificate of Incorporation of the Company | 8-K | 001-33357 | 3.1 | April 1, 2016 | |
| 3.2 | Amendment to Certificate of Incorporation of the Company | Def 14A | 001-33357 | Appen. A | July 1, 2016 | |
| 3.3 | Second Amendment to Certificate of Incorporation of the Company | Def 14A | 001-33357 | Appen. A | October 17, 2018 | |
| 3.4 | Third Amendment to Certificate of Incorporation of the Company | 8-K | 001-33357 | 3.1 | December 19, 2019 | |
| 3.5 | Fourth Amendment to Certificate of Incorporation of the Company | 10-Q | 001-33357 | 3.5 | August 15, 2022 | |
| 3.6 | Bylaws of the Company | 8-K | 001-33357 | 3.2 | April 1, 2016 | |
| 4.1 | Form of Restricted Stock Agreement/Notice | 8-K | 001-33357 | 4.1 | July 18, 2012 | |
| 4.2 | Description of Capital Stock | 10-K | 001-33357 | 4.7 | February 27, 2023 | |
| 4.3 | Form of Warrant | 8-K | 001-33357 | 4.1 | March 12, 2020 | |
| 4.4† | Form of Stock Option Agreement (Executives) | 10-Q | 001-33357 | 4.8 | August 10, 2020 | |
| 4.5 | Form of Stock Option Agreement (Standard) | 10-Q | 001-33357 | 4.9 | August 10, 2020 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4.6 | Indenture, dated as of August 24, 2021, between Protalix BioTherapeutics, Inc., the guarantors party thereto, The Bank of New York Mellon Trust Company, N.A., as trustee and Wilmington Savings Fund Society, FSB, as collateral agent | 8-K | 001-33357 | 4.2 | August 26, 2021 | |
| 4.7 | Form of Exchange Note (2024) | 8-K | 001-33357 | 4.3 | August 26, 2021 | |
| 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 Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document | | | | | X |
| 101.SCH | Inline XBRL Taxonomy Extension Schema Document | | | | | X |
| 101.CAL | Inline XBRL Taxonomy Extension Calculation Linkbase Document | | | | | X |
| 101.DEF | Inline XBRL Taxonomy Extension Definition Linkbase Document | | | | | X |
| 101.LAB | Inline XBRL Taxonomy Extension Labels Linkbase Document | | | | | X |
| 101.PRE | Inline XBRL Taxonomy Extension Presentation Linkbase Document | | | | | X |
| 104 | COVER PAGE INTERACTIVE DATA FILE (formatted as Inline XBRL and contained in Exhibit 101). | | | | | |

† Management contracts or compensation plans or arrangements in which directors or executive officers are eligible to participate.

**SIGNATURES**

Pursuant to the requirements 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.

PROTALIX BIOTHERAPEUTICS, INC.
(Registrant)

Date: May 4, 2023

By: /s/ Dror Bashan

Dror Bashan
President and Chief Executive Officer
(Principal Executive Officer)

Date: May 4, 2023

By: /s/ Eyal Rubin

Eyal Rubin
Senior Vice President and Chief Financial Officer, Treasurer and Secretary
(Principal Financial and Accounting Officer)

**EXHIBIT 31.1**

**CERTIFICATION**

I, Dror Bashan, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Protalix BioTherapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 4, 2023

/s/ Dror Bashan
Dror Bashan
President and Chief Executive Officer

**EXHIBIT 31.2**

**CERTIFICATION**

I, Eyal Rubin, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Protalix BioTherapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 4, 2023

/s/ Eyal Rubin
Eyal Rubin
Sr. Vice President & Chief Financial Officer,
Treasurer

**EXHIBIT 32.1**

**PROTALIX BIOTHERAPEUTICS, INC.**

CERTIFICATION

In connection with the quarterly report of Protalix BioTherapeutics, Inc. (the "Company") on Form 10-Q for the period ended March 31, 2023 as filed with the Securities and Exchange Commission (the "Report"), I, Dror Bashan, President and Chief Executive Officer of the Company, hereby certify as of the date hereof, solely for purposes of Title 18, Chapter 63, Section 1350 of the United States Code, that to the best of my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company at the dates and for the periods indicated.

This Certification has not been, and shall not be deemed, "filed" with the Securities and Exchange Commission.

Date: May 4, 2023

/s/ Dror Bashan
Dror Bashan
President and Chief Executive Officer

**EXHIBIT 32.2**

**PROTALIX BIOTHERAPEUTICS, INC.**

CERTIFICATION

In connection with the quarterly report of Protalix BioTherapeutics, Inc. (the "Company") on Form 10-Q for the period ended March 31, 2023 as filed with the Securities and Exchange Commission (the "Report"), I, Eyal Rubin, Senior Vice President and Chief Financial Officer of the Company, hereby certify as of the date hereof, solely for the purposes of Title 18, Chapter 63, Section 1350 of the United States Code, that to the best of my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company at the dates and for the periods indicated.

This Certification has not been, and shall not be deemed, "filed" with the Securities and Exchange Commission.

Date: May 4, 2023

/s/ Eyal Rubin
Eyal Rubin
Senior Vice President and Chief Financial Officer