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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of
the Securities Exchange Act of 1934
Date of report (Date of earliest event reported): February 28, 2023

PROMETHEUS BIOSCIENCES, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-40187	81-4282653
(State or other jurisdiction of incorporation or organization)	(Commission File Number)	(I.R.S. Employer Identification No.)

3050 Science Park Road
San Diego, California 92121
(Address of principal executive offices) (Zip Code)

858-422-4300
(Registrant's telephone number, include area code)

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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, par value $0.0001 per share	**RXDX**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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. ☐

Item 2.02. Results of Operations and Financial Condition.

On February 28, 2023, Prometheus Biosciences, Inc. issued a press release announcing its financial results for the quarter and year ended December 31, 2022. A copy of the press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

In accordance with General Instruction B.2 of Form 8-K, the information in this Current Report on Form 8-K, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, except as expressly set forth by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release issued on February 28, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PROMETHEUS BIOSCIENCES, INC.

Date: February 28, 2023

By: /s/ Timothy K. Andrews
Timothy K. Andrews
General Counsel and Secretary

Exhibit 99.1

Prometheus Biosciences Reports Fourth Quarter and Full-Year 2022 Financial Results and Highlights Recent Corporate Progress

- Reported strong efficacy and favorable safety results for PRA023 in ARTEMIS-UC and APOLLO-CD Phase 2 Studies -
- Prometheus intends to advance PRA023 into Phase 3 studies for UC and CD in 2023 -
- Initiated a third Phase 2 of PRA023 into SSc-ILD, demonstrating pipeline-in-a-product candidate potential for the program -
- Expanded clinical pipeline with advancement of PRA052, a potentially first-in-class monoclonal antibody blocking CD30L, into Phase 1 -
- Strong cash position of >$700M following full completion of recent financing -

SAN DIEGO, February 28, 2023 (GLOBE NEWSWIRE) -- Prometheus Biosciences, Inc. (Nasdaq: RXDX), a clinical-stage biotechnology company pioneering a precision medicine approach for the discovery, development, and commercialization of novel therapeutics for the treatment of immune-mediated diseases, today reported financial results for the quarter and full-year ended December 31, 2022 and highlighted recent corporate progress.

"2022 was a momentous year for Prometheus and the IBD community, highlighted by the positive readout in both PRA023 Phase 2 studies in UC and CD, which we believe set a new standard in IBD by combining high efficacy and favorable safety results," said Mark McKenna, Chairman and CEO of Prometheus Biosciences. "We continue to believe that PRA023 is a potential best-in-class and first-in-class therapeutic candidate for IBD and we intend on carrying this momentum into 2023 by advancing PRA023 into Phase 3 studies."

FOURTH QUARTER AND FULL-YEAR 2022 AND RECENT CORPORATE HIGHLIGHTS

CORPORATE HIGHLIGHTS

Reported positive results for PRA023 in both ARTEMIS-UC Phase 2 and APOLLO-CD Phase 2a studies. Prometheus reported topline results from the initial cohort of its ARTEMIS-UC Phase 2 trial and results from its APOLLO-CD Phase 2a trial of PRA023, demonstrating strong efficacy and favorable safety results in both studies in the context of very severe and refractory patient populations. The company plans to advance to Phase 3 trials in both UC and CD this year.

- Prometheus' Phase 2 ARTEMIS-UC clinical trial was a 12-week, double-blind, placebo-controlled, randomized study to evaluate the efficacy and safety of PRA023 in patients with moderate-to-severely active UC who have failed conventional or advanced therapy. PRA023 met the primary and all ranked secondary endpoints including clinical, endoscopic, histologic, and patient-reported outcome measures in the initial cohort (Cohort 1) of the trial. 68/68 (100%) of PRA023-treated patients completed the Cohort 1 study, compared to 60/67 (89.6%) in the placebo group. The topline results were as follows:
  - 26.5% of patients on PRA023 reached the primary endpoint of clinical remission (per modified Mayo Score), compared to 1.5% on placebo, for a placebo-adjusted clinical remission rate of 25.0% on the primary endpoint ($p<0.0001$)
  - 36.8% of patients on PRA023 reached the secondary endpoint of endoscopic improvement (Mayo endoscopy subscore of ≤ 1), compared to 6.0% on placebo, for a placebo-adjusted endoscopic improvement rate of 30.8% on the secondary endpoint ($p<0.0001$)
  - All secondary endpoints met with statistical significance
  - PRA023 was well tolerated with no safety signal identified
  - Cohort 1 interim analysis suggests a trend towards increased PRA023 response in CDx+ patients over all comers with clinical remission of 37.5% in Dx+ patients, compared with 25.0% for all-comers

- Prometheus' Phase 2a APOLLO-CD clinical trial was a 12-week open-label study that enrolled 55 patients with moderate-to-severely active CD with endoscopically active disease who had failed conventional or biologic therapy. The study enrolled a highly refractory patient population with 70.9% of patients previously treated with at least one biologic therapy and 52.7% treated with two or more biologic therapies. The results were as follows:
  - 26.0% of patients on PRA023 achieved endoscopic response ($p=0.002$ compared to 12% prespecified historical placebo rate)

- 49.1% of patients on PRA023 achieved clinical remission ($p<0.001$ compared to 16% prespecified historical placebo rate)
- PRA023 was well tolerated in subjects with moderately-to-severely active CD with no safety signal identified
- PRA023 showed a significant impact on multiple markers of inflammation and fibrosis

Expanded therapeutic investigation of PRA023 into SSc-ILD, a rare autoimmune disorder. Prometheus initiated its third Phase 2 study of PRA023, ATHENA-SSc-ILD, targeting both key fibrotic and inflammatory pathways for the treatment of SSc-ILD. PRA023 received Fast Track Designation from the US Food and Drug Administration (FDA) for the treatment of SSc-ILD. Systemic Sclerosis (SSc) is a rare autoimmune disorder characterized by progressive fibrosis of the skin and internal organs thought to result from inflammation and chronic immune activation. Lung involvement (SSc-ILD) is the leading cause of morbidity and mortality for individuals with the disorder. SSc-ILD has been largely irreversible with current therapeutic strategies focused on slowing progression of the disorder. Topline results from the Phase 2 study are expected in 1H 2024.

Advanced second precision program, PRA052, into Phase 1. Prometheus received IND clearance from the FDA and initiated a Phase 1 trial in normal healthy volunteers (NHVs) for PRA052, a potential first-in-class monoclonal antibody blocking CD30 ligand (CD30L). CD30L is a costimulatory molecule that has been implicated in inflammatory bowel disease (IBD) by genetic, preclinical, and human translational data. Prometheus is also developing a companion diagnostic candidate designed to select potential responders for this program. Results from the Phase 1 NHV study are expected in 4Q 2023.

Completed upsized $550M public offering of common stock. Prometheus completed an upsized public offering of common stock following the release of its Phase 2 data on PRA023, with net proceeds to the company of approximately $520 million.

UPCOMING ANTICIPATED MILESTONES AND EVENTS

- ARTEMIS-UC expansion cohort (Cohort 2) results – 2Q 2023
- Initiation of registrational studies for PRA023 in UC and CD – 2023
- R&D Day Presentation – 2H 2023
- PRA052 Phase 1 NHV results – 4Q 2023
- IND submission for PR1100 – 4Q 2023

FOURTH QUARTER AND FULL-YEAR 2022 FINANCIAL RESULTS

Cash, Cash Equivalents and Short-Term Investments. As of December 31, 2022, Prometheus had cash, cash equivalents and short-term investments of $695.8 million, compared to $257.3 million at the end of 2021. The increase is primarily due to raising approximately $470.5 million in net proceeds through an upsized underwritten public offering of common stock in Q4 2022. Subsequent to the end of the year, Prometheus raised approximately $50.1 million in additional net proceeds through the exercise of the underwriters' option to purchase additional shares.

Collaboration Revenue. Revenue was $0.7 million for the three months ended December 31, 2022, compared to $1.0 million for the three months ended December 31, 2021 and $6.8 million for the full year 2022 compared with $3.1 million for the full year 2021. The fluctuations were primarily due to revenue generated from Prometheus' collaboration with Dr. Falk Pharma GmbH.

Research and Development (R&D) Expenses. Research and development expenses were $29.9 million for the three months ended December 31, 2022 compared to $23.6 million for the three months ended December 31, 2021 and $112.8 million for the full year 2022 compared with $62.4 million for the full year 2021. The increases in R&D expenses were primarily due to advancement of PRA023 in global Phase 2 clinical trials and PRA052 into Phase 1 clinical trials, as well as advancing our other development programs.

General and Administrative (G&A) Expenses. General and administrative expenses were $12.0 million for the three months ended December 31, 2022 compared to $7.4 million for the three months ended December 31, 2021 and $39.7 million for the full year 2022 compared with $28.5 million for the full year 2021. The increases were primarily due to an increase in headcount and stock-based compensation expense.

About Prometheus Biosciences
Prometheus Biosciences, Inc. is a clinical-stage biotechnology company pioneering a precision medicine approach for the discovery, development, and commercialization of novel therapeutics for the treatment of immune-mediated diseases. The Company's target discovery engine, Prometheus360™, combines proprietary machine learning-based analytical approaches with one of the world's largest gastrointestinal bioinformatics databases to identify novel therapeutic targets and develop therapeutic candidates to engage those targets.

The company's lead candidate, PRA023, is a humanized IgG1 monoclonal antibody (mAb) that has been shown to block the tumor necrosis factor (TNF)-like ligand 1A (TL1A), a target associated with both intestinal inflammation and fibrosis. Prometheus is developing PRA023 for the treatment of immune-mediated diseases including ulcerative colitis (UC), Crohn's Disease (CD), and systemic sclerosis-associated interstitial lung disease (SSc-ILD). Prometheus plans to advance PRA023 into Phase 3 trials in UC and CD later this year.

Forward Looking Statements

Prometheus cautions readers that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. These statements are based on the company's current beliefs and expectations. Such forward-looking statements include, but are not limited to statements regarding: the potential of PRA023 to improve IBD treatment and to be both a first-in-class and best-in-class anti-TL1A mAb; the potential of PRA052 to be a first-in-class mAb blocking CD30L; the timing of results from Cohort 2 of the ARTEMIS-UC trial, topline results from the ATHENA-SSc-ILD trial, and results from the Phase 1 NHV study of PRA052; plans to advance PRA023 into Phase 3 trials in UC and CD, including the timing thereof; plans to submit an IND for PR1100, including the timing thereof; plans to develop diagnostic candidates; and the potential of Prometheus' diagnostic candidates to identify potential responders. The inclusion of forward-looking statements should not be regarded as a representation by Prometheus that any of its plans will be achieved. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in our business, including, without limitation: topline results Prometheus reports are based on preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trial and such topline data may not accurately reflect the complete results of a clinical trial; Prometheus' approach to the discovery and development of precision medicines based on Prometheus360™ is unproven; interim results of a clinical trial do not predict final results and the clinical outcomes may materially change following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues and as more patient data become available, including from Cohort 2 of the ARTEMIS-UC trial; potential delays in the commencement, enrollment and completion of clinical trials and preclinical studies; the results of clinical trials are not necessarily predictive of future results; Prometheus' dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; Prometheus' ability to develop companion diagnostics for its therapeutic product candidates; unexpected adverse side effects or inadequate efficacy of its product candidates that may limit their development, regulatory approval and/or commercialization, or may result in recalls or product liability claims; planned future trials of PRA023 may not support regulatory registration; regulatory developments in the United States and foreign countries; Prometheus' ability to maintain undisrupted business operations due to the COVID-19 pandemic, including delaying or otherwise disrupting its preclinical studies, clinical trials, manufacturing and supply chain; and other risks described in the company's prior press releases and filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in Prometheus' most recent annual report on Form 10-K and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Prometheus undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

Prometheus Biosciences, Inc.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(unaudited)
(in thousands, except share and per share data)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2022	**2021**	**2022**	**2021**
Collaboration revenue	$ 653	$ 1,037	$ 6,809	$ 3,129
Operating expenses:				
Research and development	29,942	23,564	112,848	62,427
General and administrative	12,041	7,417	39,739	28,505
Total operating expenses	41,983	30,981	152,587	90,932
Loss from operations	(41,330)	(29,944)	(145,778)	(87,803)
Other income (expense), net	2,566	26	4,026	(2,392)
Net loss	$ (38,764)	$ (29,918)	$ (141,752)	$ (90,195)
Other comprehensive loss:				
Unrealized gain (loss) on marketable securities, net	22	—	(429)	—
Comprehensive loss	(38,742)	(29,918)	(142,181)	(90,195)
Net loss per share, basic and diluted	$ (0.90)	$ (0.77)	$ (3.49)	$ (2.88)
Weighted average shares outstanding - basic and diluted	42,950,876	38,916,838	40,617,465	31,334,154

Prometheus Biosciences, Inc.
Condensed Consolidated Balance Sheets
(in thousands)
(unaudited)

	December 31, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 292,423	$ 257,254
Short-term investments	403,329	—
Other current assets	12,399	8,129
Total current assets	708,151	265,383
Other assets	32,622	2,418
Total assets	$ 740,773	$ 267,801
Liabilities and Stockholders' Equity		
Current liabilities	$ 22,817	$ 16,442
Long-term liabilities	41,988	16,204
Total liabilities	64,805	32,646
Total stockholders' equity	675,968	235,155
Total liabilities and stockholders' equity	$ 740,773	$ 267,801

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