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): May 24, 2023

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

Delaware	**001-39402**	**27-5414423**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, California 94005
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (650) 822-5500

Not Applicable
(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 $0.001 per share	ANNX	The Nasdaq Stock 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 8.01. Other Events.

On May 24, 2023, Annexon, Inc. announced topline results from its ARCHER Phase 2 trial of ANX007 in patients with geographic atrophy (GA). A copy of the press release, titled "Annexon Topline Data from ARCHER Phase 2 Trial of ANX007 in Geographic Atrophy Demonstrated Statistically Significant, Dose-Dependent Preservation of Visual Function," is filed as Exhibit 99.1 hereto and is incorporated by reference herein.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated May 24, 2023, titled "Annexon Topline Data from ARCHER Phase 2 Trial of ANX007 in Geographic Atrophy Demonstrated Statistically Significant, Dose-Dependent Preservation of Visual Function."
104.1	Cover Page Interactive Data File, formatted in inline XBRL.

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 hereunto duly authorized.

Dated: May 25, 2023

Annexon, Inc.

By: /s/ Jennifer Lew
Jennifer Lew
Executive Vice President and Chief Financial Officer

Exhibit 99.1

Annexon Topline Data from ARCHER Phase 2 Trial of ANX007 in Geographic Atrophy Demonstrated Statistically Significant, Dose-Dependent Preservation of Visual Function

ARCHER data support ANX007 as the first complement therapy to preserve visual acuity, achieving statistically significant protection against vision loss in both foveal and non-foveal patients through 12 months

Reduction in rate of geographic atrophy lesion growth did not reach statistical significance

ARCHER results support ANX007's neuroprotective mechanism of protecting photoreceptor cells, synapses and function

Company plans to engage with regulatory agencies to determine optimal path forward for ANX007

Company to hold conference call today at 1:30 p.m. PT / 4:30 p.m. ET

Brisbane, CA, May 24, 2023 – Annexon, Inc. (Nasdaq: ANNX), a clinical-stage biopharmaceutical company developing a new class of complement-based medicines for patients with classical complement-mediated autoimmune, neurodegenerative and ophthalmic disorders, today announced topline results from its ARCHER Phase 2 trial of ANX007 in patients with geographic atrophy (GA), the leading cause of blindness worldwide, demonstrating a statistically significant, dose-dependent preservation of visual function.

Results from the 12-month treatment period of ARCHER showed that patients treated monthly and every-other-month with ANX007 were protected against vision loss as measured by changes from baseline in the widely accepted functional endpoint of best corrected visual acuity (BCVA). Patients in the monthly treatment group showed a 72% reduction in risk of 15-letter loss (n=89, p=0.006), and patients in the every-other-month treatment group showed a 48% reduction in risk of 15-letter loss (n=92, p=0.064). Patients in the pooled treatment group showed a 59% reduction in risk of >15-letter loss (n=181, p=0.008). These data represent the first demonstration of a complement-based therapy to protect against vision loss in a prospective 12-month clinical trial and support the differentiated mechanism of action of ANX007, which is designed to target and preserve photoreceptor cells, synapses and function.

The primary endpoint of mean rate of change (slope) in GA lesion area compared to sham at 12 months did not reach statistical significance. A 6.2% reduction in lesion growth was observed in monthly treatment group (p=0.526), a 1.3% reduction was observed in the every-other-month treatment group (p-value=0.896) and a 3.7% reduction was observed in the pooled patient population (p-value=0.673). ANX007 was generally well tolerated as both a monthly and every-other-month treatment.

"The chronic, progressive nature of GA means a steady and inevitable loss of vision, which profoundly impacts the life of the millions of people with GA," said Jeffrey S. Heier, M.D., Director of the Retina Service and Retina Research, Ophthalmic Consultants of Boston, and an investigator in ARCHER. "The ultimate goal for any physician is to preserve vision for our patients for as long as possible. The totality of the data on ANX007 from the ARCHER trial are promising, with the demonstrated preservation of functional vision in GA patients, regardless of their lesion location or size. I am encouraged with the overall profile of ANX007 and look forward to its continued development."

GA is a disease of vision loss driven by the loss photoreceptor cells, a type of neuron. Based on Annexon's founding discovery, C1q, the initiator of the classical complement pathway, drives the elimination of functional synapses in disease, essentially driving the loss of photoreceptor cells and their function. Preclinical models have demonstrated that inhibition of C1q protects photoreceptor cell synapses, and importantly, photoreceptor cell function. Lesion growth is measured by fundus autofluorescence (FAF). FAF measures retinal pigment epithelial (RPE) cells under photoreceptors, not photoreceptor cells themselves or their function. While downstream complement inhibition protects the RPE on the edge of a growing lesion (demonstrated by FAF), a functional impact on photoreceptor cells has not been clearly demonstrated. Annexon's mechanism is distinct and designed to target functional photoreceptors throughout the macula to protect synapses and function. C1q inhibition appears to have less impact on the clearance of RPE cells on the edge of the lesion, which may be driven by downstream complement pathways.

"GA is a devastating disease of aging that greatly limits a person's ability to read, perform activities of daily living and even see the faces of their loved ones. Based on the totality of the topline data from the ARCHER trial, we believe that ANX007 has the potential to be a new and distinct treatment option for patients with GA, marking an important step toward achieving our mission of delivering game-changing therapies to patients living with complement-mediated diseases," said Douglas Love, chief executive officer of Annexon. "Protecting against vision loss for patients with GA is the ultimate clinical goal. We are grateful to the many patients, caregivers and physicians who have enabled the development of ANX007 and are encouraged by the opportunity ANX007 may have in meaningfully enhancing their lives. Based on the ARCHER trial results, we plan to engage with regulators to determine the optimal path forward to bring ANX007 to patients as expeditiously as possible."

ARCHER Phase 2 Trial Design

ARCHER is a randomized, multi-center, double-masked, sham-controlled Phase 2 clinical trial comparing the safety and efficacy of ANX007 in patients with GA secondary to AMD. The study enrolled a total of 270 patients, stratified by GA lesion size, location and choroidal neovascularization (CNV) in the fellow eye at the time of enrollment. Patients were nearly equally split between foveal (49.4% to 57.3%) and non-foveal groups, had an average age of 80 years and were balanced between female and male. Ninety-six percent of patients enrolled were from the United States.
Patients were randomized to receive an intravitreal dose of 5mg ANX007 monthly (n=89), 5mg ANX007 every other month (n=92) or sham monthly or every other month (pooled n=89) for a treatment period of 12 months, followed by a six-month off-treatment period.

The primary outcome measure of the study was the rate of change in GA lesion growth (slope) from baseline as measured by fundus autofluorescence (FAF) through 12 months for the study eye. The study included multiple pre-specified visual function measures to assess the effects of ANX007 on vision:

- Change from baseline in BCVA
- Change from baseline in low-luminance best corrected visual acuity (LLVA)
- Change in baseline from low-luminance visual acuity deficit (LLVD)

Preservation in Visual Function with ANX007

ANX007 represents the first complement therapeutic candidate to preserve visual acuity, demonstrating a statistically significant reduction of vision loss in both foveal and non-foveal patients at 12 months.

- **Best corrected visual acuity**: BCVA is widely accepted functional endpoint that measures visual acuity on a logMAR reading chart, a specialized chart of rows of letters used by ophthalmologists to estimate visual acuity. In this study, loss was defined as loss of 15 BCVA letters or more on two consecutive visits, or a loss at the end of the 12-month treatment period.

- ***Over the 12-month treatment period***, patients in the ANX007 monthly treatment group showed a 72% reduction in risk of ≥15-letter vision loss (n=89, p=0.006) and patients in the ANX007 every-other-month treatment group showed a 48% reduction in risk of ≥15-letter vision loss (n=92, p=0.064). Patients in the pooled treatment group showed a 59% reduction in risk of ≥15-letter loss (n=181, p=0.008).
- ***Through the 12-month treatment period***, as compared to baseline, ANX007 demonstrated a statistically significant protection against vision loss in both monthly and pooled treatment groups and a non-significant trend in protection in the every-other-month treatment group, compared to sham:

BCVA: Patients with > 15 Letter Loss through Month 12

	Sham (n=89)	EM (n=89)	EOM (n=92)	ANX007 Pooled (n=181)
	21.3% (19/89)	5.6% (5/89)	10.9% (10/92)	8.3% (15/181)
p-value vs sham	—	0.0021	0.055	0.0024

- When assessing the BCVA treatment effect by ***lesion location***, the combined analysis, stratified by foveal and non-foveal patients, demonstrated an overall statistically significant difference between ANX007 and sham:

BCVA by Lesion Location: Patients with ≥15 Letter Loss through Month 12

Location	Sham	EM	EOM	ANX007 Pooled
Foveal	25.0% (11/44)	5.9% (3/51)	18.4% (9/49)	12.0% (12/100)
Non-Foveal	17.8% (8/45)	5.3% (2/38)	2.3% (1/43)	3.7% (3/81)
p-value vs sham	—	0.0019	0.0439	0.0015

- When assessing the BCVA treatment effect by ***retinal health***, the combined analysis, stratified by healthier and less healthy retina, demonstrated an overall statistically significant difference between ANX007 and sham. This effect supports the potential use as an early treatment for GA:

BCVA by Retinal Health: Patients with ≥15 Letter Loss through Month 12

	Sham	EM	EOM	ANX007 Pooled
LLVD <30 (healthier)	16.9% (10/59)	0.0% (0/56)	6.3% (3/48)	2.9% (3/104)
LLVD ≥30 (less healthy)	30.8% (8/26)	16.1% (5/31)	16.3% (7/43)	16.2% (12/74)
p-value vs sham	—	0.0016	0.029	0.0009

- **Low-luminance visual acuity**: LLVA is BCVA assessed in low light conditions. ANX007 demonstrated a non-significant trend in slowing the progression of LLVA loss in the monthly, every-other-month and pooled treatment groups, which Annexon believes supports the ANX007 mechanism of action:

LLVA: Patients with > 15 Letter Loss through Month 12

	Sham (n=79)	EM (n=79)	EOM (n=85)	ANX007 Pooled (n=164)
	20.3% (16/79)	10.1% (8/79)	11.8% (10/85)	11.0% (18/164)
p-value vs sham	—	0.076	0.14	0.051

- **Low-luminance visual deficit**: LLVD is the difference between BCVA and LLVA. When assessing the LLVD treatment effect by baseline visual acuity, the combined analysis stratified by baseline vision demonstrated an overall statistically significant difference between ANX007 and sham:

LLVD: Patients with ≥15 Letter Worsening through Month 12

BCVA Score	Sham	EM	EOM	ANX007 Pooled
≥ 55 (better vision)	25.5% (13/51)	9.4% (5/53)	16.4% (9/55)	13.0% (14/108)
<55 (impaired vision)	17.9% (5/28)	7.7% (2/26)	3.3% (1/30)	5.4% (3/56)
p-value vs sham	—	0.0161	0.0597	0.0091

ANX007 Generally Well-Tolerated in Patients

Treatment with ANX007 was generally well-tolerated in the 181 GA patients treated either monthly or every other month. There was a limited incidence of choroidal neovascularization (CNV) conversion across all three groups, with 3.4% in the sham group vs. 4.5% and 4.3% in the ANX007 monthly and every-other-month groups, respectively. Among the patients treated with ANX007, three serious adverse events (SAEs) of endophthalmitis were observed, which were determined to be related to intravitreal injection procedure and not related to treatment. There were three SAEs of intraocular inflammation, suspected of being treatment-related, which were not associated with retinal vasculitis. One SAE of retinal artery occlusion was reported, suspected of being treatment-related, which was also not associated with retinal vasculitis.

Oral Presentation of ARCHER Topline Data at ASRS

Dr. Heier will present the topline data from the ARCHER trial, as well as additional findings from the 12-month treatment period, in an oral presentation at the ASRS 2023 Annual Meeting.

Details of the presentation are as follows:

- **Title:** Treatment of Geographic Atrophy Secondary to Age-Related Macular Degeneration with Intravitreal ANX007: Results of the ARCHER Study, Jeffrey S. Heier, M.D.

- **Date and Time:** Sunday, July 30, 2023 at 9:00 a.m. PT

The six-month off-treatment follow-up period of the ARCHER Phase 2 trial is ongoing, and Annexon plans to report final results following study conclusion.

Conference Call Information

Annexon management will host a conference call today at 1:30 p.m. PT / 4:30 p.m. ET. Management will be joined by leading retinal physician, Charles C. Wykoff, M.D., Ph.D., Associate Professor of Clinical Ophthalmology of the Academic Institute, Associate Clinical Member of the Research Institute at Houston Methodist, Weill Cornell Medical College, Specialist at the Retina Consultants of Texas, and an investigator in ARCHER Phase 2 trial.

The webcast and accompanying slides can be accessed under the 'Events & Presentations' section on the Investors page at www.annexonbio.com. A replay of the webcast will be archived on the Annexon website for 30 days. Dial-in information for conference participants may be obtained by registering for the event here.

About Geographic Atrophy

Geographic atrophy (GA), also known as atrophic age-related macular degeneration (AMD) or dry AMD, has a genetic link to aberrant complement activity and can lead to blindness caused by damaged and dying retinal cells. Currently, there are no approved treatment options to prevent the onset or progression of GA. It is estimated that one million people in the United States and three million people globally suffer from GA.

About Annexon

Annexon (Nasdaq: ANNX) is a clinical-stage biopharmaceutical company seeking to bring game-changing medicines to patients with classical complement-mediated diseases of the body, brain and eye. The classical complement pathway within the immune system, when overactivated, drives inflammation in a host of autoimmune, neurodegenerative and ophthalmic diseases. Annexon is advancing a new class of complement medicines targeting the early classical cascade and all downstream pathway components that contribute to disease, while selectively preserving the beneficial immune functions of other complement pathways. Annexon is rigorously developing a pipeline of diversified product candidates across multiple mid- to late-stage clinical trials, with clinical data anticipated throughout 2023 and beyond.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "positioned," "potential," "predict," "seek," "should," "suggest," "target," "on track," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. All statements other than statements of historical facts contained in this press release are forward-looking statements. These forward-looking statements include, but are not limited to, statements about: topline data from the ARCHER Phase 2 trial of ANX007 in patients with GA; continued development of ANX007; potential treatment opportunities for patients and market size; engagement with regulators to determine the optimal path forward to bring ANX007 to patients; plans to report final results following study conclusion; the potential benefits from treatment with anti-C1q

therapy; and continuing advancement of the company's portfolio. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, risks and uncertainties related to: the ongoing off-treatment follow-up portion of the ARCHER Phase 2 trial and final results from the ARCHER Phase 2 trial; the company's history of net operating losses; the company's ability to obtain necessary capital to fund its clinical programs; the early stages of clinical development of the company's product candidates; the effects of COVID-19 or other public health crises on the company's clinical programs and business operations; the company's ability to obtain regulatory approval of and successfully commercialize its product candidates; any undesirable side effects or other properties of the company's product candidates; the company's reliance on third-party suppliers and manufacturers; the outcomes of any future collaboration agreements; and the company's ability to adequately maintain intellectual property rights for its product candidates. These and other risks are described in greater detail under the section titled "Risk Factors" contained in the company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q and the company's other filings with the SEC. Any forward-looking statements that the company makes in this press release are made pursuant to the Private Securities Litigation Reform Act of 1995, as amended, and speak only as of the date of this press release. Except as required by law, the company undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

The contents of the company's website at www.annexonbio.com and the webcast and accompanying slides accessible through the company's website are not incorporated by reference into this press release.

Investor Contact:

Chelcie Lister
THRUST Strategic Communications
chelcie@thrustsc.com

Lori Murray
Annexon Biosciences
lmurray@annexonbio.com

Media Contact:

Sheryl Seapy
Real Chemistry
949-903-4750
sseapy@realchemistry.com