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): December 20, 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 7.01. Regulation FD Disclosure.

As reported under Item 8.01 of this Current Report on Form 8-K, on December 20, 2023, Annexon, Inc. ("Annexon" or the "Company") issued a press release (the "ANX007 Press Release") to announce a global registrational program for ANX007 in geographic atrophy ("GA") using vision preservation as the primary outcome measure. The Company provided an update on the planned Phase 3 trial designs and alignment with the U.S. Food and Drug Administration ("FDA") on the primary endpoint. Annexon also issued a second press release (the "ANX1502 Press Release" and collectively, the "Press Releases") reporting results from its Phase 1 study of the ANX1502 oral small molecule inhibitor of the classical complement pathway in healthy volunteers. Copies of the Press Releases are furnished herewith as Exhibits 99.1 and 99.2 and are incorporated herein by reference.

Copies of related presentations are furnished herewith as Exhibits 99.3 and 99.4 to this Current Report on Form 8-K and are incorporated by reference herein.

This information in this Item 7.01 of this Current Report on Form 8-K 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, or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in any such filing.

Item 8.01. Other Events.

ANX007

On December 20, 2023, the Company outlined its global registrational program for ANX007, a potentially best-in-class C1q and classical complement inhibitor for the treatment of GA. The Company intends to initiate a comprehensive pivotal program with (1) ARCHER II, a global sham-controlled trial designed to confirm results from the previously completed Phase 2 ARCHER trial and to potentially expedite regulatory approval in Europe and (2) a second trial, ARROW, an injection-controlled head-to-head trial against SYFOVRE® (pegcetacoplan injection), an FDA-approved therapy, to measure ANX007's critical differentiation on visual function. The Company plans to submit data from ARCHER II and ARROW to the FDA and EMA, and if successful, seek global approval for ANX007. The ARCHER II trial is expected to initiate in mid 2024 with topline data currently anticipated in the second half of 2026. The ARROW trial is expected to initiate in late 2024, following a determination by the EMA of the approval of SYFOVRE® in Europe and after assessing the potential to conduct a global comparator study with topline data currently anticipated mid-2027. The global registrational program is based on alignment between the Company and FDA on the use of vision preservation as the primary endpoint, with no requirement for a surrogate structural endpoint, and considers FDA's recommendation to use an injection comparator. The global registrational program is subject to EMA feedback, and the Company will engage with the EMA in the first half of 2024.

The ARCHER II Phase 3 trial will enroll approximately 400 patients with GA secondary to age-related macular degeneration (AMD) who will be randomized 1:1 to receive a monthly dose of ANX007 or sham. The primary endpoint will be the prevention of ≥15-letter loss of best corrected visual acuity (BCVA) (three lines on the standard ETDRS eye chart) in patients assessed through 12 months. The ARROW trial plans to enroll approximately 500 patients with GA to evaluate a monthly dose of ANX007 versus SYFOVRE®. Although SYFOVRE® was shown to slow lesion growth, published data from three prior SYFOVRE® trials that treated more than 1,400 GA patients indicate no apparent visual function benefit. Based on the generally well-tolerated safety profile and statistically significant and dose-dependent visual protection shown in the earlier Phase 2 ARCHER trial, the Company believes that ANX007 has the potential to demonstrate significant protection against vision loss as measured by BCVA ≥15-letter loss in a head-to-head study.

The following risk factor is provided to supplement Annexon's risk factors previously disclosed under the heading "Risk Factors" in Annexon's Annual Report on Form 10-K for the year ended December 31, 2022 and Annexon's Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023, June 30, 2023, and September 30, 2023.

Conducting a global, two-trial program in GA will be expensive and time consuming, and even if favorable, the FDA and comparable foreign regulatory authorities may not accept data from one or both of our trials in our global Phase 3 clinical program for ANX007.

The ARCHER II Phase 3 trial is designed to be a global sham-controlled trial and the ARROW trial is expected to be an injection-controlled head-to-head trial against SYFOVRE®. The FDA has recommended the use of an injection comparator instead of a sham control in ophthalmic trials. As a result, the data from the ARCHER II study, even if positive, may be insufficient for regulatory approval in the United States. The Company is planning to conduct the ARROW study to demonstrate ANX007's significant protection against vision loss over SYFOVRE®. However, the FDA may not agree that the data from the ARROW trial is sufficient to warrant approval of ANX007, even if the results are sufficiently positive. In such an event, we may be required to conduct one or more additional clinical trials before seeking FDA approval of ANX007, which would increase our expenses and could delay or prevent commercialization of ANX007 in GA. Moreover, there are no currently approved therapies for GA in Europe, and the results of the ARROW study may not be acceptable to the EMA or any other comparable foreign regulatory authorities.

Conducting two large Phase 3 trials in multiple jurisdictions is expensive and can take many years to complete, and we cannot guarantee that clinical trials will be conducted as planned or completed timely, if at all. In addition, there are two FDA-approved therapies for GA in the United States, which may adversely impact our ability to recruit patients into our clinical trials. We may need additional capital to complete both the ARCHER II and ARROW clinical trials and may not be able to raise sufficient capital in a timely manner. The occurrence of any such events could delay either trial, prevent us from completing one or more of our clinical trials, seeking FDA approval of ANX007 for GA, if ever, and could delay or prevent commercialization of ANX007.

In addition, none of the FDA-approved therapeutics in GA have been assessed using vision preservation as the primary endpoint. Due to the lack of BCVA ≥15-letter loss results for SYFOVRE®, we may experience difficulties in conducting the ARROW trial, including powering for statistical significance, potential delays in enrollment, emerging safety data for SYFOVRE®, and potential inability to timely obtain SYFOVRE®, which may result in substantial delays in the development of ANX007. There is no assurance that in a head-to-head study, ANX007 will result in statistically significant clinical superiority over SYFOVRE® or that he overall results will be sufficient to support marketing approval.

ANX1502

On December 20, 2023, the Company also reported results from the Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) healthy volunteer study of ANX1502, an oral, selective small molecule inhibitor that targets the active form of C1s responsible for classical pathway activation. ANX1502 was generally well-tolerated and achieved target serum levels and demonstrated pharmacokinetic (PK) measures that support advancement into a proof-of-concept clinical study to assess pharmacodynamic (PD) effect and efficacy in patients with Cold Agglutinin Disease (CAD). Based on these data, the Company intends to advance a tablet formulation of ANX1502 into a proof-of-concept study in patients with CAD, expected to initiate in 2024.

Dose-proportional PK and targeted levels of active drug were observed across both SAD and MAD cohorts of the healthy volunteer study. Single doses of 525 mg to 1025 mg of ANX1502 demonstrated suppressed C4d serum levels in healthy volunteers with higher than median baseline C4d, a biomarker of complement activation. Furthermore, across all doses evaluated, ANX1502 was observed to be generally well-tolerated with mild to moderate treatment-emergent adverse events (TEAEs), none of which exceeded Grade 2. The most frequent TEAEs were gastro-intestinal, which included nausea, emesis, and diarrhea. No serious adverse events were reported, and there were no significant clinical or lab findings.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated December 20, 2023, titled "Annexon Outlines Global Registrational Program for ANX007 in Geographic Atrophy with FDA Alignment on Vision Preservation as Primary Endpoint."
99.2	Press Release, dated December 20, 2023, titled "Annexon Reports Phase 1 Results for ANX1502, its Oral Small Molecule Inhibitor of the Classical Complement Pathway."
99.3	Annexon, Inc. Presentation dated December 2023
99.4	Annexon, Inc. Presentation dated December 2023
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: December 20, 2023

Annexon, Inc.

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

Exhibit 99.1

Annexon Outlines Global Registrational Program for ANX007 in Geographic Atrophy with FDA Alignment on Vision Preservation as Primary Endpoint

Alignment with FDA on Best Corrected Visual Acuity ≥ 15-Letter Loss as Primary Outcome Measure - Representing the Highest Value Outcome to Patients and Physicians

ARCHER II, a Global Sham-Controlled Trial Supporting a Potentially Faster Path to Registration, Expected to Initiate in Mid-2024

ARROW, a Head-to-Head Trial using SYFOVRE® as an Injection Comparator to Differentiate Vision Protection from Slowing of Lesion Growth, Expected to Initiate in Late 2024

BRISBANE, Calif., Dec. 20, 2023 - Annexon, Inc. (Nasdaq: ANNX), a clinical-stage biopharmaceutical company developing a new class of complement-based medicines for people living with devastating inflammation-related diseases, today outlined its global registrational program for ANX007, a first-in-class C1q and classical complement inhibitor, for the treatment of patients with geographic atrophy (GA).

Annexon has gained alignment with the U.S. Food and Drug Administration (FDA) on a Phase 3 registration program that includes using, for the first-time, the prevention of ≥15-letter loss of best corrected visual acuity (BCVA) as the primary outcome measure, as well as conducting a comparison of ANX007 to an injection agent, consistent with requests for trials across ophthalmic indications. Notably, the FDA has not required Annexon to study the slowing of lesion growth as measured by fundus autofluorescence (FAF), an anatomical endpoint used for the approval of other GA programs.

“We are thrilled to have aligned with FDA on vision preservation as the primary endpoint in our Phase 3 GA program, based on the statistically significant and dose-dependent visual protection ANX007 demonstrated in the Phase 2 ARCHER trial,” said Douglas Love, chief executive officer of Annexon. “Blocking C1q with ANX007 is designed to stop classical complement inflammation that drives photoreceptor damage and vision loss. Considering the robust preservation of vision demonstrated by ANX007 in the ARCHER trial, and that current FDA-approved treatments have not shown a meaningful functional benefit after years of treatment, we are encouraged by the potential for ANX007 to demonstrate significant protection against vision loss as measured by BCVA ≥15-letter loss in a head-to-head study. We are excited to embark on this global pivotal program with the aim of providing meaningful functional benefit and offering a new transformative treatment to the patients, and their families, affected by GA.”

Annexon’s registration program will initiate first with ARCHER II, a global sham-controlled trial designed to confirm the results from the Phase 2 ARCHER trial, and potentially expedite the path to regulatory approval in Europe, where there are approximately 2.5 million people living with GA. Given the availability of FDA-approved treatments in the United States, Annexon plans to conduct its injection-controlled head-to-head study, ARROW, against SYFOVRE® (pegcetacoplan injection), with the potential to underscore ANX007’s unique mechanism of action and critical differentiation on visual function. ARCHER II is expected to begin enrollment in mid-2024, followed by ARROW in late 2024.

“For the millions of patients living with GA, loss of sight is coupled with the loss of independence, leaving a significant impact on quality of life,” said Jeffrey S. Heier, M.D., director of the Retina Service and Retina Research, Ophthalmic Consultants of Boston, and an investigator in ARCHER. “It is every physician’s goal to preserve vision for as long as possible. Based on the outcome of the ARCHER trial, I am excited by the potential of ANX007 and its distinct neuroprotective mechanism of action, and I look forward to further understanding its role in the treatment of GA through its robust Phase 3 program.”

ANX007 Global GA Registrational Program Overview

- ARCHER II Global Sham-Controlled Trial: The Phase 3 ARCHER II trial is designed to enroll approximately 400 patients with GA secondary to age-related macular degeneration (AMD) who will be randomized 1:1 to receive a monthly dose of ANX007 or sham procedure. The primary endpoint will be the prevention of ≥15-letter loss of best corrected visual acuity (BCVA), which represents three lines on the standard ETDRS eye chart, in patients assessed through 12 months. BCVA ≥15-letter loss is a well-established functional endpoint that has served as the basis for numerous ophthalmology drug approvals by the FDA and EMA. Key secondary endpoints in ARCHER II include safety, low-luminance visual acuity (LLVA) and low-luminance visual deficit (LLVD).
- ARROW Head-to-Head Trial: The Phase 3 ARROW trial is designed to enroll approximately 500 patients with GA to evaluate a monthly dose of ANX007 versus SYFOVRE® as an injection comparator, an FDA-approved drug shown to slow lesion growth. The primary endpoint will be the prevention of ≥15-letter loss of BCVA assessed through 12 months and is designed to differentiate vision protection from slowing of lesion growth, offering patients a functional benefit alternative.

Annexon continues to engage with the European Medicines Agency following receipt of PRIME designation and will seek feedback from EMA on the pivotal Phase 3 program in the first half of 2024. ANX007 is the first therapeutic candidate for the treatment of GA to receive PRIME designation, which provides early and proactive support to developers of promising medicines that may offer a major therapeutic advantage over existing treatments or benefit to patients without treatment options.

About ANX007 and Phase 2 ARCHER Trial

ANX007 is a fragment antigen-binding (Fab) antibody designed as a first-in-kind therapeutic to selectively inhibit C1q, the initiating molecule of the classical complement pathway, and a key driver of neurodegeneration. In GA, C1q binds to photoreceptor synapses early in the disease process, causing aberrant activation of the classical pathway with synapse loss, inflammation and neuronal damage that results in vision loss. Intravitreal administration of ANX007 stops C1q and activation of the entire downstream classical pathway to protect photoreceptor synapses and cells essential for vision.

In the randomized, multi-center, double-masked, sham-controlled Phase 2 ARCHER clinical trial, ANX007 demonstrated consistent protection against vision loss in a broad population of patients with GA. Specifically, topline data reported in May 2023 and presented at the American Society of Retina Specialists (ASRS) Annual Meeting in July 2023 showed that ANX007 provided statistically significant, time and dose-dependent protection from vision loss in patients with GA, measured by BCVA ≥ 15-letter loss, the widely accepted and clinically meaningful functional endpoint assessing visual acuity. Protection from vision loss was also shown in multiple additional prespecified measures of BCVA and visual function, including LLVA and LLVD. ANX007's treatment effect increased over the course of the on-treatment portion of the study, suggesting that ANX007 may provide a growing and durable treatment effect over time. While benefit gained against vision lost was maintained during the subsequent six-month off-treatment period, the rate of decline for BCVA ≥ 15-letter vision began to parallel that of sham, providing additional support for the observed on-treatment protection. ANX007 treatment was generally well-tolerated, with no increase in choroidal neovascularization (CNV) rates between the treated and sham arms and no events of retinal vasculitis reported.

About Geographic Atrophy

Geographic atrophy (GA) is an advanced form of dry age-related macular degeneration (AMD), an eye disease that is the leading cause of blindness in the elderly. GA is a chronic progressive neurodegenerative disorder of the retina involving the loss of photoreceptor synapses and cells in the outer retina. GA affects an estimated one million people in the United States and eight million people globally, severely limiting their independence and causing frustration, anxiety and emotional hardship. Effective treatments that preserve vision are still needed, as no currently approved therapies have been shown in clinical trials to significantly prevent vision loss.

About Annexon

Annexon Biosciences (Nasdaq: ANNX) is a clinical-stage biopharmaceutical company utilizing a distinct scientific approach to stop C1q and all inflammatory aspects of classical complement pathway activation before it starts. As the only company solely focused on shutting down the early classical cascade, Annexon is developing a fit-for-purpose pipeline of therapeutics designed to provide meaningful benefits across multiple diseases of the body, brain and eye. With proof-of concept data in both Guillain-Barré syndrome and geographic atrophy, Annexon is rigorously advancing its mid-to late-stage clinical trials to bring their potential treatments to patients as quickly as possible. To learn more visit annexonbio.com.

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: timing of initiation of the ARCHER II and ARROW trials; ANX007's distinct potential neuroprotective mechanism of action and potential to provide protection from vision loss; the potential for robust, dose and time dependent preservation of vision loss in the broad patient population; continued development of ANX007; market size; meeting with regulators to determine the optimal path forward; expected superiority on BCVA ≥ 15-letter loss in a head-to-head study with SYFOVRE®; anticipated growing and durable treatment effect over time of ANX007; plans to report final results following study conclusion; ability to achieve regulatory approval in the United States, Europe and other large jurisdictions; potential for a global sham-controlled trial to support a faster path to regulatory approval; 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 trial and final results from the ARCHER 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 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.

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Annexon Reports Phase 1 Results for ANX1502, Its Oral Small Molecule Inhibitor of the Classical Complement Pathway

Target Levels of Active Drug Achieved in Healthy Volunteers with Oral Twice-Daily Dosing; Supportive Impact on Pharmacodynamic Biomarker of Complement Activity

ANX1502 Generally Well-Tolerated Across Cohorts with No Serious Adverse Events

Tablet Formulation of ANX1502 Expected to Advance into Proof-of-Concept Study in Patients with CAD in 2024

BRISBANE, Calif., Dec. 20, 2023 - Annexon, Inc. (Nasdaq: ANNX), a clinical-stage biopharmaceutical company developing a new class of complement-based medicines for people living with devastating inflammation-related diseases, today reported results from the Phase 1 single ascending dose (SAD) and multiple ascending dose (MAD) healthy volunteer study of ANX1502, a first-in-kind oral, selective small molecule inhibitor that targets the active form of C1s responsible for propagating classical pathway activation in association with C1q. ANX1502 achieved target serum levels and demonstrated pharmacokinetic (PK) measures that support advancement into a proof-of-concept clinical study to assess pharmacodynamics (PD) and efficacy in patients with cold agglutinin disease (CAD) in 2024.

“After more than a decade of groundbreaking research targeting the early classical complement pathway, we are excited to have reached an important step in the clinical development of ANX1502, our first-in-kind small molecule complement inhibitor that we believe can have meaningful impact on a range of autoimmune conditions,” said Ted Yednock, Ph.D., chief innovation officer of Annexon. “We’re very encouraged by the results from our Phase 1 SAD/MAD trial showing that ANX1502 was well-tolerated and achieved target drug levels with supportive impact on a key biomarker in healthy volunteers. Based on these data, we look forward to advancing a tablet formulation of ANX1502 into a proof-of-concept study in patients with CAD, which enables us to further explore larger opportunities in serious autoimmune diseases.”

The completed Phase 1 clinical trial is a randomized, double-blind, placebo-controlled SAD and MAD study to assess the safety, tolerability, PK and PD of ANX1502 liquid suspension formulation in healthy adults. The study evaluated single ascending doses of ANX1502 ranging from 25 mg to 1050 mg and multiple ascending doses of ANX1502 ranging from 200 mg twice daily to 525 mg twice daily. Results of the study were as follows:

- Dose-proportional PK and targeted levels of active drug were observed across both SAD and MAD cohorts
- Single doses of 525-1025 mg ANX1502 suppressed C4d serum levels in healthy volunteers with higher than median baseline C4d
- Across all doses evaluated, ANX1502 was generally well tolerated with mild to moderate treatment-emergent adverse events (TEAEs). The most frequent TEAEs were gastro-intestinal, which included nausea, emesis, and diarrhea.
- No serious adverse events were reported, and there were no significant clinical or lab findings.

Following the successful completion of the proof-of-concept study in patients with CAD, Annexon intends to evaluate ANX1502 in serious complement-mediated autoimmune diseases with the aim of providing enhanced efficacy and offering convenient dosing administration for long-term treatment of chronic conditions.

About Annexon

Annexon Biosciences (Nasdaq: ANNX) is a clinical-stage biopharmaceutical company utilizing a distinct scientific approach to stop C1q and all inflammatory aspects of classical complement pathway activation before it starts. As the only company solely focused on shutting down C1q, Annexon is developing a fit-for-purpose pipeline of therapeutics designed to provide meaningful benefits across multiple diseases of the body, brain, and eye. With proof-of concept data in both Guillain-Barré syndrome and geographic atrophy, Annexon is rigorously advancing its mid-to late-stage clinical trials to bring their potential treatments to patients as quickly as possible. To learn more visit annexonbio.com.

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Exhibit 99.3

ANNEXON biosciences

STOP THE START

of classical complement-driven diseases

ANX007 Phase 3 GA Program

December 2023

Overview of ANX007 Geographic Atrophy Program

Pioneering upstream classical complement trial with demonstrated functional benefit

- ✓ Unique MOA targeting classical complement inflammation where it starts
- ✓ Preclinical classical complement inhibition protected photoreceptor cell loss and function
- ✓ ARCHER 1st clinical demonstration of significant, dose & time-dependent vision preservation
- ✓ Vision preservation supported by multiple lines of evidence, including: 12 months on-treatment, fellow-eye, foveal status and off-treatment analyses
- ✓ Clinical impact consistently improved over time on fundus autofluorescence (FAF) lesion and BCVA ≥15-letter loss measures
- ✓ ANX007 1st and only EMA PRIME Designation in GA – based on preclinical & ARCHER data set
- ✓ Actively pursuing global Phase 3 program to confirm ARCHER findings

ANX007 GA Phase 3 Program Overview: Potential Best-in-Class Approach

- **Aligned with FDA on BCVA ≥15 letter loss functional endpoint, with no requirement for surrogate structural endpoint**, consistent with ARCHER Ph2 results
- FDA recommends injection comparator as control (e.g., placebo or approved drug); EMA advisor feedback & precedent for sham control with currently no EU-approved comparator

- **ANNX to conduct global sham-controlled trial ASAP: ARCHER II Study (mid-2024)**
  - EMA-centric approach (no comparators); replicates ARCHER I & potentially fastest path to EU approval. ~2.5M EU pts; ~1M US pts
- **ANNX to stagger second, injection comparator trial against Syfovre: ARROW Study (2H 2024)**
  - Satisfy FDA recommendation re injection control, and no apparent Syfovre functional benefit over 3 trials
  - Potential 'Best in class' program disconnecting lesion surrogate from vision endpoint (own narrative & drive value during trial)
  - Provides additional shot on goal for approval
  - Initiate post-EMA determination of Syfovre approval to finalize EU / global trial feasibility

Two Study Global P3 Approach Balances POS, Cost and Time

Clinical	Regulatory	Other Considerations
1 Maximize clinical PTS	**2 Achieve global regulatory approval**	**3 Minimize cost, time, operational complexity**
• Sham controlled trial highest PTS* (replicate ARCHER) • Evidence of 007 potential to be superior to Syfovre on BCVA ≥15 (three prior Syfovre trials)	• EMA: Sham precedent & no comparator • FDA: Injectable control recommended – active comparator only feasible option	• Reasonably sized trials • Essentially one trial per jurisdiction, each of which has potential to support BLA • Rapid path to EMA label

2 studies with distinct comparators
- **ARCHER II: Sham controlled**
- **ARROW: Syfovre controlled**

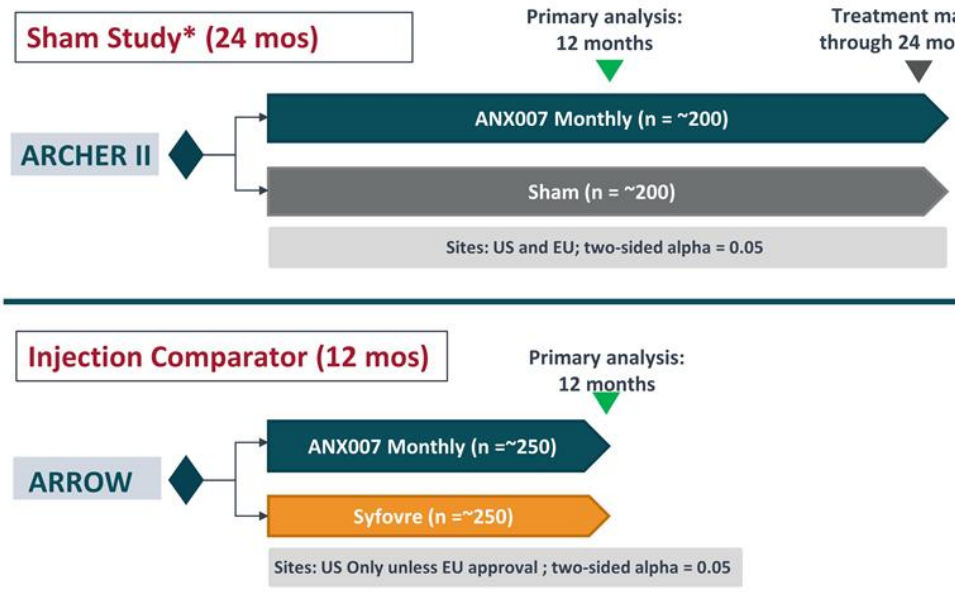
- Initiate ARCHER II first: potentially highest PTS and fastest path to EU approval
- Addresses divergent regulatory recommendations
- Builds strength of evidence: 2 successful Ph3 studies
- Monitoring evolving Syfovre situation (e.g., tolerability profile, EMA approval)

*probability of technical success

ANNEXON biosciences

ANX007 GA P3 Trials Overview: Replicate ARCHER & Support Global Approvals

Estimated program cost ~$140M for two trials



Primary Endpoint

- Persistent ≥15-Letter BCVA Loss through 12 months, or accumulation of appropriate # of events

POTENTIAL SECONDARY / EXPLORATORY ENDPOINTS

- LLVA / LLVD
- Ellipsoid Zone (EZ) attenuation / lesion growth

Study Design Elements

- Replicate ARCHER (e.g., inclusion/ exclusion, assessments etc.)
- Possible enrichment criteria for sham study (based on ARCHER data)

*Archer was a 270 patient trial

**24 mos. total treatment per regulatory direction

ANNEXON biosciences

Syfovre: An "Active Control" with No Observed Effect on Visual Acuity

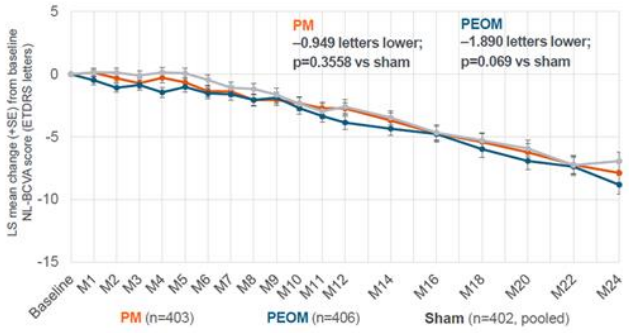
No apparent treatment effect on BCVA 15 across three trials and >1,400 GA patients observed

Summary: BCVA Findings for Syfovre

OAKS and DERBY combined

BCVA in the study eye over 24 months

OAKS DERBY



Visual function endpoints:

No statistically significant differences across study arms on key secondary endpoints at 24 months

- BCVA
- Maximum reading speed
- Functional Reading Independence Index
- Microperimetry: Mean threshold sensitivity (OAKS only)

In nonsubfoveal subgroup, lesion distance to foveal center at baseline was larger in sham pooled (370 microns) than in PM (337 microns) and PEOM (340 microns)

LS means estimated from MMRM analysis. The mITT population was used for the analysis, defined as all randomized patients who received at least 1 injection of pegcetacoplan or sham and have baseline and at least one post-baseline value of GA lesion area in the study eye. BCVA=best-corrected visual acuity; ETDRS=Early Treatment of Diabetic Retinopathy Study; GA=geographic atrophy; LS=least square; M=month; mITT=modified intent-to-treat; MMRM=mixed-effects model for repeated measures; NL=normal luminance; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error. From Heier, Retina Society, November 2-5, 2022. 13

- **Recruited generally similar patient population as ARCHER**
- **No Syfovre BCVA ≥15-letter loss data reported**
  - Modeling: best, non-significant effect would be <4% compared to sham
- **Low likelihood based on our modeling that similar 4th Syfovre study demonstrates positive visual acuity**

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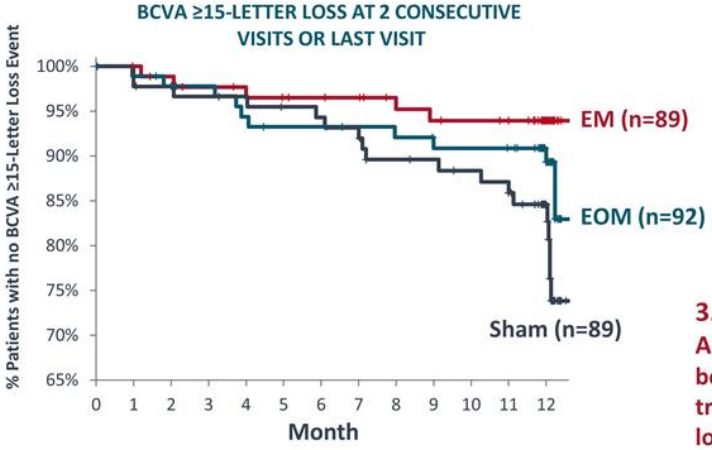
ARCHER I Vision Protection Supported by Three Lines of Evidence

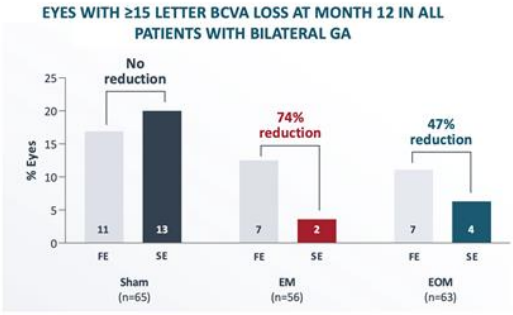
1. Observed significant time and dose-dependent protection against vision loss vs sham (BCVA)

- 72% risk reduction in EM arm (p=0.006)
- 48% risk reduction in EOM (p=0.064)

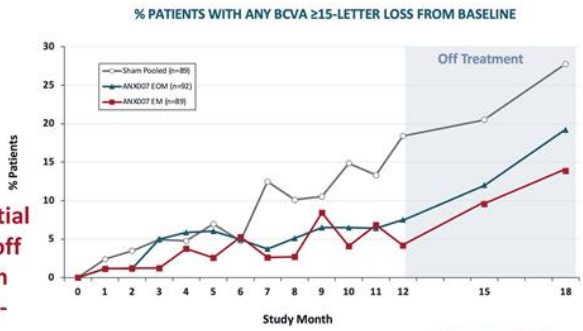


HR, hazard ratio; Nominal log-rank test (versus sham) p-values are presented

2. Fellow-Eye Analysis (comparing treated eye w/ non-treated fellow eye) showed protection in treated eye



3. Off-Treatment Analysis showed initial benefit maintained off treatment, but vision loss accelerates post-treatment



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Next Steps

- Finalize design elements for ARCHER II and ARROW Ph3 trials
  - Enrichment criteria for sham study
  - Potential modifications to year 2 of sham trial (e.g., incorporate EOM dosing)
  - Design features to ensure appropriate number of BCVA 15 events
- Continued partnership with EMA under PRIME designation for what we believe is the most expeditious path to approval
- Complete clinical feasibility assessment and trial initiation activities – targeting trial initiation mid-2024

Exhibit 99.4

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STOP THE START

of classical complement-driven diseases

ANX1502 First In Human SAD / MAD Data Overview

December 2023

Overview of ANX1502 Program

- Potential first oral small molecule inhibitor of the classical pathway in development, targeting the active form of C1s
- Successfully completed single and multidose Phase I study in healthy volunteers with liquid suspension formulation
- Observed desired PK (well above minimum targeted drug levels), consistent with BID dosing
- Obtained supportive PD data in subjects with higher C4d baseline measures
- Data support advancing to tablet bridging study to assess ANX1502 efficacy in CAD patients

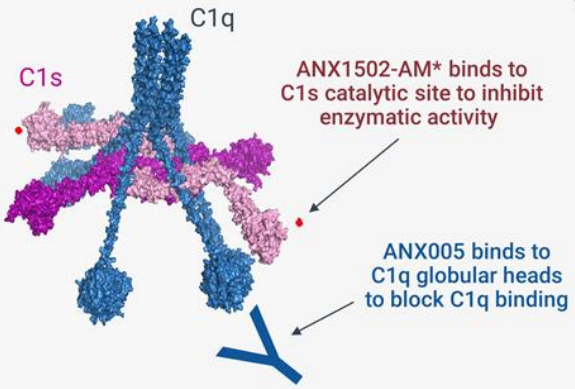
ANX1502: First Oral, Small Molecule Inhibitor of Classical Complement Pathway in Development

Orally administered prodrug **ANX1502** which releases the active moiety **ANX1502-AM***

Targeting active form of C1s responsible for transmitting classical pathway activation from C1q

Potent and selective inhibitor of C1s (serine protease): selective over related proteases (200 – 50,000-fold)

Highly specific for classical pathway



* ANX1502-AM: ANX1502 Active Moiety

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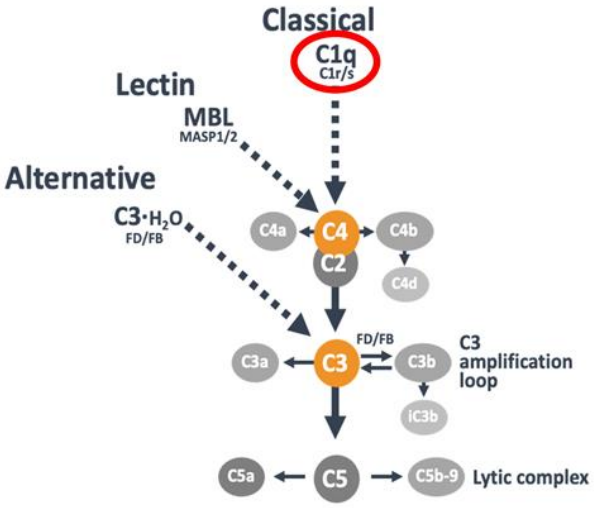
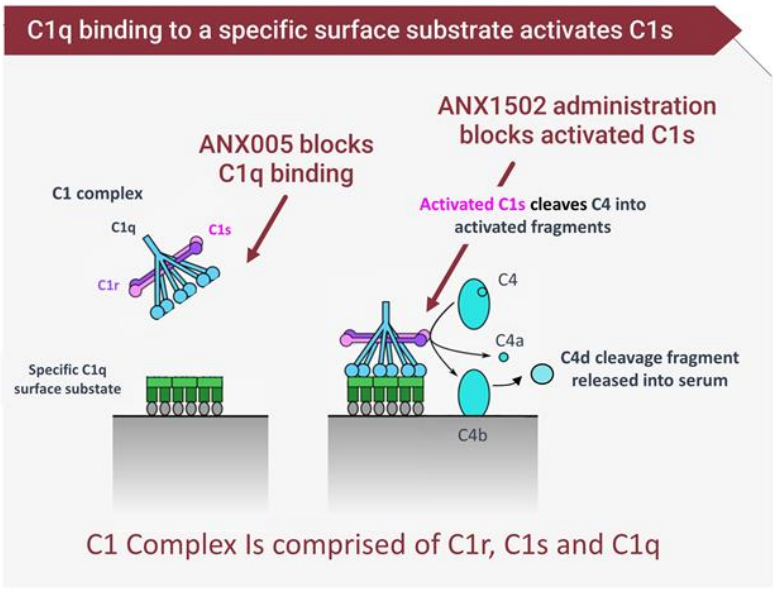
Following C1q Binding to a Specific Target Surface, ANX1502-AM* Observed to Inhibit Activated C1s to Block the Classical Cascade



* ANX1502-AM: ANX1502 Active Moiety



Modified from Sharp et al, *PNAS*, 2019

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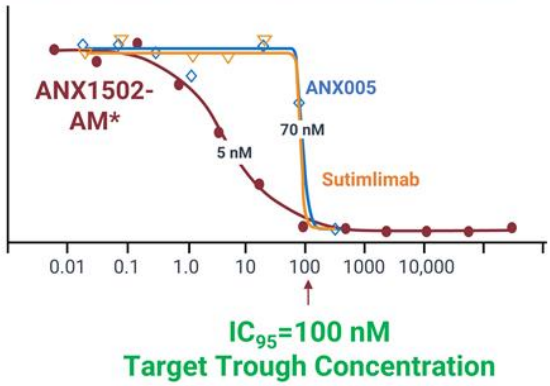
Minimum Target Drug Level (100 nM) ANX1502-AM* for Robust Functional Inhibition of Classical Complement Pathway

- ANX1502-AM* demonstrated **robust functional inhibition of classical pathway** (IC_{50} = 5 nM)
  - Comparable to ANX005 and sutimlimab
  - *In vitro* hemolysis assay w/ high serum (30%)
- Normal sigmoidal dose response vs. antibodies likely due to rate-limiting concentrations of activated C1s
- **Minimum target drug levels for IC_{95}, desired at trough, set conservatively at 100 nM**

Potent for *In Vitro* Hemolysis in 30% Human Serum



IC_{95}=100 nM Target Trough Concentration

* ANX1502-AM: ANX1502 Active Moiety

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Achieved Objectives for ANX1502 Ph 1 Program (Healthy Volunteers)

- Demonstrate favorable tolerability of ANX1502 in initial liquid suspension formulation ✓
- Achieve target levels of active drug consistent with BID dosing ✓
- Upside: demonstrate initial *in vivo* pharmacodynamic (PD) signal with biomarkers of complement activation in healthy volunteers ✓

ANX1502 Phase 1 Study Design (Healthy Volunteers)

Initial suspension formulation, dosed up to 1050 mg in SAD and 525 mg BID in MAD

- **Single Ascending Dose (SAD):**
  - 6 ANX1502 + 2 placebo subjects per dose cohort
  - Doses from 25 mg to 1050 mg evaluated
- **Multiple Ascending Dose (MAD):**
  - 9 ANX1502 + 3 placebo subjects per dose cohort
  - Twice daily dosing for 2 weeks (BID)
  - Doses from 200 mg BID to 525 mg BID evaluated

ANX1502 Suspension Formulation Generally Well-Tolerated Across SAD & MAD Cohorts in Healthy Volunteers

Manageable GI tolerability issues

Safety Results from Phase 1

- **ANX1502 generally safe and well tolerated through the highest dose level tested**
- All treatment-emergent adverse events (TEAEs) mild or moderate
- Most frequent TEAEs are gastro-intestinal and include nausea, emesis, and diarrhea
- **No serious adverse events (SAEs) observed**
- **No significant clinical/lab findings** (e.g., liver function enzymes, serum chemistry, hematology) observed

Subjects with TEAEs	SAD (Single Dose)						MAD (BID Dose)			
	25mg (N=6)	150mg (N=6)	450mg (N=6)	525mg (n=6)	1050mg (N=6)	**Placebo (N=10)**	200mg BID (N=9)	325mg BID (N=9)	525mg BID (N=9)	**Placebo BID (N=9)**
Subjects with any TEAE (%)	4 (66.6)	2 (33.3)	4 (66.6)	5 (83.3)	6 (100.0)	**6 (60.0)**	7 (77.7)	8 (88.9)	6 (66.6)	**7 (77.7.)**
Subjects with TEAE reported as related (%)	3 (50.0)	2 (33.3)	4 (66.6)	4 (66.6)	6 (100.0)	**4 (40.0)**	6 (66.6)	8 (88.9)	5 (55.5)	6 (66.6)
Subjects with any ≥ Grade 2 TEAE* (%)	1	0	0	0	0	**0**	0	2 (22.2)	1 (11.1)	**1 (12.5)**
Subjects with any Serious TEAE (%)	0	0	0	0	0	**0**	0	0	0	0

***No AEs higher than Grade 2**

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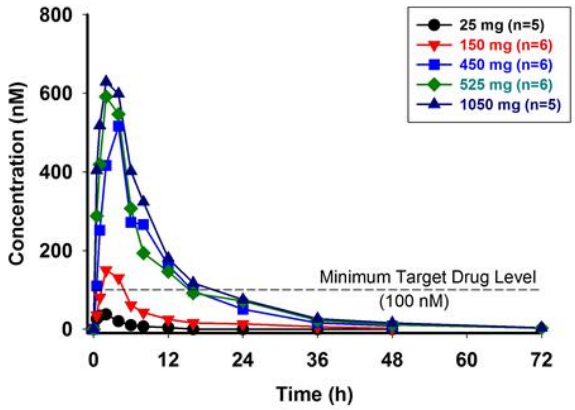
SAD Data: Target Concentration Achieved at Single Doses of ANX1502 of 525-1050 mg

PK Results from SAD

- Dose-proportional PK (AUC) in SAD cohorts across 25 mg – 525 mg cohorts
- Mean target drug level of 100 nM at 12h observed at single doses ≥ 525 mg
- Enabled BID dosing regimen in MAD study as planned



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Serum C4d as a Biomarker of C1s Activation *In Vivo*

In vivo activation of C1s leads to cleavage of C4 and release of C4d into the serum

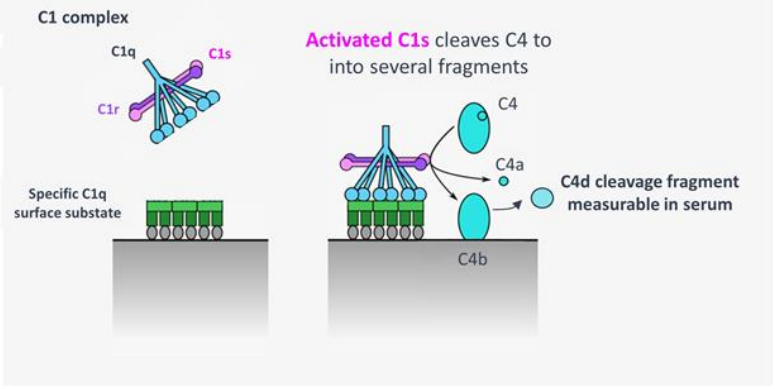
- Proximal biomarker of C1s activation
- C4d serum levels are low in healthy individuals, but elevated in LN and CAD patients

Circulating C4d levels decrease with C1q inhibition in CAD patients (ANX005 Ph2)

C4d used as a biomarker reflects drug's _in vivo_ impact on C1s activation

- CH50 *ex vivo* measures not relevant because involves 100-fold serum dilution / dilution of drug prior *to ex vivo* C1s activation

C1q binding to specific surface substrate activates C1s



Modified from Sharp et al, *PNAS*, 2019

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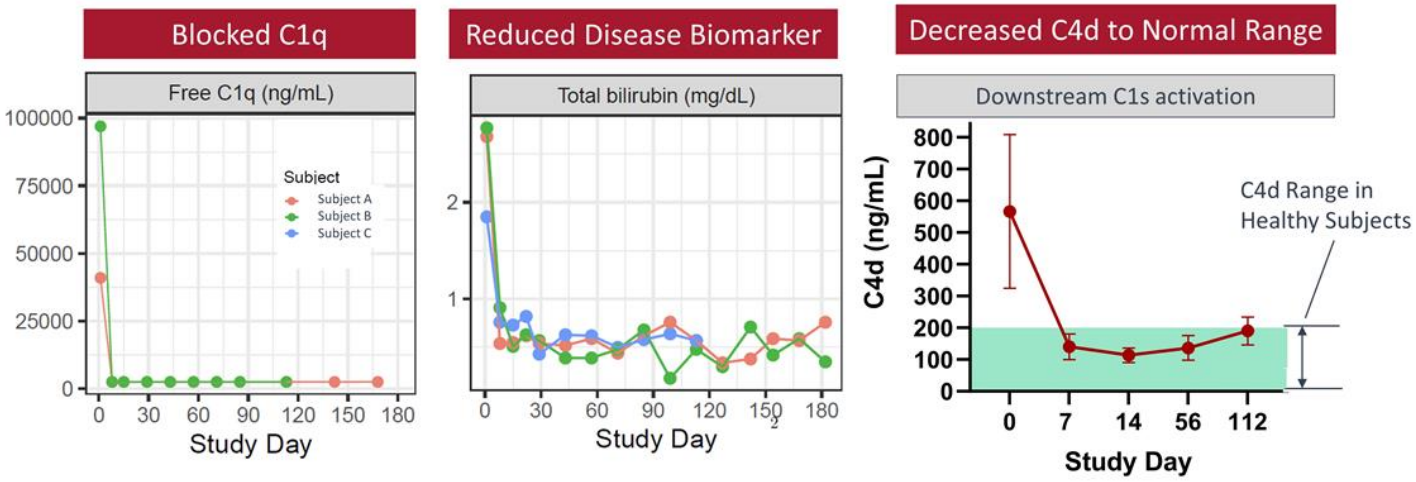
C4d Previously Validated as a Biomarker of C1 Inhibition with ANX005 in a Classical Complement Driven Disease

ANX005 blocked C1q, reduced bilirubin (disease-specific biomarker) and decreased serum C4d in Cold Agglutin Patients (CAD)



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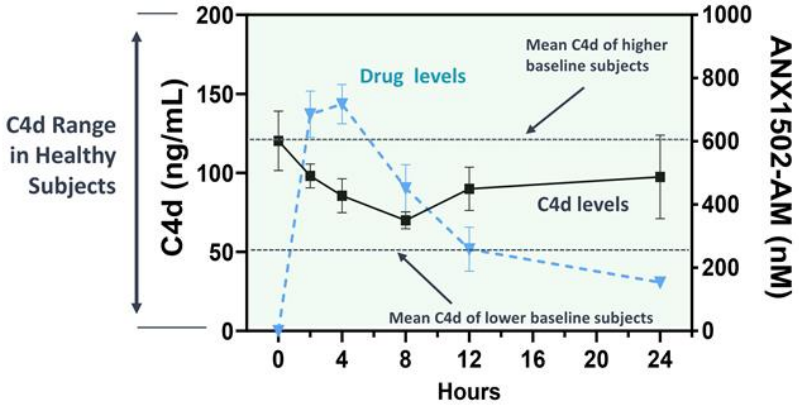
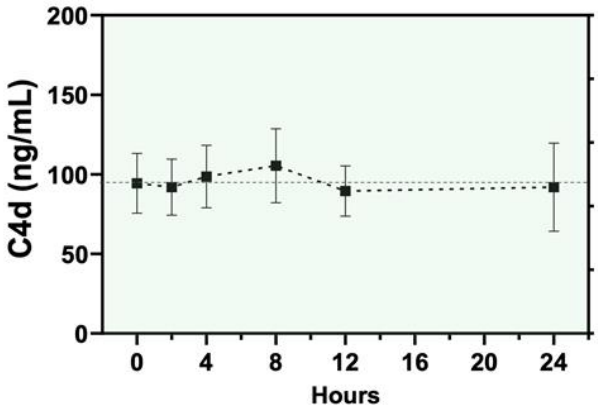
SAD PK/PD: ANX1502 (Single Doses of 525–1025 mg) Suppressed C4d Serum Levels in Healthy Volunteers w/ Higher than Median Baseline C4d

Drop in C4d in Subjects with Higher Baseline C4d Levels is Associated with Drug Exposure (n=6)



C4d Levels Did Not Change in Placebo Subjects (n=10)



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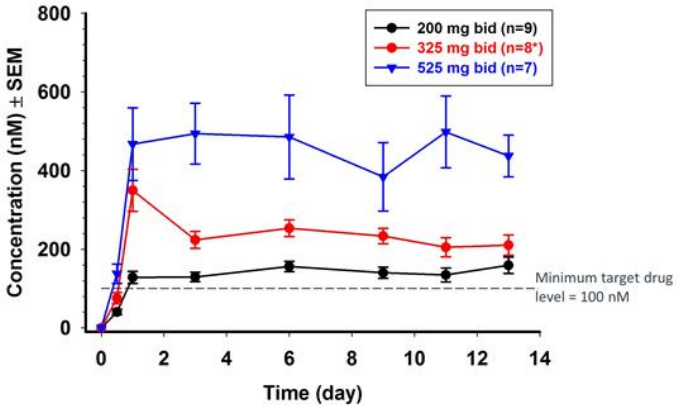
MAD Data: ANX1502 Dosing at 325 and 525mg BID Achieved Target Trough Exposures in 14-Day MAD Cohorts

- Dose-proportional PK (AUC) was observed in the MAD cohorts
- At 325 mg BID, and above, steady state drug levels above 100 nM achieved by Day 3 in all subjects
- At 525 mg BID, steady state drug levels well within range associated with significant C4d reduction in SAD cohorts
- Low baseline C4d levels fluctuate over multi-day period, preventing day-to-day monitoring of drug impact on steady state levels

PK Results from MAD



*n=4 from Day 1 to Day 3

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ANX1502 Small Molecule Program Summary & Next Steps

- Observed-targeted serum drug levels with suspension formulation of 1502 in healthy volunteers
- Obtained supportive PD data in subjects with higher C4d baseline measures
- Data support advancing tablet formulation of 1502 into clinic for assessing efficacy in CAD patients

Represents 1st oral upstream inhibitor of classical complement cascade in development as potential therapy in a host of autoimmune conditions