ANNEXON biosciences

GAME-CHANGING MEDICINES FOR COMPLEMENT-MEDIATED DISEASES

INVESTOR PRESENTATION MARCH 2023

Nasdaq: ANNX
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A bold mission to free the body, brain and eye from complement-mediated disease
Annexon Overview: On a Mission to Drive Significant Value

Pioneering Classical Complement Platform in Autoimmunity, Neurodegeneration & Ophthalmology

- Complement clinically / commercially validated with downstream approaches (C1s, C3, C5)
- ANNX building on prior learnings to block both up & downstream complement where it starts
  - Pursuing indications where (i) C1q localizes on disease tissue to anchor complement activation & (ii) complement activity drives disease progression
- Multi-faceted ‘beach-head’ portfolio with ‘informed signal finding’ and ‘confirming’ trials
- Clinical POC with lead drug candidate (ANX005) in multiple indications: GBS, HD, CAD, ALS

Significant ‘Enterprise Value’ Potential with multiple drivers over the next 3 years

- Targeting both Orphan and large patient population diseases with 4 Flagship Programs -- ~$10B market opportunity*
- Multiple expected value driving clinical readouts over 2023 & 2024, including GA & GBS efficacy trials
- Potential 1st-in-class GBS commercialization & initiation of potential 1st-in-class anti-complement HD trial
- Potential 1st-in-class oral compound for Autoimmune diseases

Well-Capitalized with Additional Opportunities

- Robust IP estate
- Wholly-owned with specific therapeutic-area partnering opportunities

* Based on market data and company estimates
Revolutionizing Complement Biology in Pursuit of Our Mission

Targeting C1q & classical complement cascade to treat autoimmune and neurodegenerative disease

C1q initiates a powerful inflammatory cascade that can lead to tissue damage

- Complement inhibition is a validated clinical and commercial approach
- Annexon’s next-generation approach blocks both upstream & downstream complement for enhanced outcomes

Robust Clinical Target Engagement of C1q Demonstrated in the Body, Brain & Eye

Full C1q Inhibition in Serum with ANX005

Full C1q Inhibition in CSF with ANX005

Full C1q Inhibition in Aqueous Humor with ANX007

CSF Levels ANX005

CSF C1q (µg/mL)

Mean ± SD
Clinical Proof-of-Concept Demonstrated in Both Autoimmune and Neurodegenerative Indications

**Guillain-Barré Syndrome (GBS)**
- 1. Slight symptoms
- 2. Walk / no running
- 3. Walk with support
- 4. Bedridden / chair bound
- 5. Ventilator-assisted breathing
- 6. Death

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 pt improvement</td>
<td>28%</td>
</tr>
</tbody>
</table>

ANX005 28% patients ≥3 pt improvement

**Huntington’s Disease (HD)**

Composite Unified Huntington’s Disease Rating Scale

ANX005 75% patients improved

**Cold Agglutinin Disease (CAD)**

**Amyotrophic Lateral Sclerosis (ALS)**

ANX005 All patients improved or maintained progression rate during treatment

Both patients that stayed on drug continued to improve

All patients who went off treatment declined
Achieving Our Mission With **FOUR FLAGSHIP PROGRAMS**

**Stopping Harmful Inflammation and Tissue Damage in the Body, Brain & Eye**

1. **Guillain-Barré Syndrome (GBS)**
   - **AUTOIMMUNE**
   - Well-validated MOA
   - Fast path to market in rare disease
   - 1st placebo-controlled trial in ~40 years

2. **Huntington’s Disease (HD)**
   - **NEURODEGENERATION**
   - Pioneering MOA
   - No disease-modifying treatments available
   - 1st complement inhibition in a brain disorder

3. **Geographic Atrophy (GA)**
   - **OPHTHALMOLOGY**
   - Well-validated MOA
   - Localized inhibition in eye
   - 1st up & downstream complement approach

4. **Oral Small Molecule**
   - **AUTOIMMUNE**
   - Well-validated MOA
   - Potential ease and convenience of oral dosing
   - 1st oral compound targeting classical complement
### Flagship Programs Advancing in Mid-stage and Pivotal Trials

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<th>INDICATION</th>
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<th>PHASE 1</th>
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<th>2023 ANTICIPATED MILESTONES</th>
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<tr>
<td>Guillain-Barré Syndrome</td>
<td>ANX005</td>
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<td>Complete Phase 3 enrollment in 2H 2023</td>
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<td>Huntington’s Disease</td>
<td>ANX005</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 2/3 trial 2023</td>
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<tr>
<td>Geographic Atrophy</td>
<td>ANX007</td>
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<td></td>
<td>Report Phase 2 data mid-2023</td>
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<tr>
<td>Autoimmune Indications</td>
<td>ANX1502</td>
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<td></td>
<td></td>
<td></td>
<td>Complete MAD trial and initiate POC trial in patients</td>
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</table>

**Guillain-Barré Syndrome**: ANX005 is expected to complete Phase 3 enrollment in 2H 2023.

**Huntington’s Disease**: ANX005 will initiate a Phase 2/3 trial in 2023.

**Geographic Atrophy**: ANX007 will report Phase 2 data mid-2023.

**Autoimmune Indications**: ANX1502 will complete a MAD trial and initiate a POC trial in patients.
Flagship Programs

- Guillain-Barré Syndrome (GBS)
- Huntington’s Disease (HD)
- Geographic Atrophy (GA)
- Oral small molecule
ANX005 Designed to Powerfully Inhibit C1q and Entire Classical Complement Pathway in the Body and Brain

Key Attributes

- **Diverse**: Utilized in autoimmune & neurodegenerative trials
- **Potency**: High binding affinity to C1q (<10 pM)
- **Target Engagement**: Full C1q inhibition observed in blood and CSF
- **Safety Results**: Generally well-tolerated in acute and chronic trials
  - No drug-related deaths & no serious infections observed
  - No autoimmune events observed post enhanced ANA screening / monitoring
- **Clinical**: Rapid clinical benefit demonstrated in GBS, HD, CAD & ALS

Administered to >200 patients to date
ANX005 Generally Well-Tolerated in Several Patient Populations

**KEY TAKEAWAYS**

**Leveraged learnings to optimize safety profile**
- Low grade, transient IRRs during first infusion: managed by infusion rate and pre-medication
- Single serious event of autoimmunity (SLE/lupus-like syndrome): no further events of autoimmunity observed post enhanced ANA screening / safety monitoring to date

**No drug related deaths & no serious infections observed throughout all studies to date**

**6 completed and 2 ongoing acute and chronic autoimmune & neurodegenerative trials**
- >100 patients from completed trials
- >110 patients in ongoing trials
- Exposure up to 1 year
### Study Deaths and Serious Adverse Events

- No deaths and no serious infections observed
- 3 observed serious adverse events related to ANX005
  - 1 IRR in NHV prior to dosing optimization
  - 2 in HD P2a trial (lupus like syndrome and idiopathic pneumonitis) prior to implementation of ANA screening and safety monitoring plan

### Adverse Events of Note

- Infusion Related Reactions (IRR) primarily first dose effect across indications (~95%) and commonly associated with transient rash
  - Adverse events coded as rash were primarily IRR
  - No IRR observed after 2nd dose of ANX005
- Elevated creatine phosphokinase (CPK) seen in placebo and ANX005 treated GBS patients – consistent with GBS

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### Treatment Emergent Adverse Events (TEAE)

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events (TEAE)</th>
<th>Safety Population (N=116*)</th>
<th>All CTCAE Grades N (%)</th>
<th>CTCAE Grade ≥3 N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any reported TEAEs, N (%)</td>
<td>114 (98.3)</td>
<td>29 (25.0)</td>
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</tr>
<tr>
<td>Most Common TEAE, N (%)</td>
<td></td>
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<tr>
<td>Infusion Related Reaction (IRR)</td>
<td>38 (32.8)</td>
<td>3 (2.6)</td>
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<tr>
<td>Most Common TEAEs (non-IRR), N (%)</td>
<td></td>
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<tr>
<td>Headache</td>
<td>37 (31.9)</td>
<td>0 (0)</td>
<td></td>
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<tr>
<td>Pain in extremity</td>
<td>24 (20.7)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Rash**</td>
<td>26 (22.4)</td>
<td>2 (1.7)</td>
<td></td>
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<tr>
<td>Pyrexia</td>
<td>18 (15.5)</td>
<td>0 (0)</td>
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<tr>
<td>Lab abnormality - CPK</td>
<td>15 (12.9)</td>
<td>6 (5.2)</td>
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<tr>
<td>Constipation</td>
<td>13 (11.2)</td>
<td>0 (0)</td>
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<tr>
<td>Pruritus</td>
<td>13 (11.2)</td>
<td>0 (0)</td>
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<tr>
<td>Serious TEAEs, N (%)</td>
<td>9 (7.8)</td>
<td>8 (6.9)</td>
<td></td>
</tr>
<tr>
<td>Related to ANX005</td>
<td>3 (2.6)</td>
<td>3 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

* All completed and open label studies with ANX005 (data cutoff 10/8/22); Includes: FIH, GBS P1b, GBS DDI, HD P2a, ALS P2a, CAD P2, wAIHA P2 trials
** Primarily initial dose IRRs, but coded under preferred term rash
Potential First-In-Class Treatment for GBS

Acute, *antibody-mediated autoimmune disease driven by aberrant C1q activation*

**GBS Overview**
- Rapid onset of **neuromuscular weakness** and paralysis
- 12,000 patients diagnosed/year in North America & Europe
- No FDA-approved therapies

**Role of C1q**
- **C1q binds autoantibodies** on nerve components, anchoring complement activation, inflammation & tissue damage
- **ANX005 blocks all inflammatory / damaging components of classical pathway** for rapid recovery

**ANX005**
- ✓ Fast Track & Orphan Drug Designations
- ✓ Pursuing monotherapy label
- ✓ Phase 3 pivotal trial ongoing
- ✓ Productive engagement with FDA on the statistical analysis plan for the ongoing pivotal trial
ANX005 Demonstrated Clinical POC in GBS Placebo-Controlled Trial

*Early improvement in muscle strength and reduction in neuronal damage preceding gain of function*

**Impact on Muscle Strength**
- Rapid increase in muscle strength within first week of treatment

**Impact on Key Neuronal Biomarker**
- Statistically significant early NfL reduction (weeks 2-4)
  - ANX005 (18-75 mg/kg)
  - Placebo

**Impact on Clinical Function**
- Patients achieving ≥3 point improvement in 8 weeks
  - ANX005
  - Placebo

All graphs: ANX005 n=18, Placebo, n=8
ANX005 GBS Phase 3 Pivotal Trial Underway

On track to complete expanded enrollment in 2H23 with Phase 3 data expected in 1H24

**Trial Design***

- Placebo (n~75)
- ANX005 30 mg/kg (n~75)
- ANX005 75 mg/kg (n~75)

**Day 1:** Single Dose

**6-month Off-treatment Follow-up**

**Specifications***

- Randomized, double-blind trial (N~220)
- Recently diagnosed severe patients (3 or higher on GBS-DS)
- Primary endpoint: GBS Disability Scale at week 8
- Patients stratified for baseline muscle strength and time from symptom onset
- Productive engagement with FDA on the statistical analysis plan for the ongoing pivotal trial
  - Increased study population by ~40 patients

*Pending planned protocol amendment*
Potential First-In-Class Treatment for HD

**Progressive neurodegenerative disease involving excessive synapse loss and neuronal damage**

**HD Overview**
- Progressive, inherited neurodegenerative disorder
- 80K people affected globally; ~300K at-risk
- No approved treatments that reverse or slow disease progression

**Role of C1q**
- C1q triggers synapse damage, synapse removal and neuroinflammation
- ANX005 blocks classical complement activation to protect synapses, reduce neuroinflammation and improve clinical outcomes

**ANX005**
- Phase 2 results demonstrated positive clinical outcomes
- Orphan Drug Designation
- Productive engagement with FDA
- Phase 2/3 trial design aimed at slowing rate of disease progression
- Phase 2/3 trial expected to initiate in 2023

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ANX005 Improved Clinical Outcomes in HD Phase 2 Trial

Reduced Downstream Complement
CSF C3 levels decreased in all patients during on and off treatment period

Reduced Neuroinflammation
HD inflammation marker (YKL-40*) reduced in patients with high baseline complement activity (C4a/C4)

Improved Clinical Function
Benefit at all time points in high complement group (cUHDRS)

*Produced by activated glia - Elevated in HD and other neurological diseases
ANX005 Phase 2/3 HD Trial Expected to Initiate in 2023

**Trial Design**
- Randomized, double-blind, placebo-controlled
- Leveraging precision medicine approach for patients with elevated baseline complement levels

**Patient Population**
- Patients with manifest and pre-manifest HD
- CAP score > 400
- UHDRS independence score ≥ 80

**Key Objectives**
- **Disease progression** measured by cUHDRS and TFC
- Confirm observations with rapid drug impact on high complement baseline patients
- Patient motor, cognition, behavior, functional capacity and quality of life assessments
- Safety and tolerability of ANX005

EXPECT TO INITIATE PHASE 2/3 IN 2023
Potential First-In-Class for Early Complement Inhibition in GA

Progressive neurodegenerative retinal disease involving C1q-driven synapse and photoreceptor loss

**GA Overview**

Leading cause of blindness in the elderly

1M people diagnosed in US; 5M people globally

Current approaches target downstream complement

**Role of C1q**

C1q drives tissue damage in the retina by anchoring complement activation on drusen, photoreceptor cells and synapses

ANX007 has potential to provide more complete protection by shutting down all classical pathway components

**ANX007**

✓ Targeting up and downstream complement activation

✓ Aim to slow rate of lesion growth

✓ Fast Track Designation

✓ Administered to 200 patients to date

✓ Phase 2 data anticipated mid-2023

1^Annexon data on file
ANX007 Designed to Powerfully Inhibit C1q & Classical Pathway in All Layers of the Retina

Key Attributes

✓ Potency: <10 pM Fab antibody formulated for intravitreal administration
✓ Target Engagement: Complete C1q inhibition in the eye for at least 4 weeks
✓ Safety Results: Generally well-tolerated in Phase 1b trial
✓ Preclinical Data: Demonstrated protection of photoreceptor cells and retinal function
✓ Dosing: Pharmacokinetics in patient aqueous humor supports monthly/every other month dosing; optimizing formulation for less frequent dosing

Administered to 200 patients to date
Targeting C1q’s Dual Role in Vision Loss in GA

C1q drives inflammation in retina and specific mechanism of synapse loss on photoreceptor neurons

C1q Well Positioned to Drive Retinal Damage

C1q localized on drusen (hallmark pathology of GA)

C1q anchors classical complement activation on drusen

C1q tags photoreceptor synapses to drive inflammation and neuronal damage

C1q guides microglial cells to target synapses in GA

C1q initiates & propagates neuroinflammation in the retina

Retina specimens from GA patients were procured from the San Diego Eye Bank; Annexon data on file; Tassoni et al, IOVS 2022 (ARVO Abstract)
Broader Overview of C1q’s Role in GA Progression

C1q accumulates in all layers of the outer retina and positioned as key driver of complement activation

- Drusen contain activating C1q substrates
- **C1q activation / inflammation contributes to retinal damage**
- Microglia/macrophages infiltrate the retina, expressing more C1q
- **C1q directly recognizes components of photoreceptor neurons → cell damage**
- **C1q tags photoreceptor synapses on stressed neurons → synapse pruning / degeneration**

1. Annexon data on file; 2. Katschke, 2018; 3. Jiao, 2018
ANX007 Inhibits C1q Throughout the Retina

C1q Occupancy by ANX007 Following Intravitreal Administration in Primates

- **Choroid**: Sham 150, 2.5 mg 50, 5 mg 0
- **Retina**: Sham 150, 2.5 mg 50, 5 mg 0
- **Vitreous**: Sham 150, 2.5 mg 50, 5 mg 0
- **Aqueous**: Sham 150, 2.5 mg 50, 5 mg 0

*Within resolution limits of assay*

\[
\text{D30} = \text{Day 30 (30 days post-2^{nd} ANX007 dose)}
\]

Two doses of 5 mg ANX007 administered by IVT 28 days apart in cynomolgus monkeys

C1q Occupancy by ANX007 In Patient Aqueous Supports Monthly/Every Other Month Dosing

- **Sham**: 100%
- **2.5 mg**: 75%
- **5 mg**: 50%

\[
\text{D1} = \text{Day 1 (before ANX007 dosing)}
\]

\[
\text{D29} = \text{Day 29 (post-1}^{st}\text{dose)}
\]

Grover et al, IOVS (in press); Sun et al, AAO Annual Meeting 2020; Annexon Data on File
Blocking C1q Protected Photoreceptor Structure and Function in Mouse Light Damage Model

Protection of Retinal Layer Thickness / Cell Number

Protection of Photoreceptor Cell Function

Anti-C1q Protected Photoreceptor Cells / Retinal Thickness

Protected Retinal Function

* p < 0.05

Jiao, 2018
Ongoing ANX007 Phase 2 GA Trial with Data Expected Mid-2023

**ARCHER Trial Design**

- ANX007 5.0 mg/eye once monthly (n=~90)
  - Sham once monthly (n=~45)
- ANX007 5.0 mg/eye every 2 months (n=~90)
  - Sham every 2 months (n=~45)

12-month Treatment Period 6-month Off-treatment Follow-up

**Specifications**

- Randomized, double-masked, sham-controlled trial (N~270)
- Patients stratified based on lesion size and location (>45% patients with non-foveal lesions)
- Primary endpoint: Rate of change (slope) in GA lesion area assessed by fundus autofluorescence (FAF)
- >50% of patients through 12-month treatment period with >90% adherence with office follow-ups*

**PHASE 2 DATA EXPECTED MID-2023**

* As of December 8, 2022
ANX1502: First Oral, Small Molecule for Classical Complement-Mediated Autoimmune Diseases

**Opportunity**

Autoimmune indications with strong scientific rationale, including:
- Multifocal motor neuropathy (MMN)
- Lupus Nephritis
- Myasthenia gravis
- Cold agglutinin disease (CAD)

**Role of C1s**

Enzyme carried by C1q responsible for classical complement pathway activation

Targeting active form of C1s inhibits complement only at sites of activation

**Highly specific effect on classical pathway**

**ANX1502**

- **Orally administered prodrug** for chronic therapy in disease
- **Converts to highly selective active compound ANX1439** on administration
- **Achieved target drug levels** in on-going Phase 1 SAD trial
- **Conducting MAD in healthy volunteers**
- **Initiating POC in 2023**

*Active compound of ANX1502*
Following C1q Binding to a Surface, Small Molecule Rapidly Inhibits Activated C1s

Modified from Sharp et al, PNAS, 2019
ANX1502: Structure-Based Screening and Design

ANX1502 Discovery From HTS To CTA Submission

**HTS**
- HTS: identification of initial inhibitors
- Obtained crystal structure with early hits to identify C1s binding mode

**Hit to Lead**
- Structure-driven drug design leads to high potency and selectivity
- Tops HITs based on structure with C1s
  - IC₅₀ ~1 μM
  - Marginal Stability

**Lead Optimization**
- Optimized potency, selectivity, stability, oral availability, etc.
- LEAD
  - IC₅₀ ~1 nM
  - Highly Selective
  - Marginal Stability

**Candidate Selection**
- Introduction of prodrug increases stability and improves bioavailability
- Active Compound ANX1439
  - IC₅₀ ~1 nM
  - Functional Activity
  - Highly Selective
  - Low in vivo clearance
  - Moderate oral bioavailability
- ANX1502
  - Improved oral bioavailability
- Initiate Phase 1

**Timeline**
- 2017
- 2018
- 2019
- 2021
- 2022

- HTS
- Hit to Lead
- Lead Optimization
- Candidate Selection
ANX1502 Delivers a Highly Potent and Selective Inhibitor of C1s

Active Compound ANX1439:

- High affinity for C1s: 0.6 nM (Biacore)
- Potent inhibitor: 1 nM purified enzymatic assay
- Selective over related serine proteases (200 – 50,000-fold)
- Robust functional inhibition of classical pathway (comparable to sutimlimab)
  - In vitro hemolysis assay (IC$_{50}$ = 5 nM)
  - Clinical target concentration =100 nM

*Active compound of ANX1502*
ANX1502 Well-Tolerated in Ongoing Phase 1 SAD Trial; Pharmacokinetic Results Support Twice Daily Dosing

Safety Results*

- ANX1502 generally well-tolerated
- Maximum tolerated dose not yet reached
- All treatment-emergent adverse events (TEAEs) mild or moderate
- No serious adverse events (SAEs)
- No significant clinical/lab findings (e.g., liver enzymes, serum chemistry, hematology)

*As of October 23, 2022

Single Dose of 450mg Achieved Target Drug Levels

Active compound levels >100 nM for 12 hours, supports twice daily dosing

Plasma levels after single dose**

Active Compound Concentration (nM)

0 100 200 300 400 500 600

0 6 12 18 24 30 36 42 48

Time (hr)

450 mg
150 mg
25 mg

Target drug levels

$T_{1/2} = 9-10$ hours

**Cohorts where ANX1502 was administered without food
## ANX1502 Advancing Into Multiple Clinical Trials for Development in Autoimmune Indications

### ANX1502 Development Plan

- **Complete Phase 1 SAD / MAD study in healthy volunteers**
  - Establish dose for patient studies
- **Demonstrate rapid POC in CAD**
  - Establish 1502 PK/PD in a short duration trial with objective readout
- **Expand autoimmune franchise into multifocal motor neuropathy (MMN)**
  - Strong scientific rationale; supporting data from mechanistically-related GBS indication

### Next Steps for Program Expansion

- **Additional franchise expansion informed by emerging data 2H23**
  - Ph 1b LN data expected in 1H23; informs late-stage trial related diseases
  - Ongoing assessment of Myasthenia gravis (MG) and other indications

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**Phase 1 data expected 2023**

**POC trial initiation expected 2023**

**P2 trial initiation expected 2024**

**Expansion expected 2H23**
MMN: Progressive Disability Despite Treatment With Standard Therapy

Disease Overview

• **Clinical features**
  - Slowly progressive asymmetrical distal limb weakness
  - Muscle wasting over time

• **Patients**
  - ~12K in US / EU
  - Commonly middle-aged men

• **Pathophysiology**
  - Anti-GM1 antibodies
  - Motor conduction block

• **Treatment**
  - Treated with IVIg, but progressive nerve damage continues
  - Life-long and time-consuming treatment

Nerve Damage Mediated by Classical Complement in MMN

INTACT NERVE

- GM1 gangloside to muscle

MMN

- C1 complex
- IgM
- Complement activation Axon and myelin damage
- GM1 gangloside to muscle

Axon and myelin damage

National Organization for Rare Diseases
https://rarediseases.org/rare-diseases/multifocal-motor-neuropathy/
Viarn, Lotte et al., Neuroimmunology Neuroinflammation, 2015
Strong Rationale for C1 Inhibition as Therapy for MMN

*IgM driven disease related to GBS*

**Classical Complement Activation in MMN**

Patient sera: C1q, C4b and C3b deposition on GM1 ganglioside *in vitro* correlates with anti-GM1 IgM titers

Yuki, et al., J Neurol Neurosurg Psychiatry 2011

**Complement Activation Correlates with Severity**

Patient sera: *In vitro* complement deposition on GM1 ganglioside correlates with MMN disease severity

Vlam, et al., Neurology 2015

**C1 Inhibition Reduces Effect of MMN Antibodies**

Neuronal culture: Anti-C1q blocks neurotoxic calcium influx caused by IgM GM1 antibodies

Harschnitz, et al., Annals Neurol 2016
Early Plans for MMN Study With ANX1502

**Trial Design**
- Randomized, double-blind trial assessing efficacy of ANX005 vs. IVIg
- IVIg rescue provided

**Key Objectives**
- Safety and tolerability
- Confirm first use of oral drug candidate in MMN patient population
- Measures of peripheral muscle strength using MRC sum score and hand-held dynamometry
- Patient function
- Need of IVIg retreatment

**Target Patient**
- "Early" MMN and documented response to IVIg (run-in period)

**TIMELINE:** INITIATE IN 1H 2024
Additional Near-Term Opportunities
## Numerous Opportunities with Next Wave Programs

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<td>Report Phase 2 data in 2023</td>
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<tr>
<td>Lupus Nephritis (LN)</td>
<td>ANX009</td>
<td></td>
<td></td>
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<td>Report Phase 1 data in 1H 2023</td>
</tr>
<tr>
<td>Autoimmune/ Neuro</td>
<td>ANX105</td>
<td></td>
<td></td>
<td></td>
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<td>Report Phase 1 data in 2023</td>
</tr>
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</table>
Potential First-In-Class Treatment for ALS

Targeting up & downstream complement activity in both the brain and peripheral nerves

**ALS Overview**

Rapidly progressing neurodegenerative disorder (fatal within 3-5 years from diagnosis)

Affects ~19,000 **people each year** in the US

**Role of C1q**

C1q targets both central and peripheral nerve components – motor neurons (MN) and peripheral neuromuscular junction (NMJ)\(^1,2,3\)

C1q activation drives inflammation and neurodegeneration\(^1,2\)

**ANX005**

Differentiated, targeting both central and peripheral nervous system

Aim to slow rate of disease progression

Phase 2a trial actively enrolling, data expected 2023

**ANX005**

- **Open-Label Treatment Period**: 3-6 Months\(^1\)
- **Off-Treatment Period**: 3 months

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\(^1\)Protocol amendment extended treatment period from 3 months to 6 months

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ANX005 Preliminary ALS Phase 2a 12-Week Data Show Disease Progression Slowed During Treatment, Increased Off-treatment

**Reduction in Plasma NfL**

- **Reduction trend in plasma NfL during treatment period**
- **Increased in off-treatment period**

**Impact on ALSFRS Rate of Progression**

- **All patients showed improvement or maintenance of progression rate during treatment**
- **Both patients that stayed on drug continued to improve**
- **All patients who went off treatment declined**

**On-treatment: N=8; Off-treatment: n=6 (all patients who completed 12-week treatment protocol): Data as of 12/6/2022**

**N=8 (All patients who completed 12 or 24-week treatment protocol): Data as of 12/6/2022**

- On treatment
- Off treatment
ANX009 Selectively Inhibits Complement Activation in Vascular Space

Key Attributes

- Subcutaneous formulation of an antigen-binding fragment (Fab)
- Target Engagement: Selectively inhibits C1q in the vascular space
- Safety: Well-tolerated in Phase 1 trial, twice weekly dosing provided sustained C1q inhibition in the circulation
- Dosing: Designed to enable chronic dosing for use in future trials of autoimmune indications
Potential First-In-Class Approach for Lupus Nephritis; Data Expected 1H23

Endogenous, pathogenic autoantibodies against C1q enhance its activity and uniquely amplify kidney inflammation and damage

LN Overview

~60,000 US patients/year

Pathogenetic autoantibodies against C1q (PACAs) enhance LN disease activity

Role of C1q

C1q and PACAs amplify kidney inflammation and damage

ANX009 blocks binding, activation & tissue damaging inflammation in LN

ANX009

Targeting patients with high baseline complement activity by increased C4d/C4

Well-tolerated in Phase 1 trial, twice weekly dosing provided sustained C1q inhibition in the circulation

Phase 1b signal-finding trial underway, with initial data expected in 1H23

*Induced by injection of auto-reactive antibodies against kidney glomerular basement membrane antigens

Selectively Inhibiting C1q to Stop Complement-Mediated Disease

High baseline complement activity correlated with disease activity

Full inhibition of C1q in serum with ANX009 in Phase 1 study

Patients most likely to respond to ANX009

Healthy volunteers; Dosing on days 0, 3, 7 and 10

Annexon data on file
ANX105 Next Generation Inhibitor of C1q & Classical Pathway

Key Attributes

✓ Full-length mAb for IV administration

✓ Target Engagement: Designed to fully inhibit C1q in blood and CSF

✓ Dosing: Designed with potentially improved dosing properties for use in future trials of autoimmune and neurodegenerative indications

✓ Phase 1 SAD study in normal healthy volunteers ongoing
A Mission to Enable People to Live Freely from Complement-mediated Diseases
Game-Changing Opportunity for C1q-directed Complement Therapies in Current Indications and Beyond

Significant Unmet Need

- C1q-directed complement agents on the market or in late-stage development
- Disease-modifying treatments available for GBS or HD
- Treatments that target **both up and downstream** complement pathway for GA
- Orally administered, small molecule complement treatments available

Multi-Billion Market Opportunity

- Expansion into additional complement-mediated diseases of the body, brain and eye
- **>$10 BILLION**

*Based on market data and company estimates*
2023 Clinical Milestones Primed to Unlock Significant Value

**Well capitalized with runway into 2025***

- **Demonstrate efficacy signal in “next wave” indication**
  - ANX009 Phase 1 LN data expected in 1H 2023

- **Demonstrate clinical efficacy in GA**
  - ANX007 Phase 2 GA data expected in mid-2023

- **Demonstrate efficacy signal in “next wave” indication and target engagement with next generation mAb**
  - ANX005 Phase 2 ALS data expected in 2023
  - ANX105 Phase 1 data expected in 2023

- **Initiate placebo-controlled HD trial**
  - ANX005 Phase 2/3 initiation expected in 2023

- **Characterize dosing properties and initiate clinical POC trial with oral, small molecule**
  - ANX1502 Phase 1 MAD data in healthy subjects and POC trial initiation in CAD patients expected by end of 2023

- **Complete enrollment in pivotal GBS trial**
  - ANX005 Phase 3 complete enrollment expected in 2H 2023 with pivotal data anticipated in the first half of 2024

*62.7 million in cash and cash equivalents as of December 31, 2022*