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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

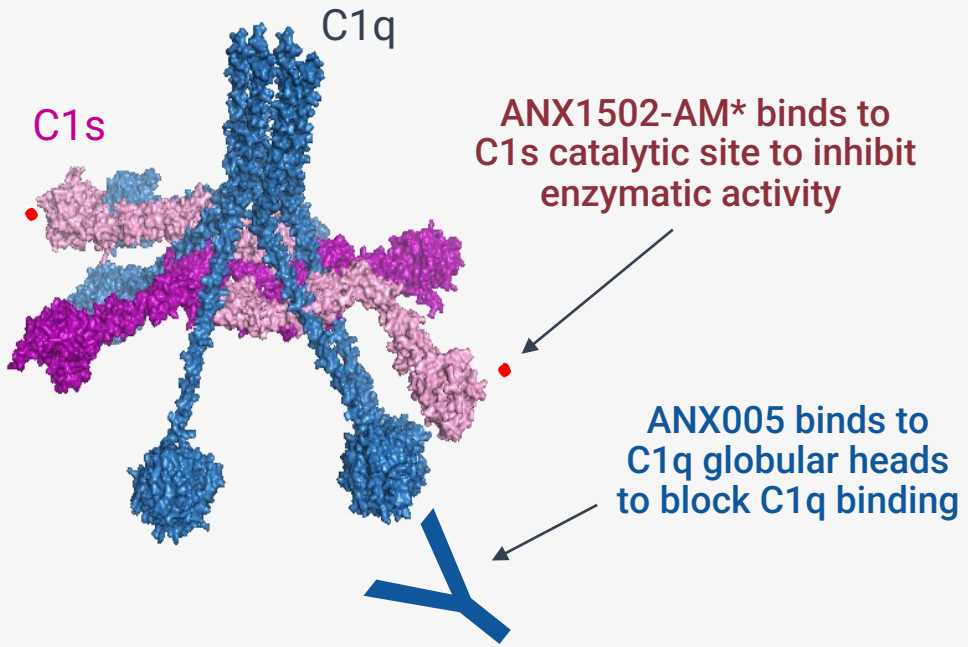
ANX1502: First Oral, Small Molecule Inhibitor of Classical Complement Pathway in Development

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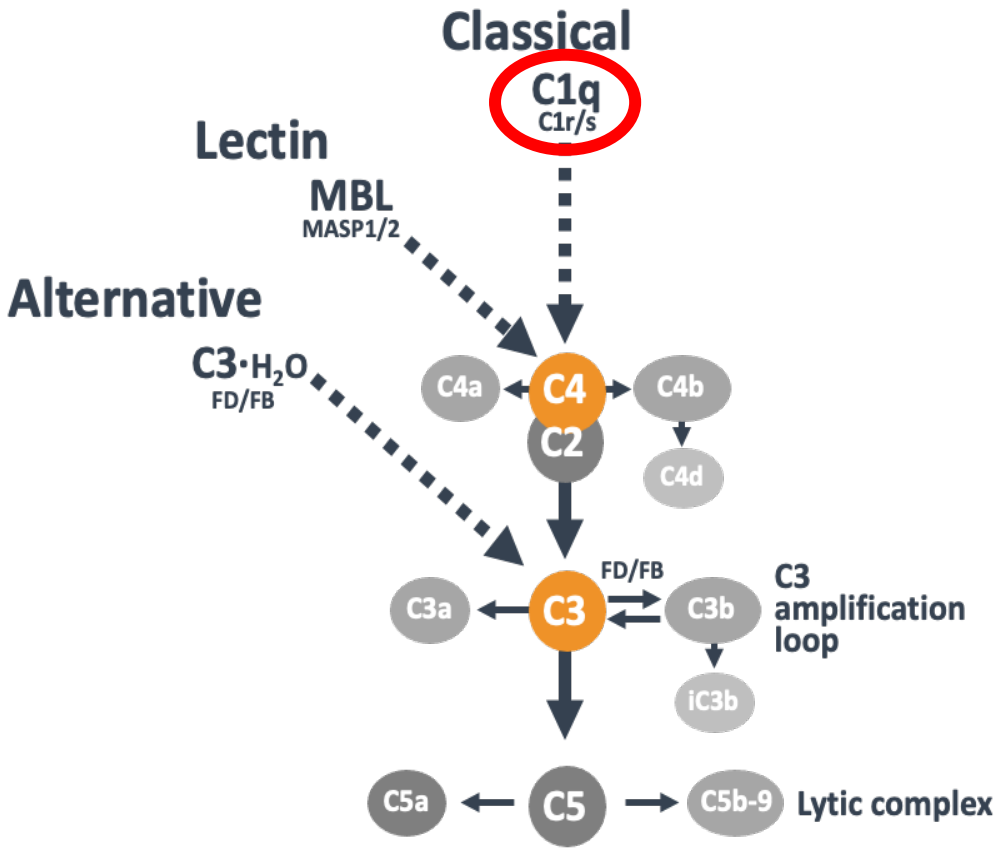
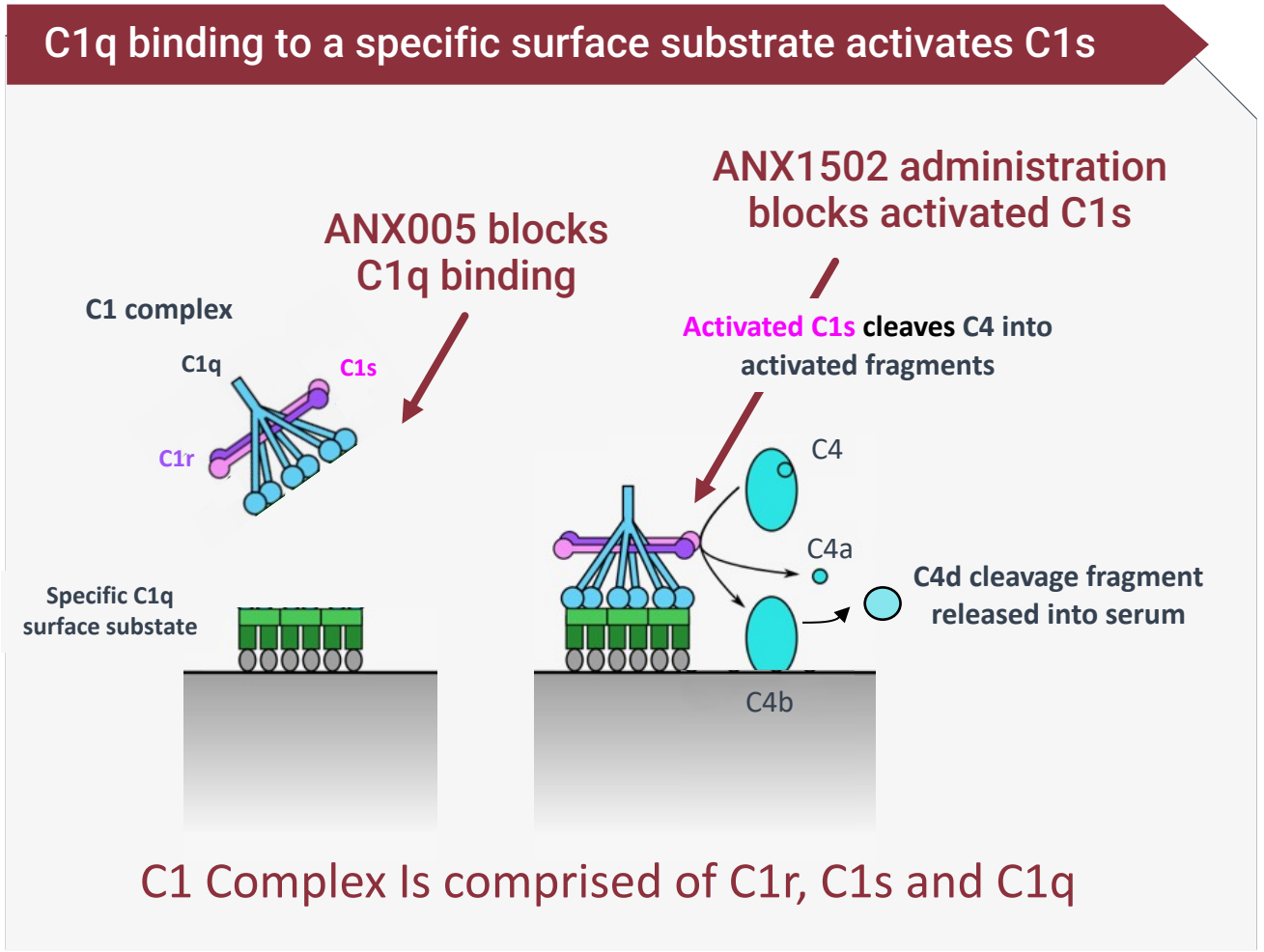
Following C1q Binding to a Specific Target Surface, ANX1502-AM* Observed to Inhibit Activated C1s to Block the Classical Cascade





* ANX1502-AM: ANX1502 Active Moiety

Modified from Sharp et al, *PNAS*, 2019

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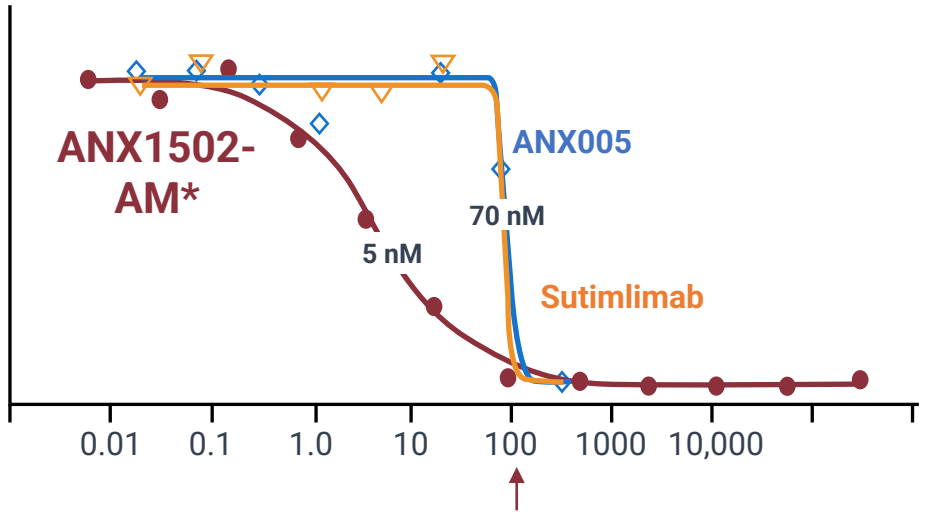
Minimum Target Drug Level (100 nM) ANX1502-AM* for Robust Functional Inhibition of Classical Complement Pathway

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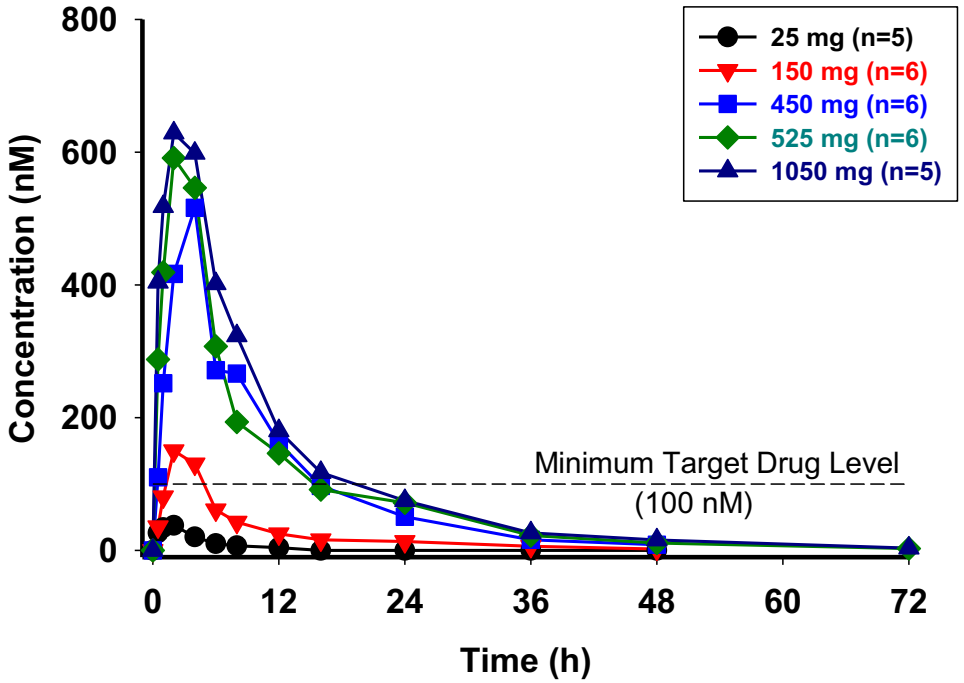
SAD Data: Target Concentration Achieved at Single Doses of ANX1502 of 525-1050 mg

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

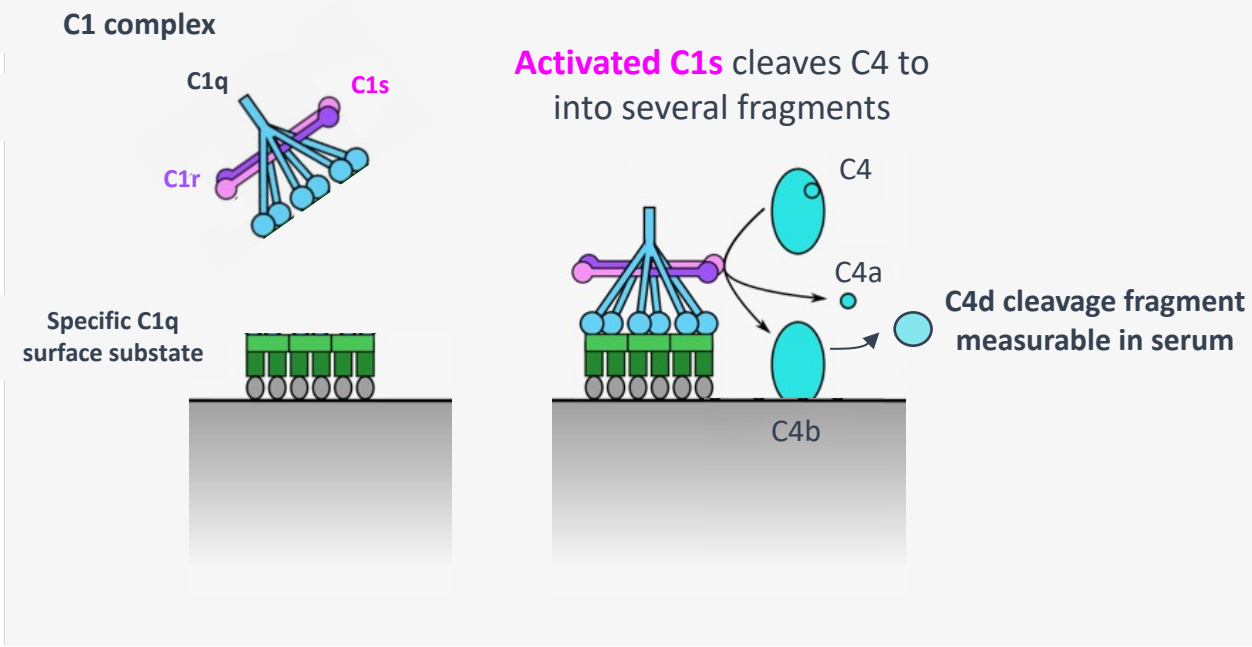
- Proximal biomarker of C1s activation
- C4d serum levels are low in healthy individuals, but elevated in LN and CAD patients

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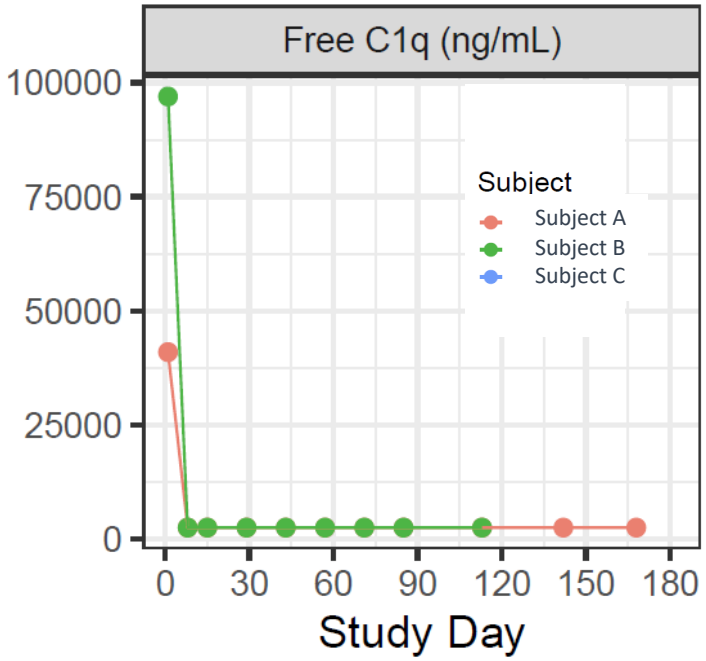
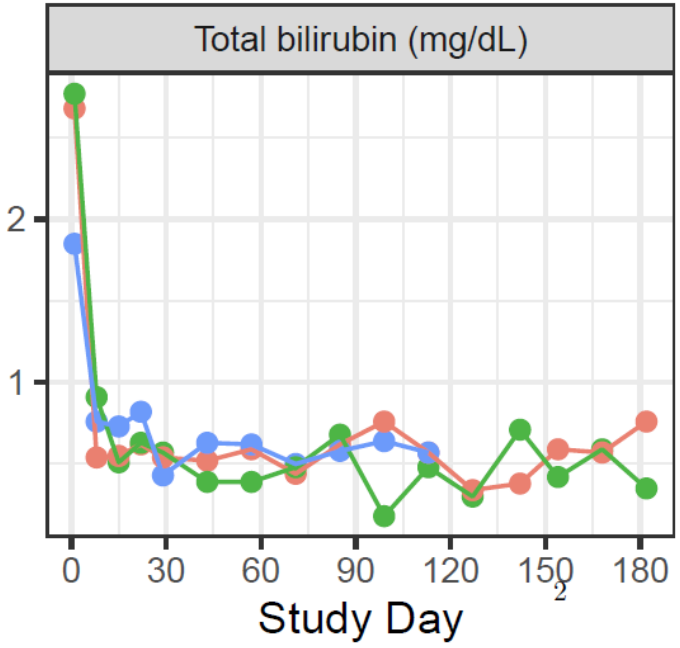
C4d Previously Validated as a Biomarker of C1 Inhibition with ANX005 in a Classical Complement Driven Disease

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

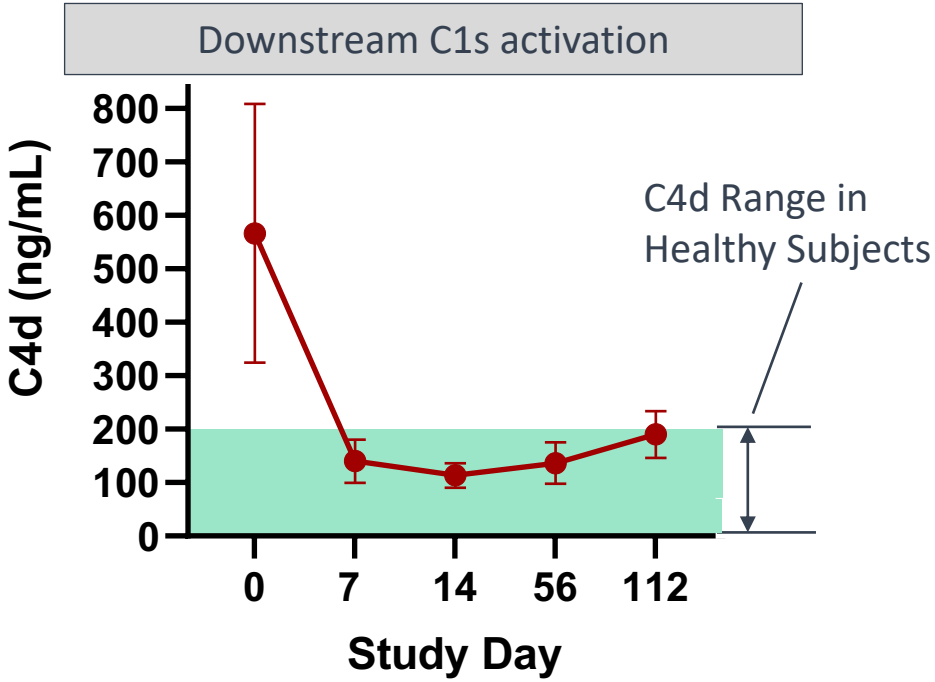
Blocked C1q



Reduced Disease Biomarker



Decreased C4d to Normal Range



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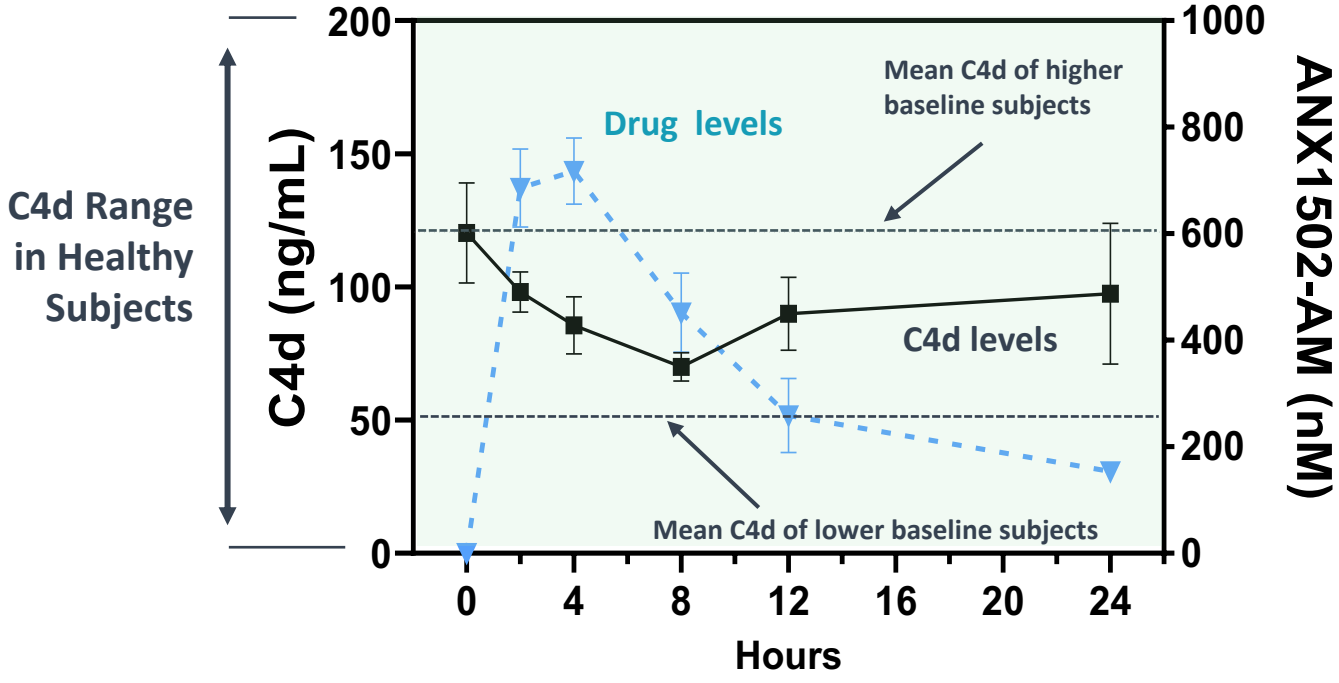
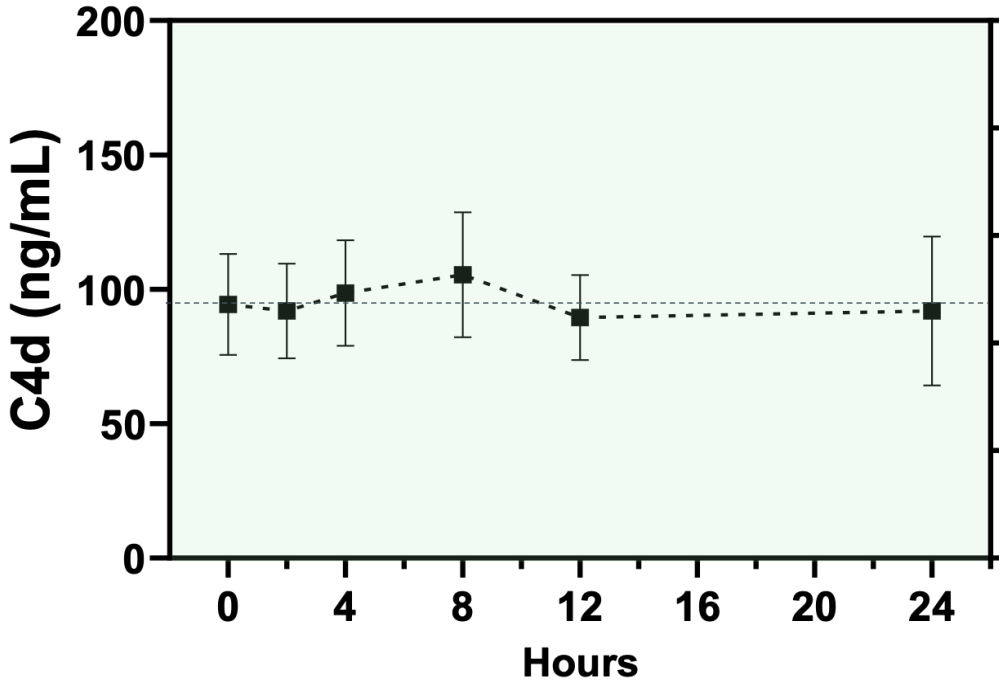
SAD PK/PD: ANX1502 (Single Doses of 525–1025 mg) Suppressed C4d Serum Levels in Healthy Volunteers w/ Higher than Median Baseline C4d

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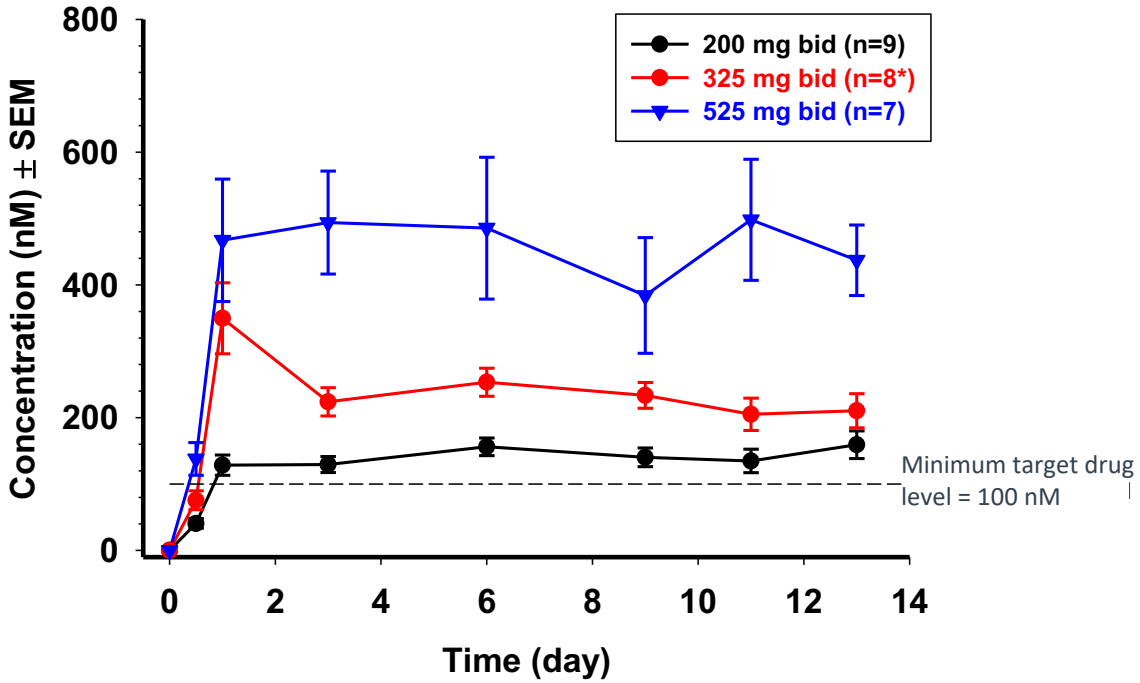
MAD Data: ANX1502 Dosing at 325 and 525mg BID Achieved Target Trough Exposures in 14-Day MAD Cohorts

- 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

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