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STOP THE START of classical complement-driven diseases

ANX1502 First In Human SAD / MAD Data Overview
August 2024

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

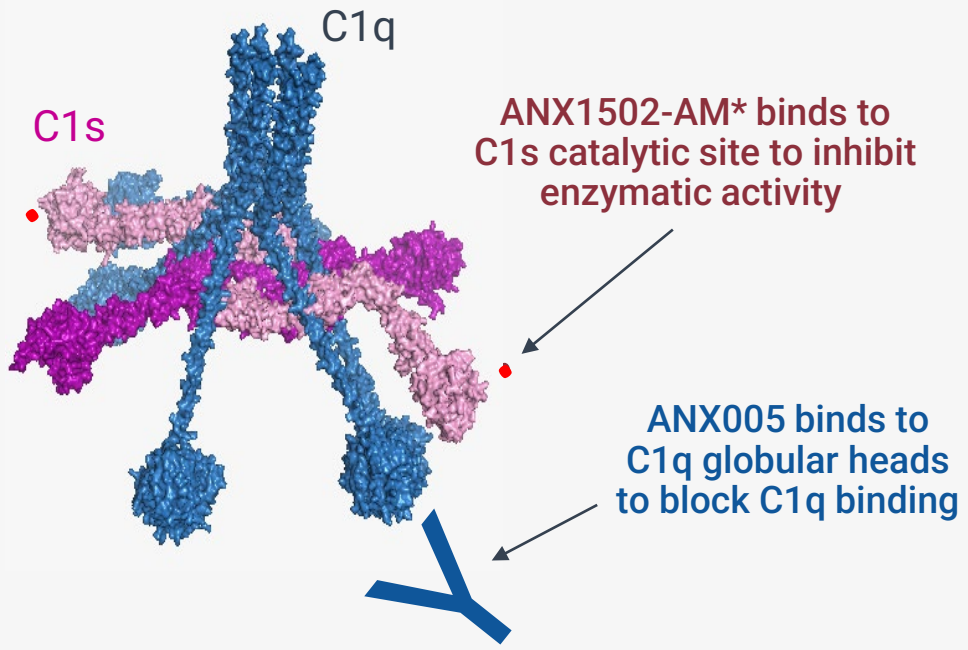
ANX1502: First Oral, Small Molecule Inhibitor of Classical Complement Pathway in Development

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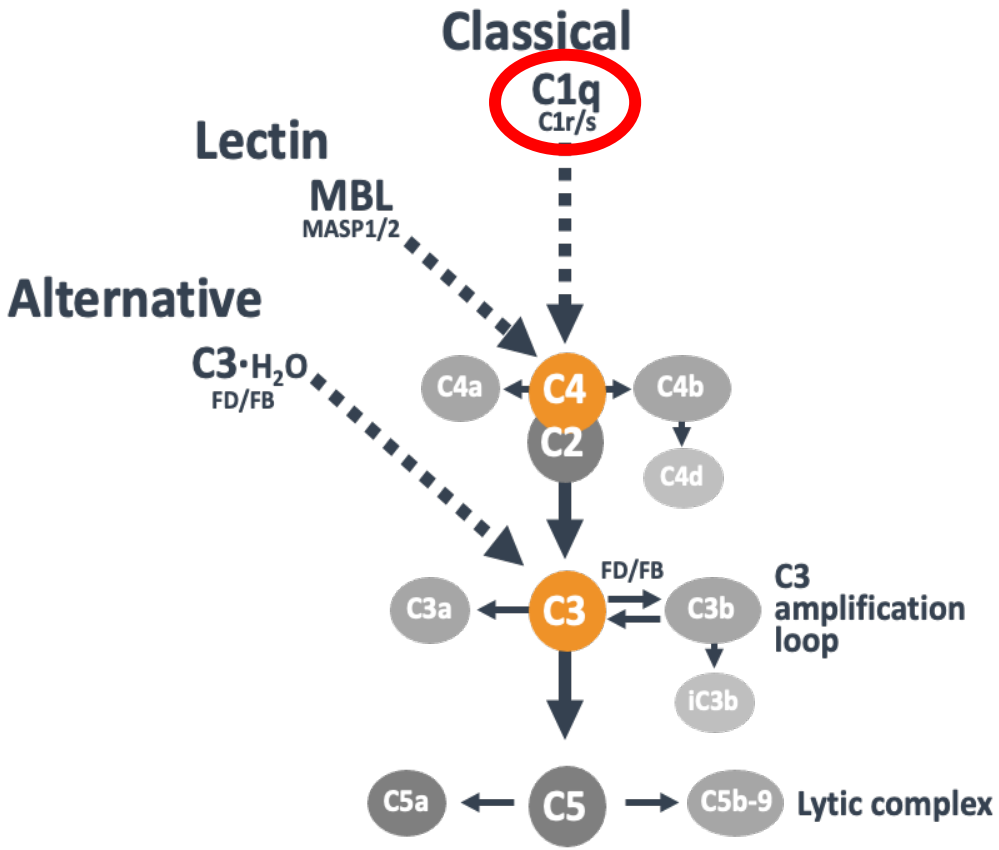
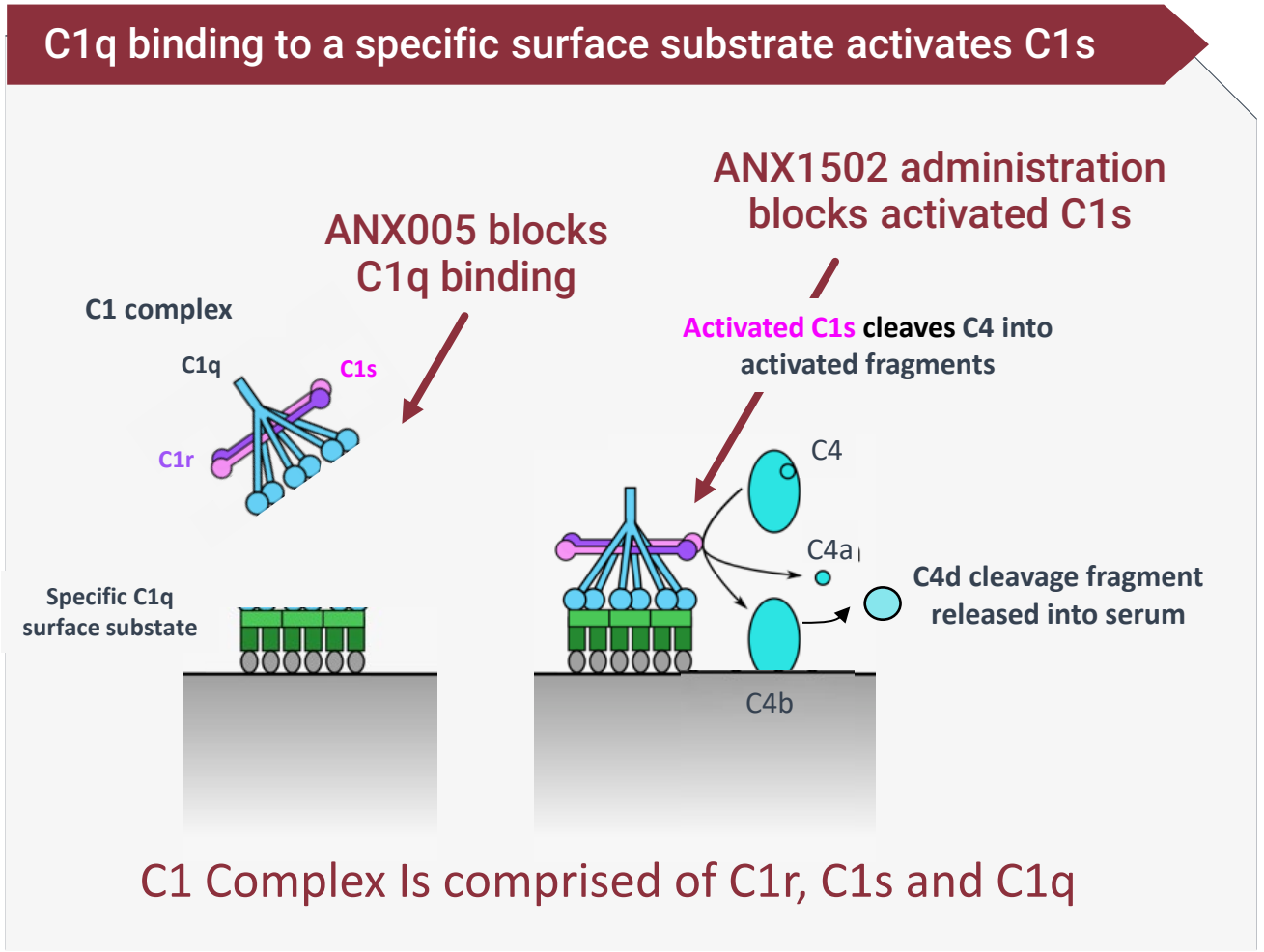
Following C1q Binding to a Specific Target Surface, ANX1502-AM* Observed to Inhibit Activated C1s to Block the Classical Cascade





* ANX1502-AM: ANX1502 Active Moiety

Modified from Sharp et al, *PNAS*, 2019

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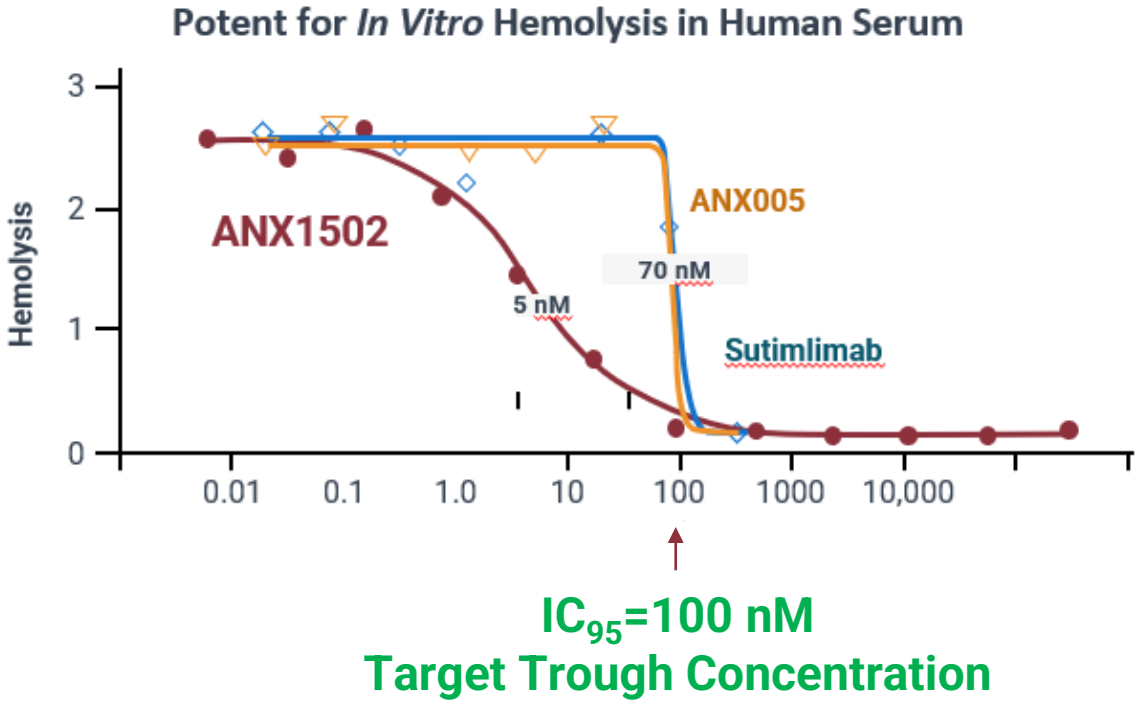
Minimum Target Drug Level (100 nM) ANX1502-AM* for Robust Functional Inhibition of Classical Complement Pathway

- 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**



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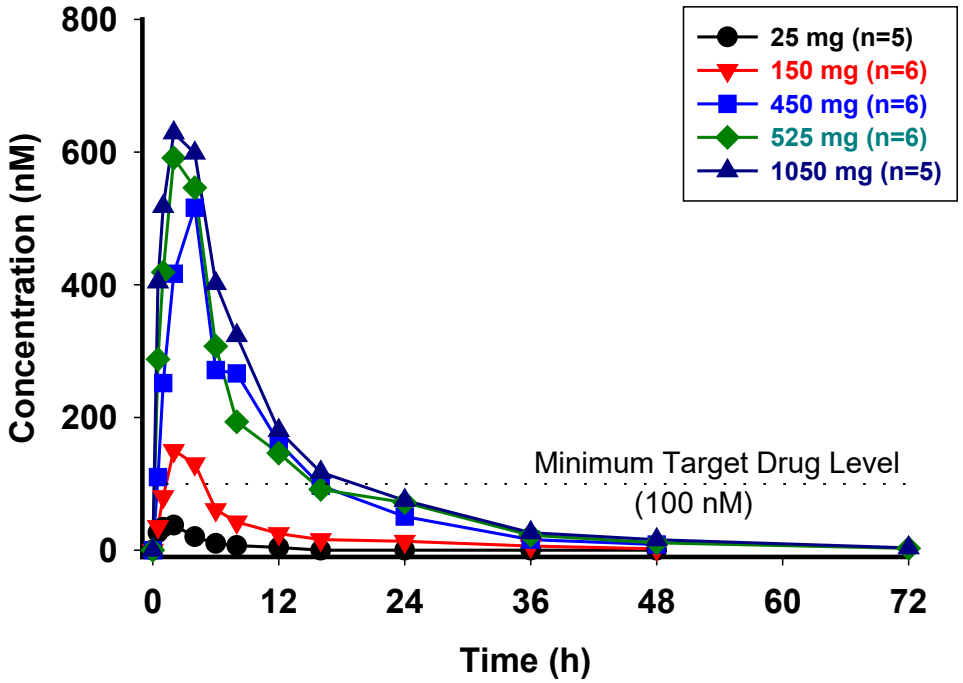
SAD Data: Target Concentration Achieved at Single Doses of ANX1502 of 525-1050 mg

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

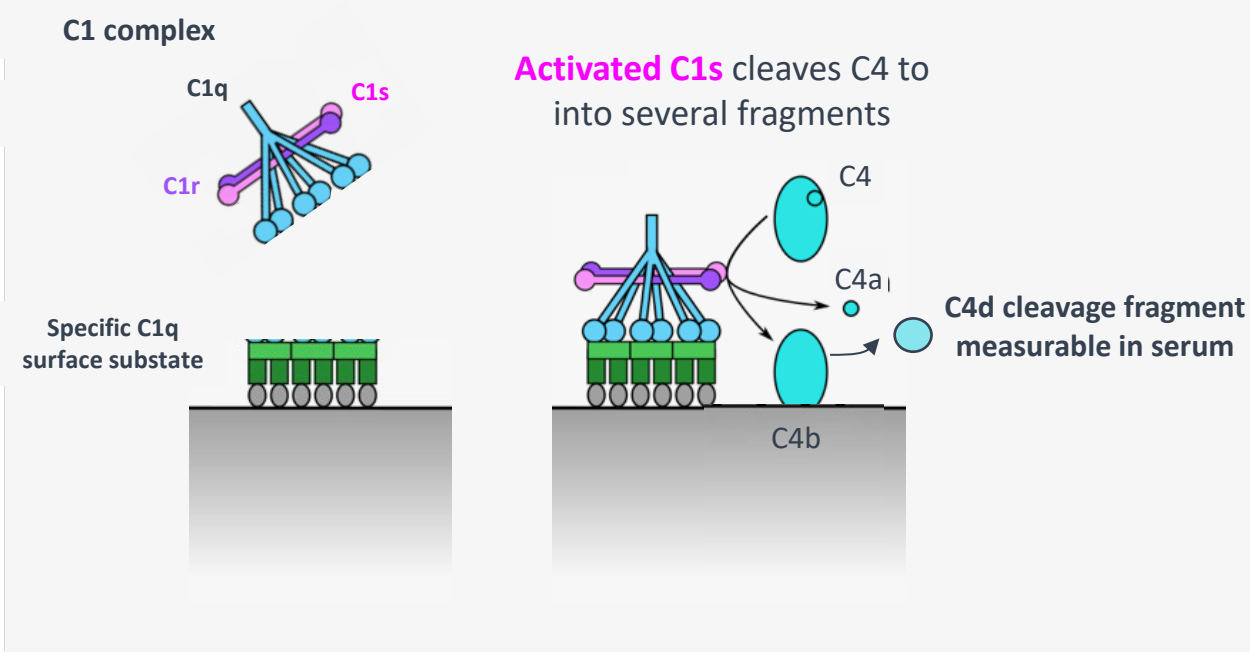
- Proximal biomarker of C1s activation
- C4d serum levels are low in healthy individuals, but elevated in LN and CAD patients

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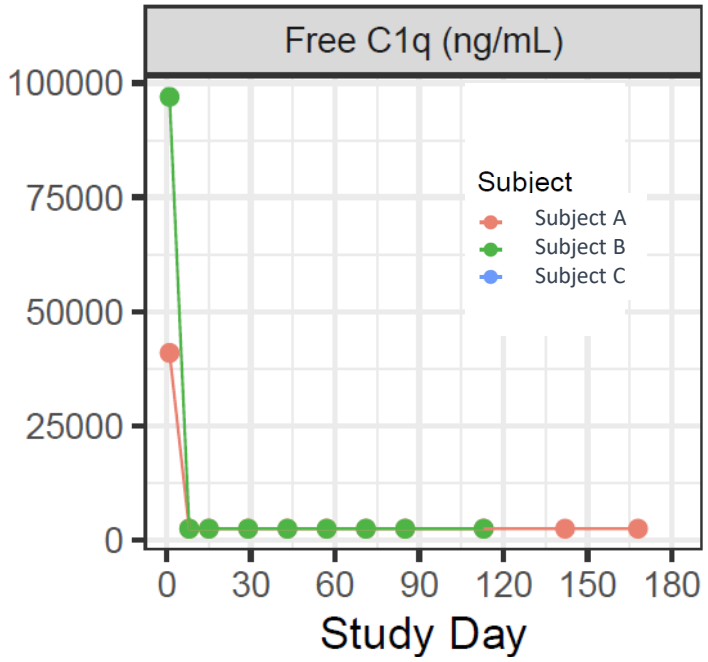
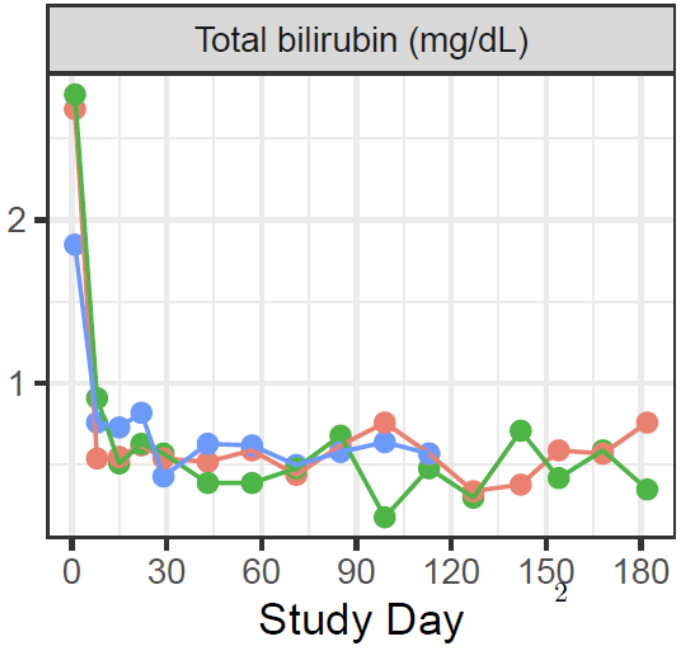
C4d Previously Validated as a Biomarker of C1 Inhibition with ANX005 in a Classical Complement Driven Disease

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

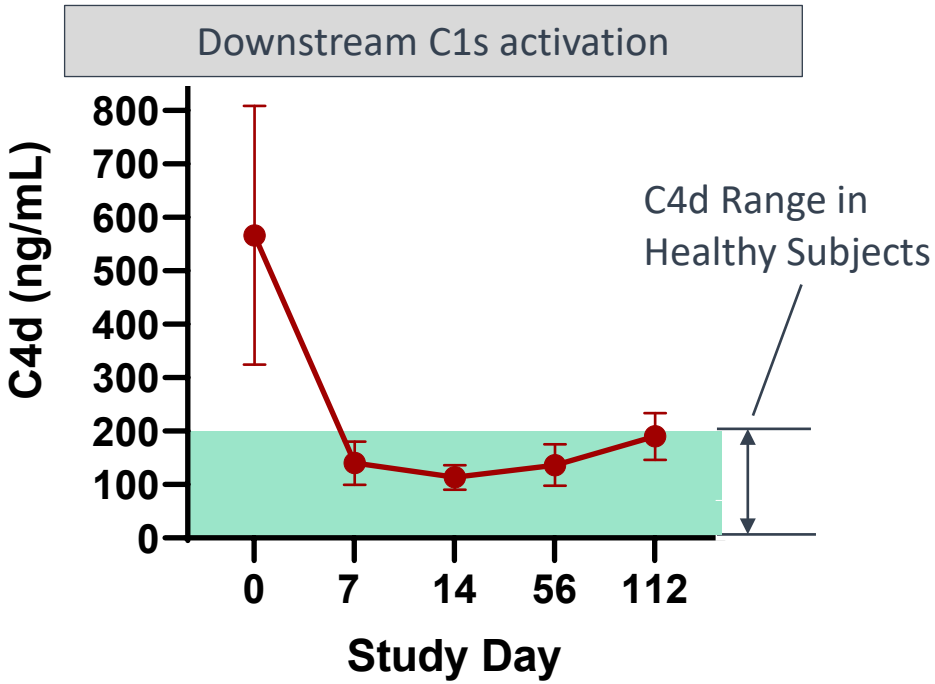
Blocked C1q



Reduced Disease Biomarker



Decreased C4d to Normal Range



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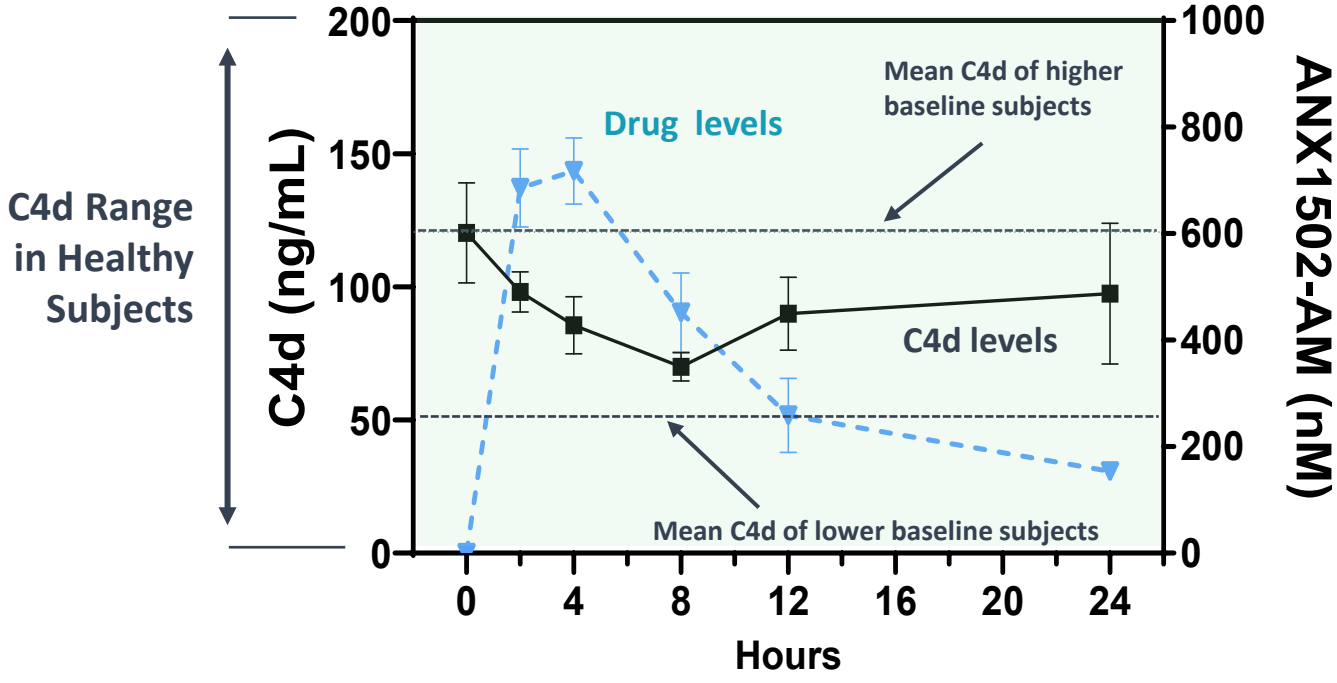
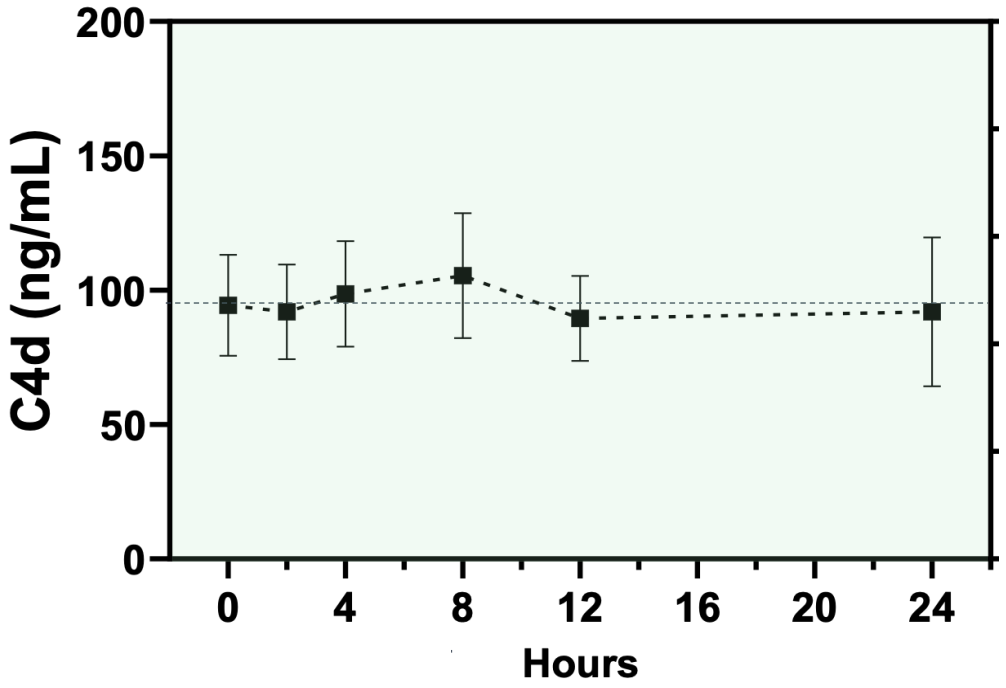
SAD PK/PD: ANX1502 (Single Doses of 525–1025 mg) Suppressed C4d Serum Levels in Healthy Volunteers w/ Higher than Median Baseline C4d

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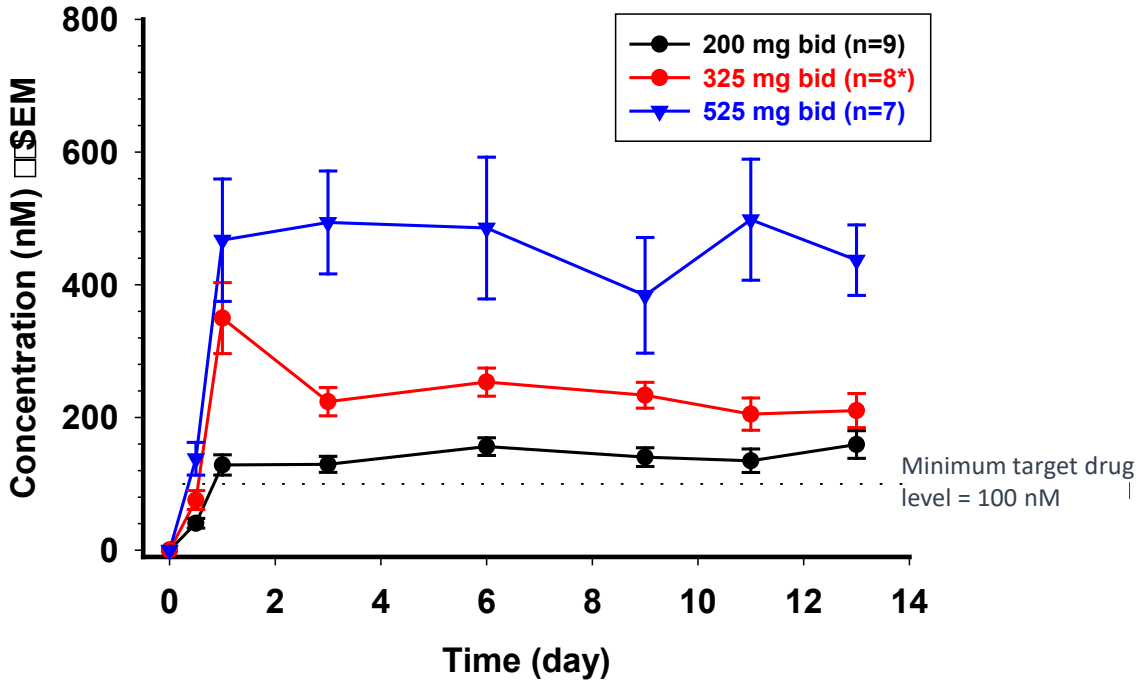
MAD Data: ANX1502 Dosing at 325 and 525mg BID Achieved Target Trough Exposures in 14-Day MAD Cohorts

- 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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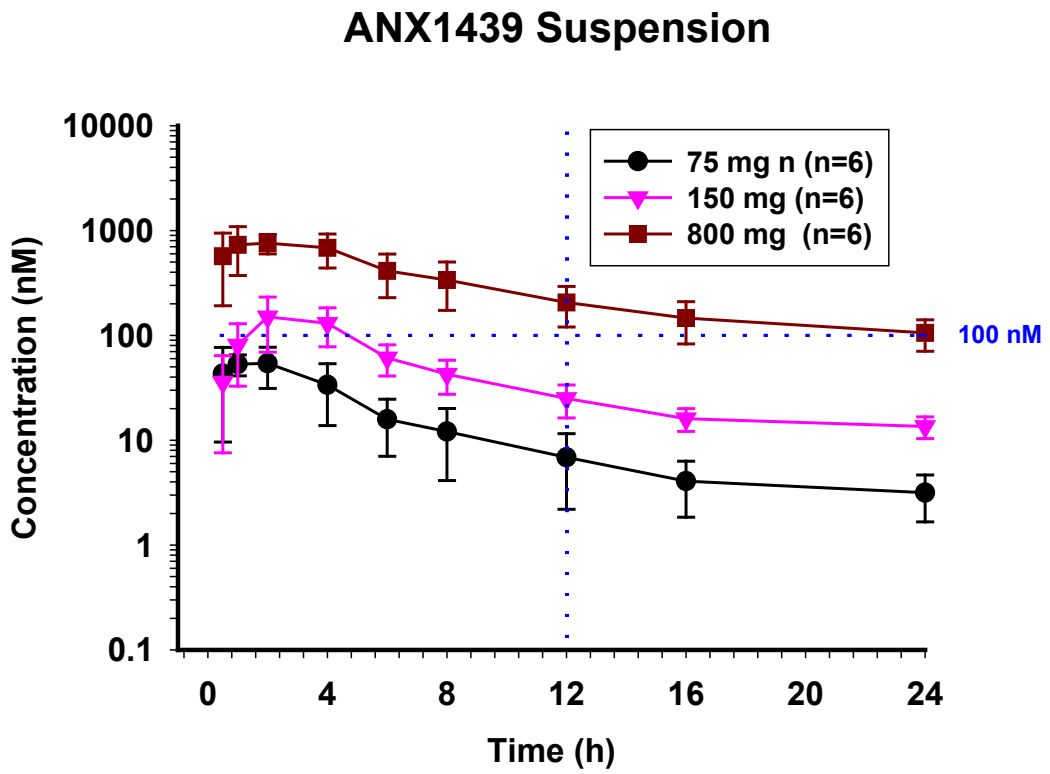
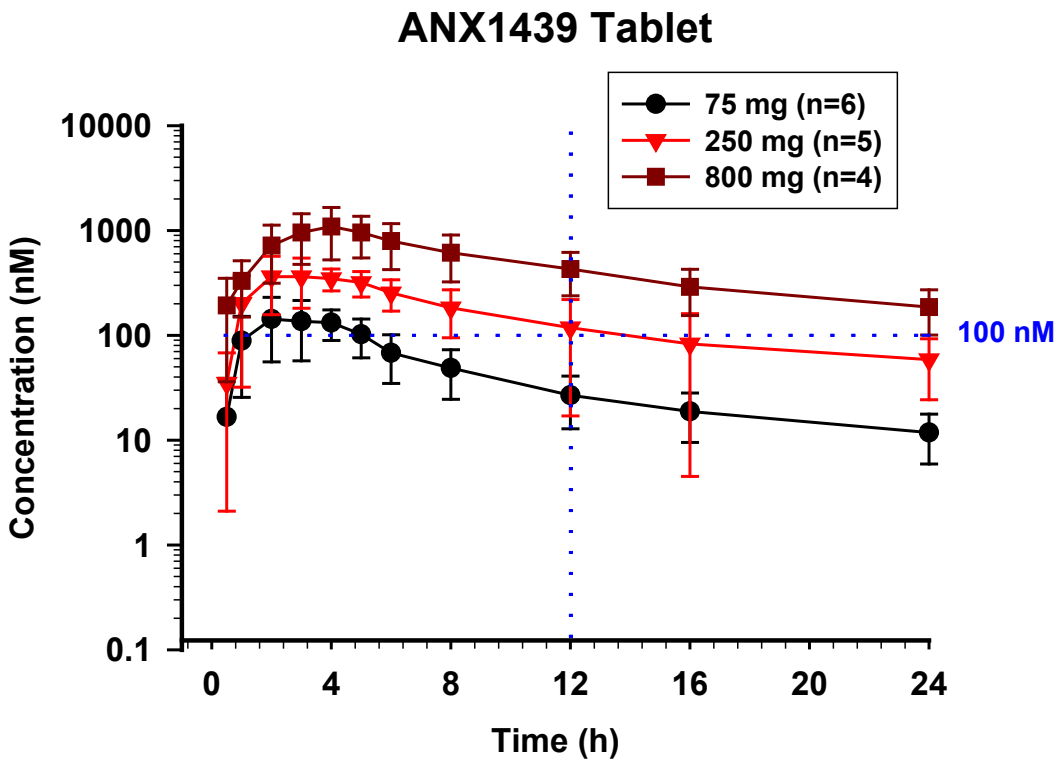
PK Comparable Between Suspension and Tablet

Observed results indicate ability to achieve target concentrations with BID dosing of tablet



Concentrations were BLQ post 36h for 75 mg dose and post 48h for 150mg and 800 mg



Concentrations were BLQ post 36h for 75 mg dose

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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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