Q1 2023 Investor Conference Call

May 8, 2023

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Agenda

Opening Remarks

Douglas Manion, Chief Executive Officer

Clinical Development Update and HS Trial

Gail Cawkwell, Chief Medical Officer

ATI-450 Pharmacodynamic Analysis

Joe Monahan, Chief Scientific Officer

Financial Results

Kevin Balthaser, Chief Financial Officer

Closing Remarks

Douglas Manion, Chief Executive Officer

Q&A Session

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Drug Development Pipeline

Drug Candidate/Program	Target	Route of Administration	Indication	Development Phase	Topline Data Expected
Immuno-Inflammatory					
Zunsemetinib (ATI-450)	MK2 inhibitor	Oral	Rheumatoid arthritis (moderate to severe)	Phase 2b	Q4 2023
			Psoriatic arthritis (moderate to severe)	Phase 2a	H1 2024
ATI-1777	"Soft" JAK 1/3 inhibitor	Topical	Atopic dermatitis (mild to severe)	Phase 2b	H2 2023
ATI-2138	ITK/JAK3 inhibitor	Oral	T cell-mediated autoimmune diseases	Phase 1 Multiple Ascending Dose	H2 2023
Gut-Biased Program	JAK inhibitor	Oral	Inflammatory bowel disease	Discovery	
Oncology					
ATI-2231	MK2 inhibitor	Oral	Metastatic breast cancer	Preclinical	
			Pancreatic cancer		

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ATI-1777 (Topical “Soft” JAK Inhibitor) (Investigational Drug Candidate)

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Aiming to Develop an Effective and Safe Therapy for Atopic Dermatitis

Atopic dermatitis (AD) is a chronic, pruritic inflammatory skin condition[1]

- The U.S. prevalence of AD is reported to be 11.3–12.7% in children and 6.9–7.6% in adults[2]
- Market projected to be $8-12 billion at peak (moderate to severe AD)[3]
- Systemic and topical JAK inhibition has demonstrated promising results in AD clinical trials[4]

Goal

- Comparable efficacy to other topical JAKs but a “soft” drug to minimize the potential for systemic toxicities
- JAK1/3 selective to minimize JAK2 mediated hematopoietic effects
- Patients with mild to severe AD
- Deliver in a patient-friendly formulation

ATI-1777 (investigational compound)

- First-in-human Phase 2a trial in subjects with moderate to severe AD completed
- Phase 2a - 4-week trial in subjects with moderate to severe AD completed with primary endpoint of % change from baseline in mEASI
- Phase 2b dose ranging study underway in mild-severe, including children down to 12 years

1. Medscape. Accessed January 7, 2023. https://emedicine.medscape.com/article/1049085-overview. 2. Silverberg J. Dermatol Clin. 2017;Jul;35(3):283-289; 3. Auster M, et al. Something Big Is Getting Bigger [research note]. Credit Suisse Equity Research; 2019; 4. Shreberk-Hassidim R, et al. J Am Acad Dermatol. 2017;Apr;76(4):745-753.

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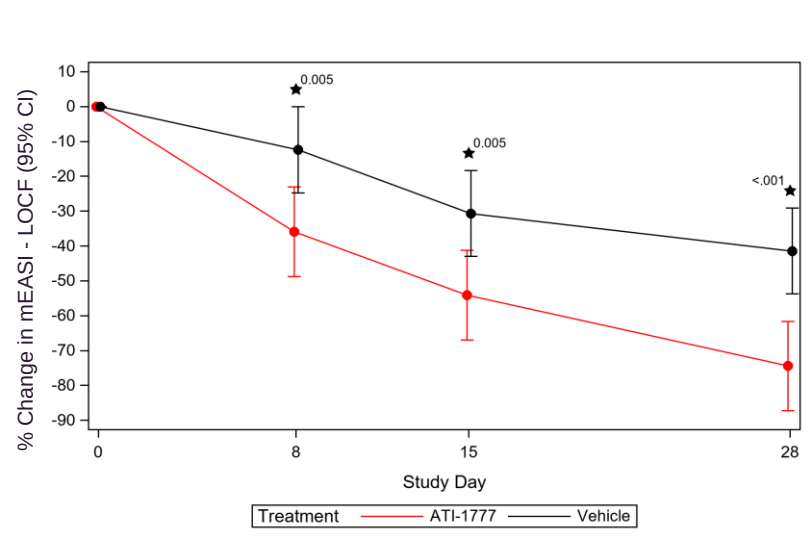
Positive Data Demonstrated in ATI-1777 Phase 2 Study in Atopic Dermatitis

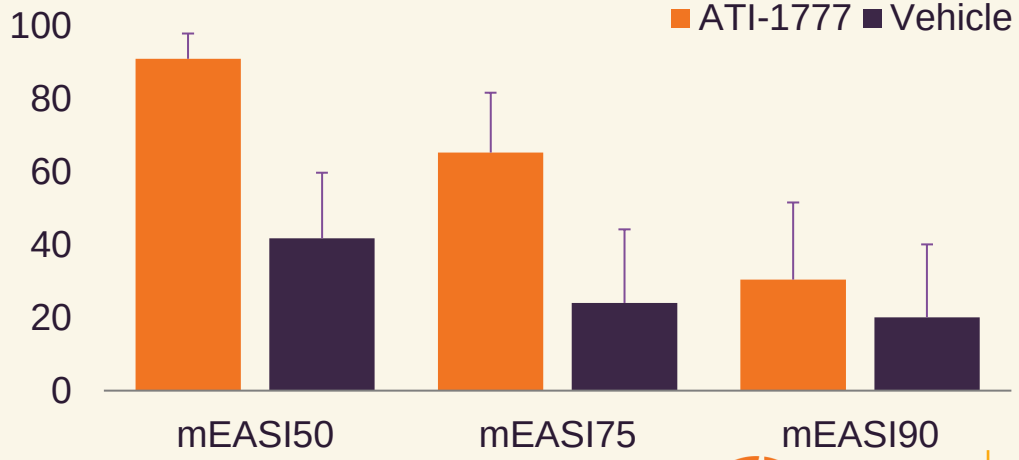
Phase 2a Trial Highlights

- ATI-1777 achieved statistically significant result in the primary efficacy endpoint at week 4
- Positive trends were observed in secondary endpoints including improvement of itch, percent of mEASI-50 responders, IGA responder analysis and reduction in BSA impacted by disease
- ATI-1777 was generally well tolerated

Primary Efficacy Endpoint: % Change in mEASI – LOCF (FAS)



Secondary Efficacy Endpoint: mEASI50/75/90 at Day 28 (FAS)



Note: (FAS): Full Analysis Set

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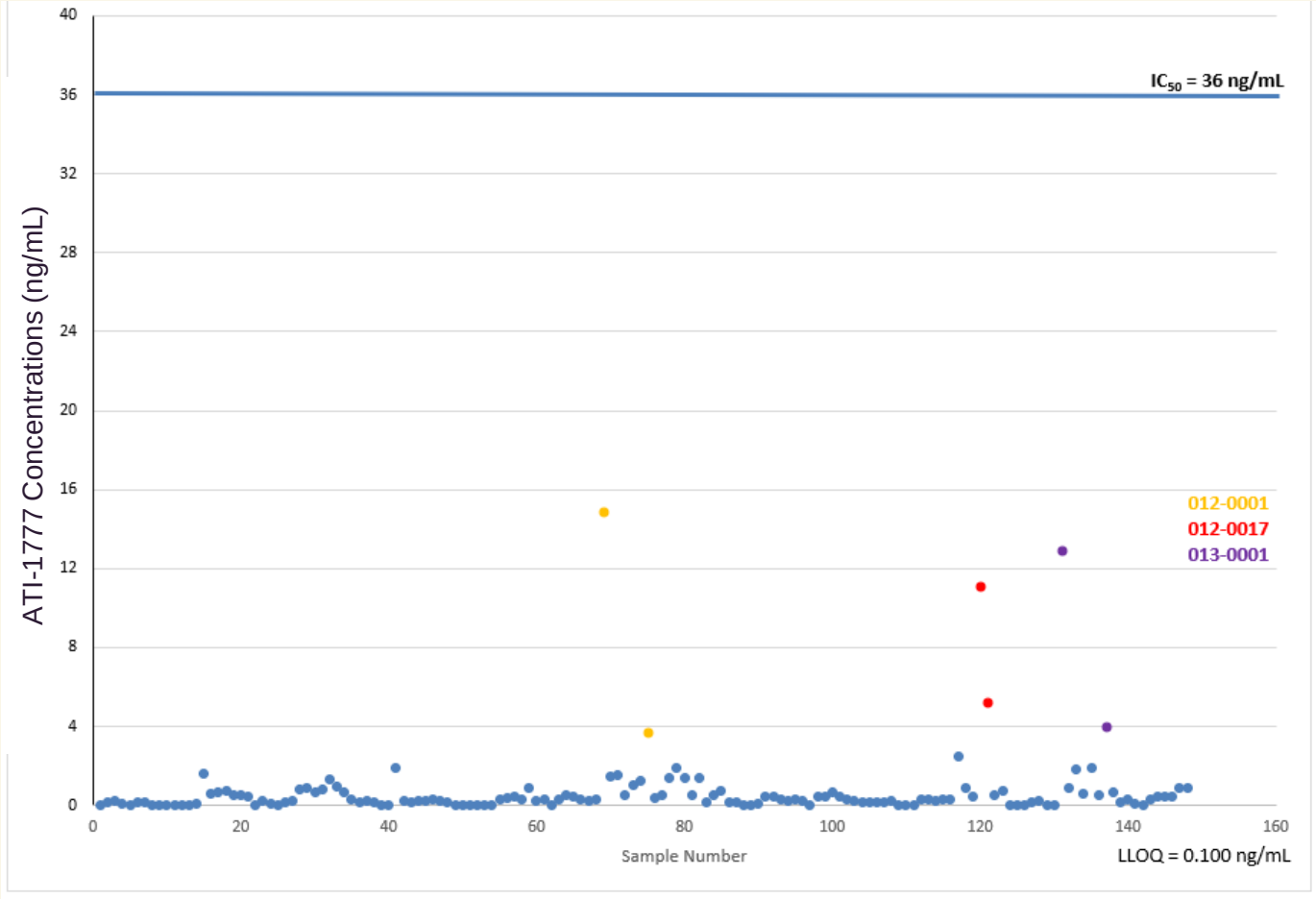
Low Plasma Levels of ATI-1777 Following Topical Application

PK Plasma Concentrations of ATI-1777 in Subjects



- >86% of samples tested following ATI-1777 administration exhibited blood levels below the detectable level
- Average concentration in subjects receiving ATI-1777 solution was never >5% the IC_{50}
- Only 3 subjects (6 out of 148 total samples) with concentrations > 1/10th the IC_{50}

Note: Data on file

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Phase 2a Study of Zunsemetinib in Hidradenitis Suppurativa

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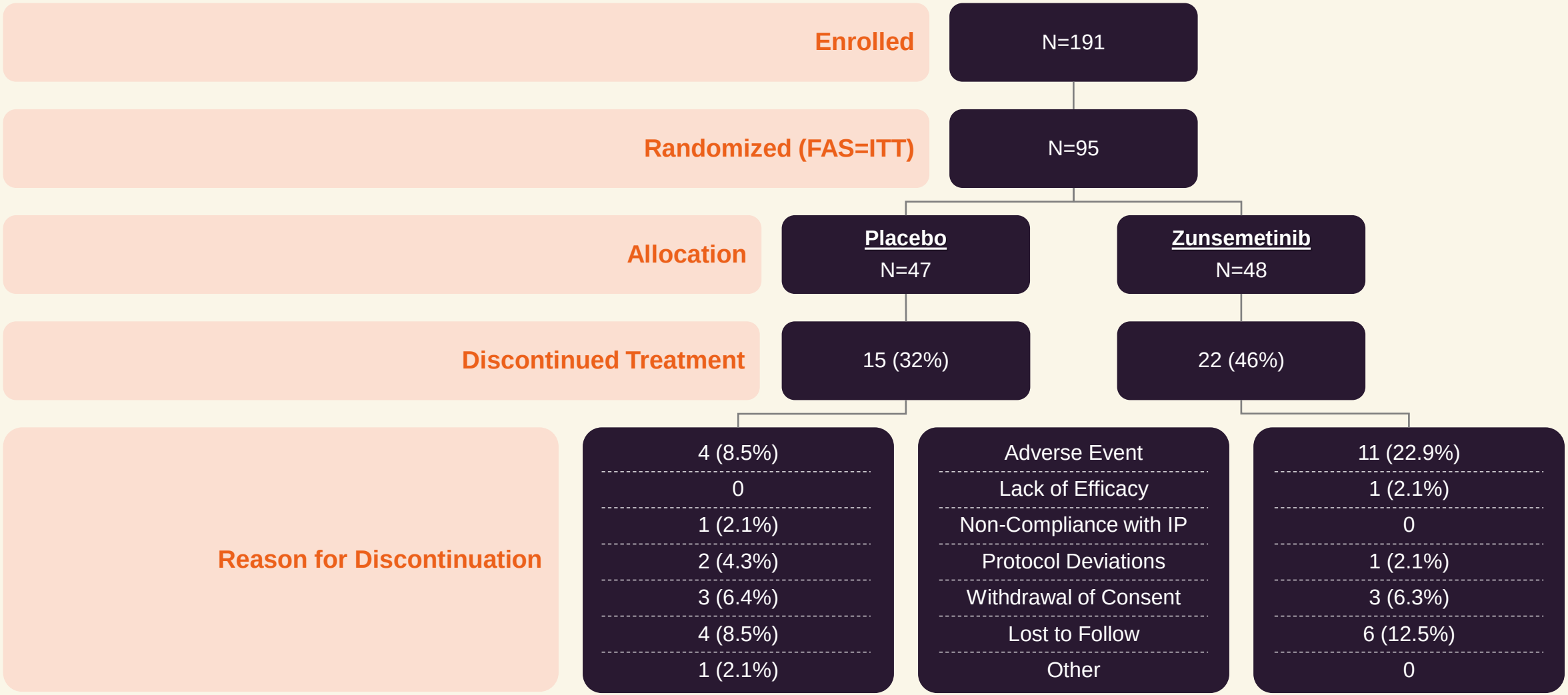
Subject Disposition and Discontinuations



Demographics and Baseline Characteristics

		Placebo (N=47)	Zunsemetinib (N=48)
Age in years	Mean (SD)	36.6 (9.32)	35.1 (9.87)
Female (at birth)		40 (85.1%)	39 (81.3%)
White – African American - Other		57.4 - 42.6 - 0%	58.3 - 37.5 - 4.2%
Duration of HS in years	Mean (SD)	13.5 (9.97)	11.3 (8.28)
Baseline Inflammatory Nodule/Abscess Count (AN)	Mean(SD)	11 (10.2)	11 (6.4)
Baseline AN Count	Min, Max	5, 67	4, 31
Baseline HS-Physician's Global Assessment	Mean (SD)	4 (0.9)	4 (0.8)
Baseline Patient's Global Assessment of Skin Pain	Mean (SD)	5 (2.3)	5 (2.8)
Baseline Hurley Stage	Mild – Mod – Severe	6.4 - 74.5 - 19.1 %	10.4 - 62.5 - 27.1%

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TEAEs in >1 Patient on Either Treatment Arm

The most common TEAEs on zunsemetinib were dizziness, headache, diarrhea and acne

Treatment-Emergent Adverse Event Preferred Term	Placebo (N=47)	Zunsemetinib (N=48)
Dizziness	0	8 (16.7%)
Headache	2 (4.3%)	6 (12.5%)
Diarrhea	4 (8.5%)	6 (12.5%)
Acne	0	5 (10.4%)
Blood CK increased	0	4 (8.3%)
Mouth ulceration	0	3 (6.3%)
Fatigue	0	3 (6.3%)
Nausea	3 (6.4%)	2 (4.2%)
Vomiting	1 (2.1%)	2 (4.2%)
Abdominal pain	0	2 (4.2%)
Upper respiratory tract infection	1 (2.1%)	2 (4.2%)
Tremor	0	2 (4.2%)
Nasopharyngitis	5 (10.6%)	1 (2.1%)

Most TEAEs were mild or moderate

Overall Infections were evenly balanced (13 patients on placebo, 12 on zunsemetinib within infection grouping) – none serious or opportunistic

Headache and dizziness were generally mild-moderate, occurred early and generally resolved with continued treatment

3 patients had possibly/probably related acne, confounded by known increased HS-acne comorbidity

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Discontinuations due to AEs

11 patients on zunsemetinib and 4 patients on placebo discontinued study treatment due to adverse events. Most of these:

- Were due to events that have been seen in other zunsemetinib clinical trials
- Occurred early in the course of the study
- Only one patient (on placebo) had serious adverse event of HS worsening

Discontinuations were generally individual events except:

- HS worsening, HS complications or HS co-morbidities led or were contributing TEAEs in 4 on zunsemetinib and 1 on placebo
- Diarrhea led to discontinuation in 2 on zunsemetinib and 1 on placebo

Of the 11 patients who discontinued on zunsemetinib due to TEAEs:

- AN count was no better or worse in most (7 of 11)
- Severity of TEAEs was mild-to-moderate in most (7 of 11)

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CK Elevations Were Common on Zunsemetinib and Placebo and all Were Without Muscle Symptoms

Maximum CK during the study at any point	ATI-450	Placebo
Grade 1 (>ULN - 2.5 x ULN)	7	5
Grade 2 (>2.5 x ULN - 5 x ULN)	3	0
Grade 3 (>5 x ULN - 10 x ULN)	2	1
Grade 4 (>10 x ULN)	1	0
CK increased before treatment (with reduction or no further increase during treatment)	2	5

- 26 patients had a CK elevation at some point during the study
  - 15 on zunsemetinib and 11 on placebo
- There were no adverse events of myalgia or weakness
- When fractionated, no evidence of cardiac involvement

- Many patients had CK elevations before treatment
- Randomly, more meaningful pre-treatment CK elevations observed in patients were on zunsemetinib

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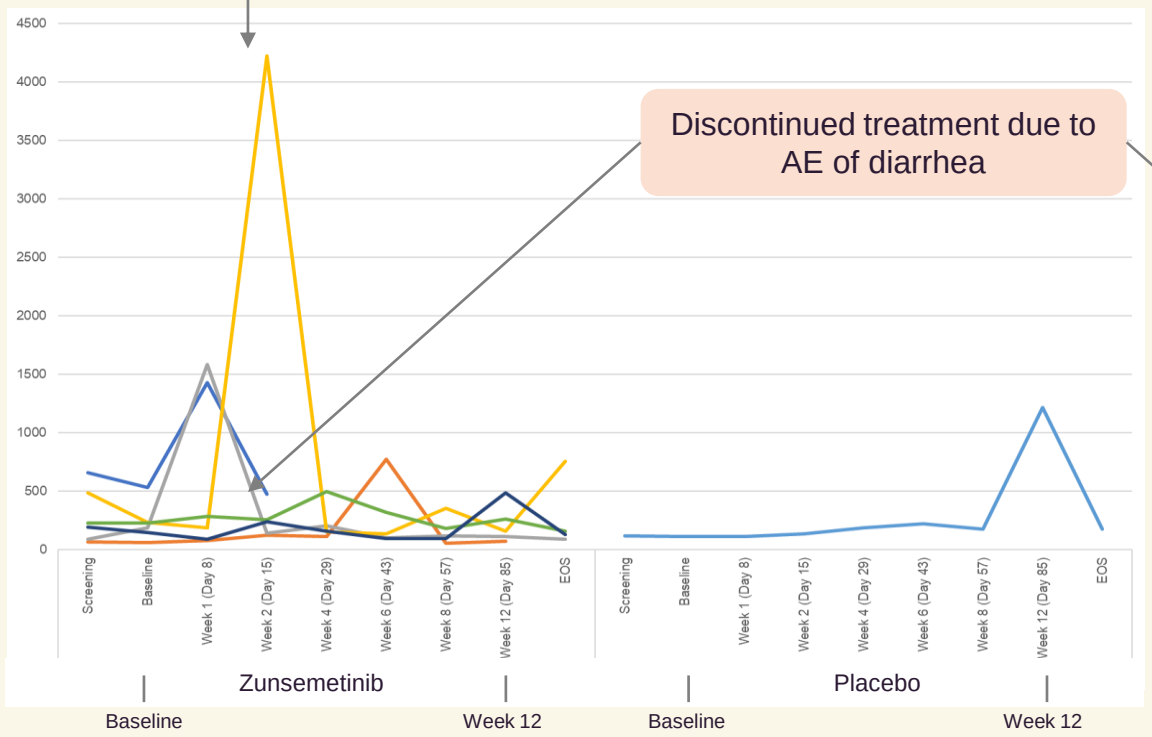
CK Elevations Generally Transient and Generally Resolved on Treatment

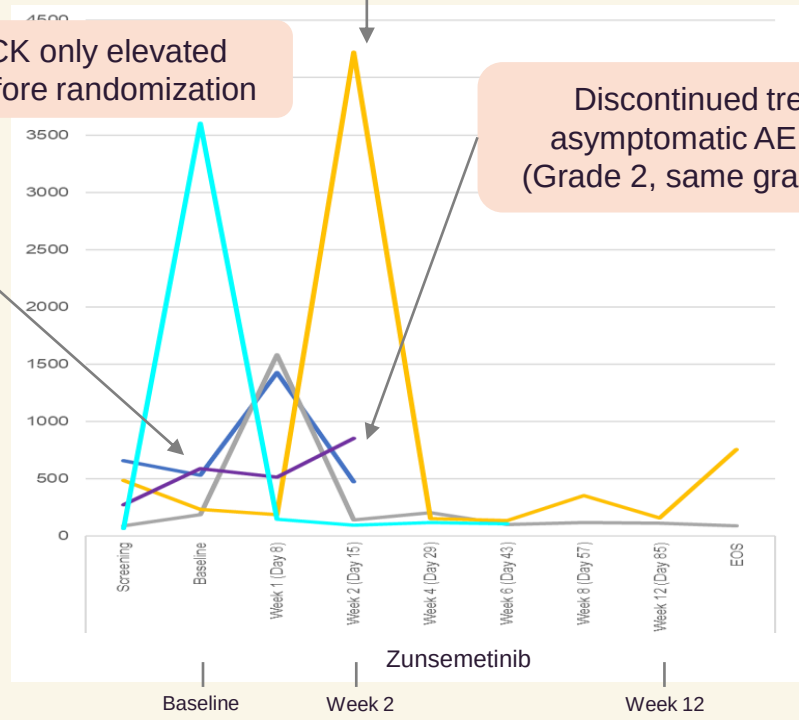
Subject noted intense exercise
CK increase assessed as unrelated to study treatment by the investigator



Discontinued treatment due to AE of diarrhea

CK only elevated before randomization

Discontinued treatment due to asymptomatic AE of CK elevation (Grade 2, same grade as at baseline)



Treatment Emergent CK Elevations ≥Grade 2

Were generally transient and generally returned to baseline while continuing study treatment

CK Elevations Reported as AEs

5 originally reported corrected to 4,
as 1 was baseline only (pre-treatment)
3 of 5 continued treatment with subsequent normalization of CK

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Zunsemetinib in HS: Safety Profile was Generally Consistent with Previous Zunsemetinib Studies, while Efficacy was Not Demonstrated

- ATI-450-HS-201 50 mg BID did not demonstrate efficacy in the Hidradenitis Suppurativa study
- PK and PD were generally consistent with prior zunsemetinib studies
- No increased risk of infections and no serious or opportunistic infections occurred
- Discontinuation due to TEAEs were higher in active than placebo (11 vs 4)
- Lack of improvement or worsening AN in 7 (64%) of those who discontinued zunsemetinib due to a TEAE
- Adverse event profile was as expected
- The most common TEAEs (>10% on zunsemetinib) were dizziness, headache, diarrhea and acne
- Asymptomatic CK elevations were seen and generally resolved with continued treatment

Addition of 47 patients randomized to zunsemetinib 50 mg for 12-week treatment period meaningfully increases the safety database, with no meaningfully different findings identified

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Zunsemetinib HS-201 Exploratory PD Efforts – Looking toward RA2b

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HS-201: Exploratory Pharmacodynamic Analysis

Analysis of Cytokines in Ex vivo Stimulated Patient Blood

- Assay - **Ex vivo** LPS stimulated cytokine production in whole blood
- Samples from both placebo and Zunsemetinib treated HS patients plus healthy donor controls
- Small sample set – 5 patients total
- Cytokines – TNFα, IL1β, IL6 & IL8

Analysis of HS Patient Endogenous Plasma Cytokines

- Assay – Measurement of endogenous cytokines,chemokines and markers of inflammation in plasma from zunsemetinib or placebo treated HS patients
- All 95 patients in the study plus healthy donor controls
- Patient sample set = Days 1, 29, 57 & 85. Fifty-seven complete/thirty-eight partial sets.
- Analytes measured – IFNγ, IL-1α, IL-1β, IL-6, IL-8, IL-10, TNFα, IL-12/IL23p40, IL-1RA, IL-17A/F, IP10, MIP1β, SAA, CRP

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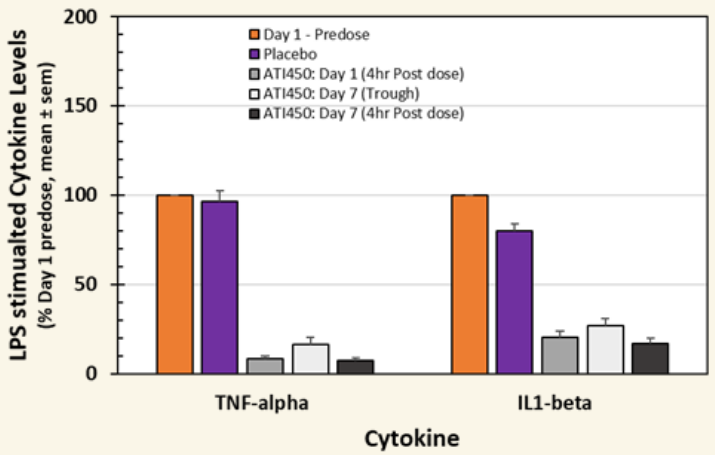
MK2 Pathway Cytokine Dependence and Response Durability

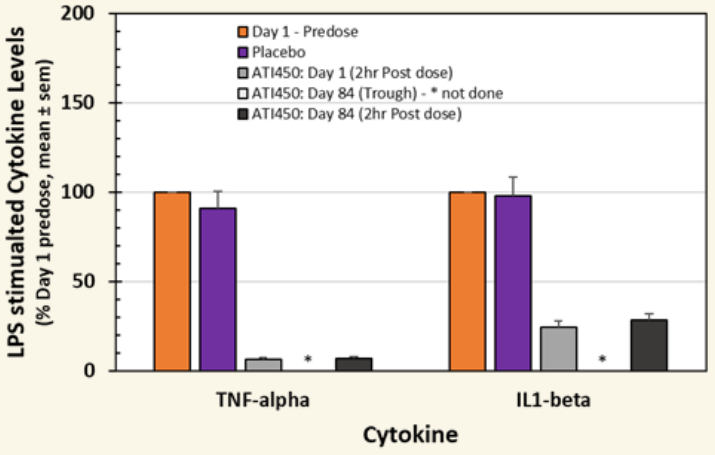
Ex vivo LPS-Stimulated Blood Analyses Across Zunsemetinib Studies

Phase 1 | **Phase 2a**

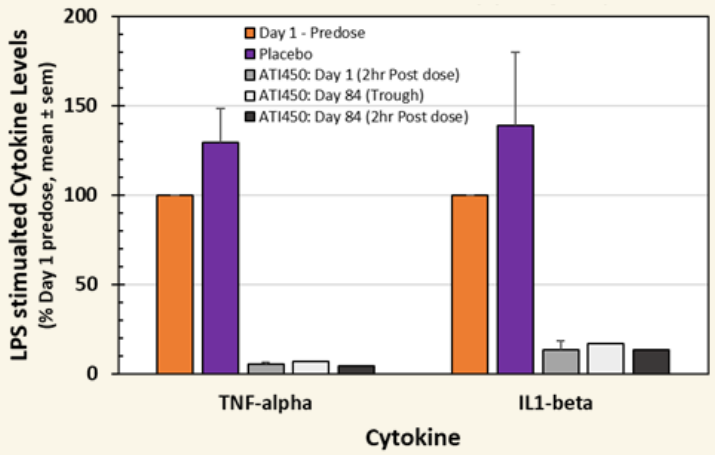
Phase 1 : MAD



Phase 2a : RA



Phase 2a : HS[1]



- Zunsemetinib potently inhibited TNFα and IL1β on day 1 suggesting that proinflammatory cytokine production in healthy subjects, RA and HS patients is dependent on the MK2 pathway
- Zunsemetinib potently inhibited TNFα and IL-1β following prolonged dosing (MAD: 7 days BID; RA 2a: 84 days BID; HS 2a: 84 days BID) consistent with lack of pathway reprogramming and tachyphylaxis in all studies

1. Subset of patients

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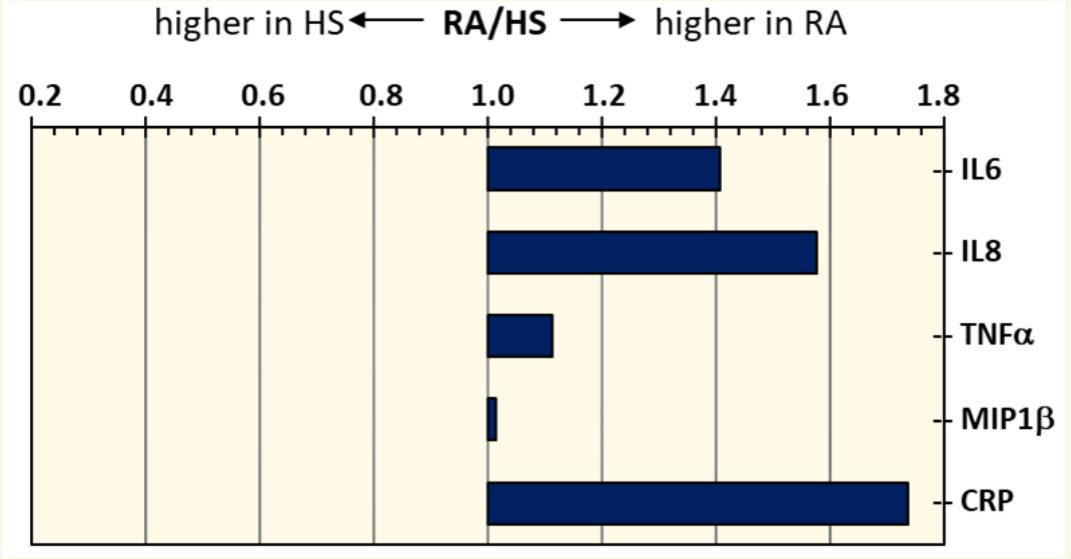
Lower Endogenous Plasma Cytokines Observed in HS vs in RA Phase 2a Studies

Median Cytokine Levels Pre-Dose

Cytokine	HS Patient Day 1 Levels		RA Patient Day 1 Levels	
	median (pg/ml)	Q1 ; Q3 (pg/ml)	median (pg/ml)	Q1 ; Q3 (pg/ml)
IL6	1.72	0.9; 2.79	2.42	1.27 ; 4.22
IL8	6.01	3.91 ; 9.77	9.47	6.39 ; 15.5
TNFa	1.06	0.79 ; 1.36	1.18	0.79 ; 1.44
MIP1b	54.67	41 ; 72.19	55.50	44.9 ; 78.61
CRP*	7.84	4.26 ; 14.01	13.60	6.23 ; 22.5

*CRP = mg/L

Ratio of RA/HS Cytokine Levels



Endogenous proinflammatory cytokines and CRP were lower in the HS phase 2a study compared with the RA phase 2a study consistent with a lower level of systemic inflammation

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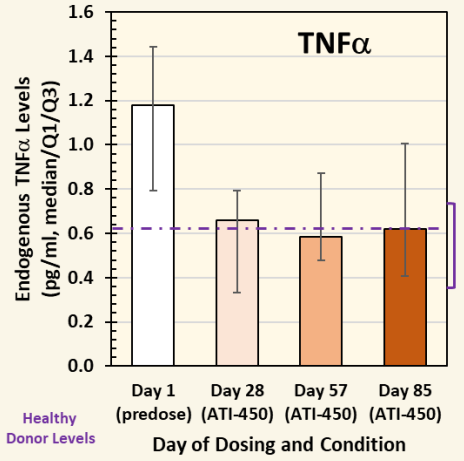
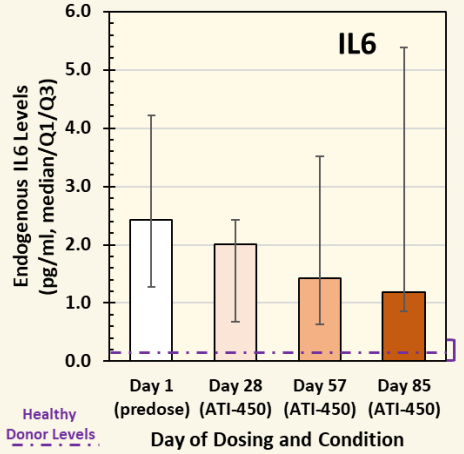
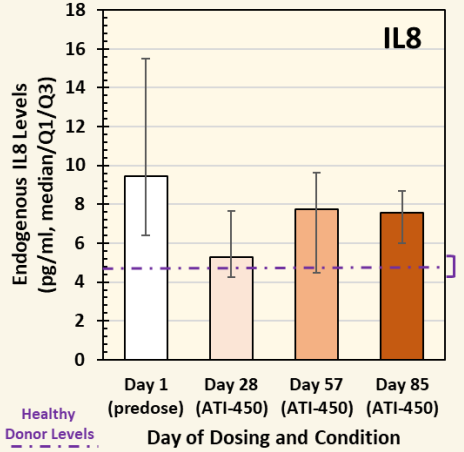
Zunsemetinib Modulation of Endogenous Cytokines

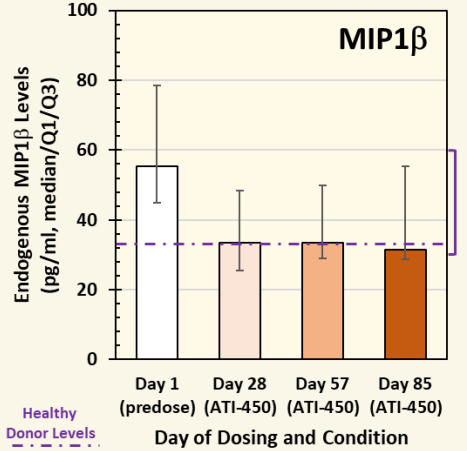
Comparison of RA and HS Phase 2a Studies

RA Study

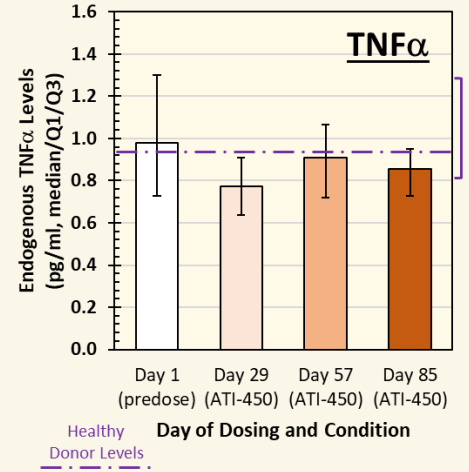


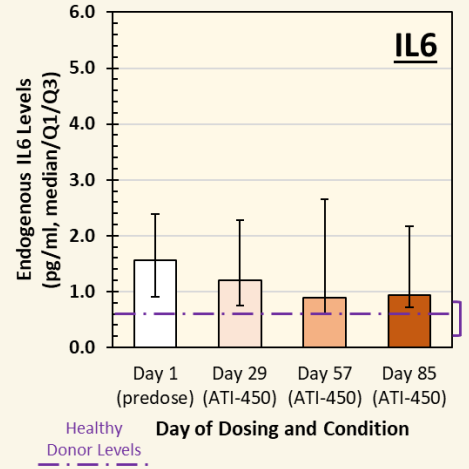


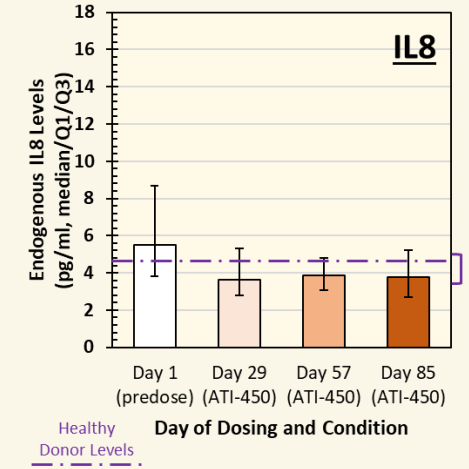


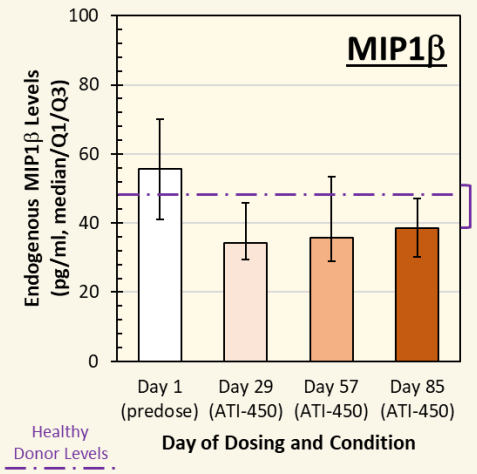


HS Study









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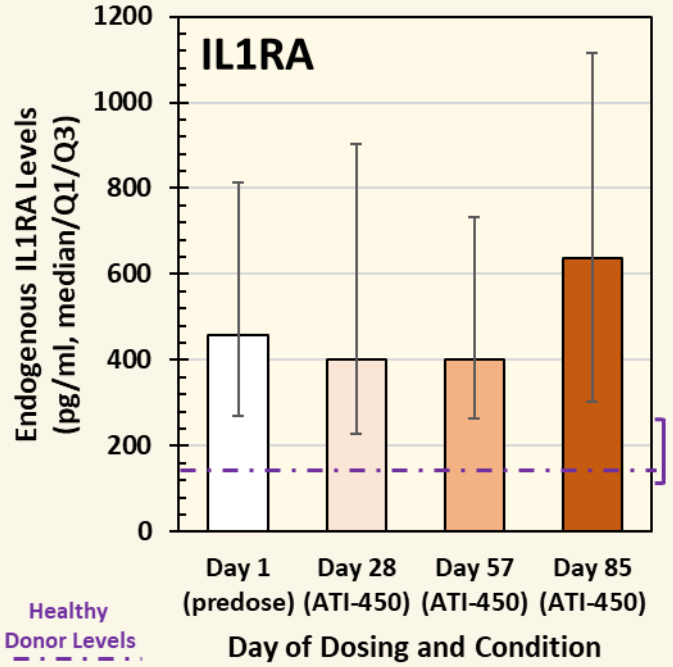
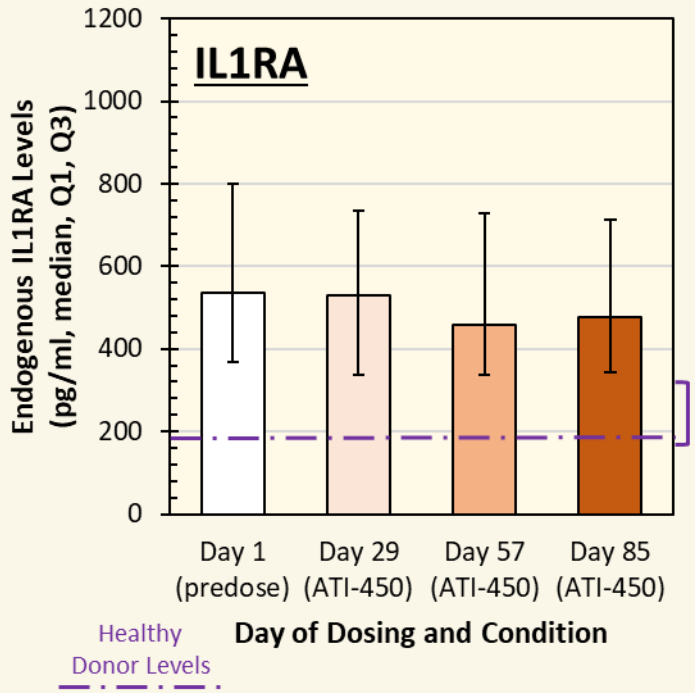
Zunsemetinib Did Not Inhibit the Anti-Inflammatory IL-1 Receptor Antagonist (IL-1RA) Cytokine in either HS or RA Phase 2a Studies

RA Phase 2a Study



HS Phase 2a Study



The anti-inflammatory cytokine IL-1RA was elevated in both HS and RA patients and was not inhibited by zunsemetinib in contrast to the proinflammatory cytokines

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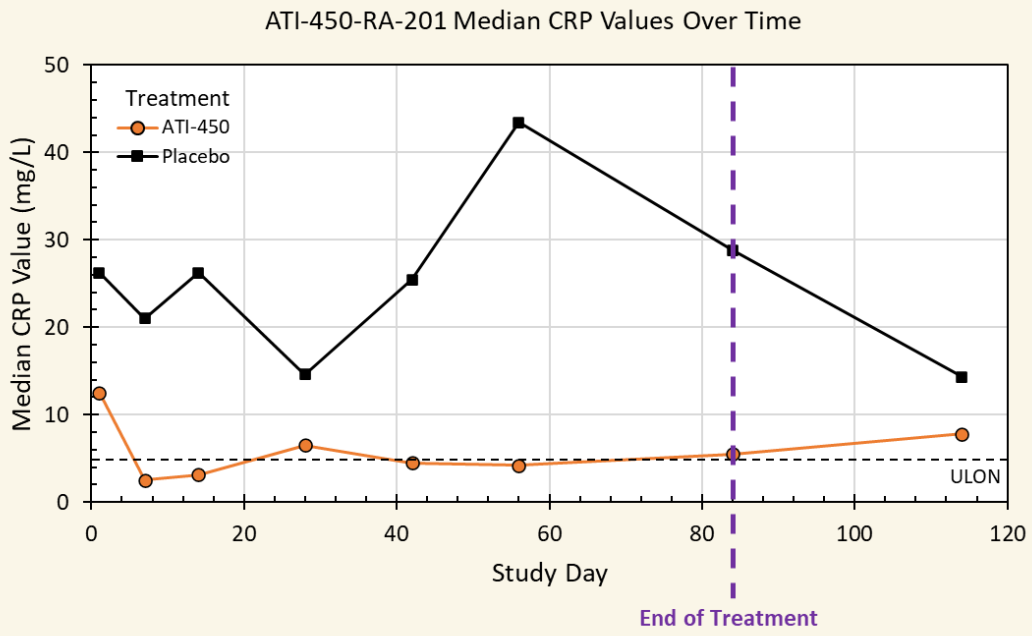
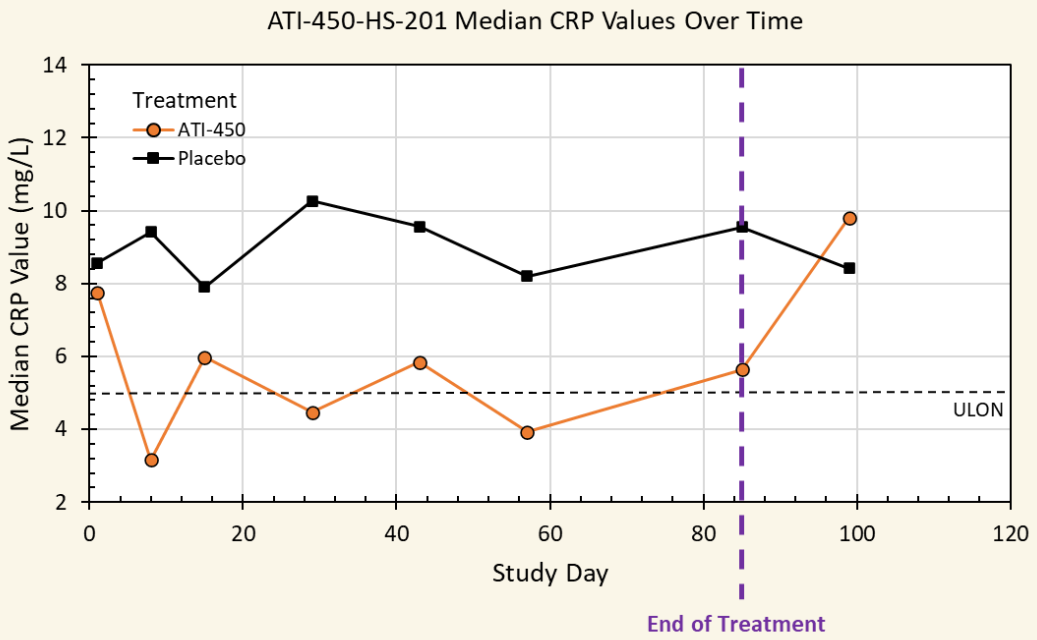
Zunsemetinib Treatment Resulted in a Sustained Inhibition of CRP in both RA-201 and HS-201 Studies

RA Phase 2a Study



HS Phase 2a Study



Sustained inhibition of plasma CRP in HS patients was observed with zunsemetinib treatment similar to that observed in the RA-201 Phase 2a study

Summary and Conclusions

- **Ex vivo stimulated cytokine inhibition in whole blood**
  - Consistent results across three studies demonstrate marked and sustained inhibition of proinflammatory cytokines and no evidence of tachyphylaxis
- **Endogenous pharmacodynamic plasma biomarker analysis**
  - A subset of cytokines elevated in HS blood relative to healthy donor but to a lesser extent than observed in the RA-201 study
  - Zunsemetinib inhibition trends with proinflammatory cytokines were similar in both the HS and RA phase 2a studies
  - The elevated anti-inflammatory cytokine (IL1RA) was not modulated by zunsemetinib in either the HS or RA phase 2a studies
  - Acute phase systemic inflammation markers CRP and IL-6 were inhibited by zunsemetinib in both the HS and RA phase 2a studies
- **RA and HS phase 2a pharmacodynamic analyses demonstrate persistent systemic anti-inflammatory activity for zunsemetinib**

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Q1 2023 Financial Results Highlights

Q1 2023 total revenue of $2.5M, up 74% YoY

- Licensing revenue increased driven primarily by higher royalties from licensed IP

Q1 2023 net loss of $28.2M, up 50% YoY

- Research and development expense increased by $8.3M, driven by
  - Zunsemetinib clinical trials in RA
  - ATI-1777 in AD
  - ATI-2138 multiple ascending dose study
  - Personnel and stock-based compensation
- General and administrative expense increased by $2.7M, driven by
  - Personnel and stock-based compensation

Financial Strength – Cash runway through the end of 2025

- March 31, 2023 cash, cash equivalents and marketable securities balance of $204M
- Issued placement notice to sell 3.4M shares under at-the-market facility during the first quarter
  - Aggregate net proceeds of $26.7M
  - Transaction closed in April and therefore is not included in the March 31, 2023 cash balance

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Q&A Session