Immunic Therapeutics

IMU-856: Phase 1 SAD/MAD Data in Healthy Human Subjects

NASDAQ: IMUX | September 20, 2022

Cautionary Note Regarding Forward-Looking Statements

This presentation contains “forward-looking statements” that involve substantial risks and uncertainties for purposes of the safe harbor 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. These include statements regarding management’s intentions, plans, beliefs, expectations or forecasts for the future, and, therefore, you are cautioned not to place undue reliance on them. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Immunic undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise, except to the extent required by law. We use words such as “anticipates,” “believes,” “plans,” “expects,” “projects,” “future,” “intends,” “may,” “will,” “should,” “could,” “estimates,” “predicts,” “potential,” “continue,” “guidance,” and similar expressions to identify these forward-looking statements that are intended to be covered by the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995.

Such forward-looking statements are based on our expectations and involve risks and uncertainties; consequently, actual results may differ materially from those expressed or implied in the statements due to a number of factors, including, but not limited to, risks relating to strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives of management. Risks and uncertainties that may cause actual results to differ materially from those expressed or implied in any forward-looking statement include, but are not limited to: Immunic’s plans to develop and commercialize its product candidates, including IMU-838, IMU-935 and IMU-856; the timing of initiation of Immunic’s planned clinical trials; the potential for IMU-856 and the Company’s other product candidates to safely and effectively target and treat the diseases mentioned herein; the impact of future preclinical and clinical data on IMU-856 and the Company’s other product candidates; the availability or efficacy of Immunic’s potential treatment options that may be supported by trial data discussed herein; expectations regarding potential market size; the timing of the availability of data from Immunic’s clinical trials; the timing of any planned investigational new drug application or new drug application; Immunic’s plans to research, develop and commercialize its current and future product candidates; Immunic’s ability to successfully collaborate with existing collaborators or enter into new collaboration agreements, and to fulfill its obligations under any such collaboration agreements; the clinical utility, potential benefits and market acceptance of Immunic’s product candidates; Immunic’s commercialization, marketing and manufacturing capabilities and strategy; Immunic’s ability to identify additional products or product candidates with significant commercial potential; developments and projections relating to Immunic’s competitors and industry; the impact of government laws and regulations; COVID-19 and the armed conflict in Ukraine; Immunic’s ability to protect its intellectual property position; Immunic’s listing on The Nasdaq Global Select Market; expectations regarding the capitalization, resources and ownership structure of the company; the executive and board structure of the company; Immunic’s estimates regarding future revenue, expenses, capital requirements and need for additional financing; the nature, strategy and focus of the company; and the other risks set forth in the company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the Securities and Exchange Commission.

Forward-looking statements included in this presentation are based on information available to Immunic as of the date of this presentation. Immunic does not undertake any obligation to update such forward-looking statements except as required by applicable law.

Advanced Clinical Pipeline

Three Differentiated Programs in Various Phases of Clinical Development

Program	Target	Preclinical	Phase 1	Phase 2	Phase 3	Key Milestones
Vidofludimus Calcium (IMU-838)	DHODH	Relapsing Multiple Sclerosis (RMS) – ENSURE Trials				▪ RMS interim analysis planned after approx. half of the events occurred ▪ PMS interim analysis planned after half of the patients completed 24 weeks of treatment
		Progressive Multiple Sclerosis (PMS) – CALLIPER Trial				
		Primary Sclerosing Cholangitis (PSC)				
IMU-935	IL-17 / RORγt	Psoriasis				▪ Q4/2022: initial phase 1b psoriasis data expected
		Castration-Resistant Prostate Cancer (CRPC)				
IMU-856	Intestinal Barrier Function	Celiac Disease				▪ 2023: initial phase 1b celiac disease data expected

■ Completed or ongoing ■ In preparation or planned

Immunic THERAPEUTICS

IMU-856: Phase 1 SAD/MAD Data in Healthy Human Subjects

01 Phase 1 Clinical Trial of IMU-856

- Trial Design and Study Population
- Results Part A: Single Ascending Doses
- Results Part B: Multiple Ascending Doses
- Ongoing Part C in Patients with Celiac Disease

02 Summary and Outlook

03 Extended Information Section

Immunic THERAPEUTICS

01

Phase 1 Clinical Trial of IMU-856

Trial Design and Status

Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

Ongoing Part C in Patients with Celiac Disease

01

Phase 1 Clinical Trial of IMU-856

Trial Design and Status

Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

Ongoing Part C Patients with Celiac Disease

Phase 1 Clinical Trial: Trial Design and Current Status

PART A ✓

Evaluation of
single ascending doses (SAD)

—

Healthy human subjects
randomized to receive single
dose of IMU-856 or placebo

- Planned dose escalation completed:
  10, 20, 40, 80, 120 and 160 mg of IMU-856
- 45 subjects enrolled (IMU-856: n=33)
- IMU-856 was well-tolerated and showed dose-linear pharmacokinetics

PART B ✓

Evaluation of
multiple ascending doses (MAD)

—

Healthy human subjects
randomized to receive 14-day
treatment of IMU-856 or placebo

- Planned dose escalation completed:
  40, 80 and 160 mg QD of IMU-856
- 26 subjects enrolled (IMU-856: n= 19)
- IMU-856 was well-tolerated and steady-state trough levels were achieved within first week of dosing

PART C

Evaluation of
patients with celiac disease
receiving 28-day
treatment of
IMU-856 or placebo

- Dosing: 80 and 160 mg QD of IMU-856
- Approximately 42 patients are planned to be enrolled
- Currently ongoing and actively recruiting

QD: quaque die = once-daily;

01

Phase 1 Clinical Trial of IMU-856

Trial Design and Status

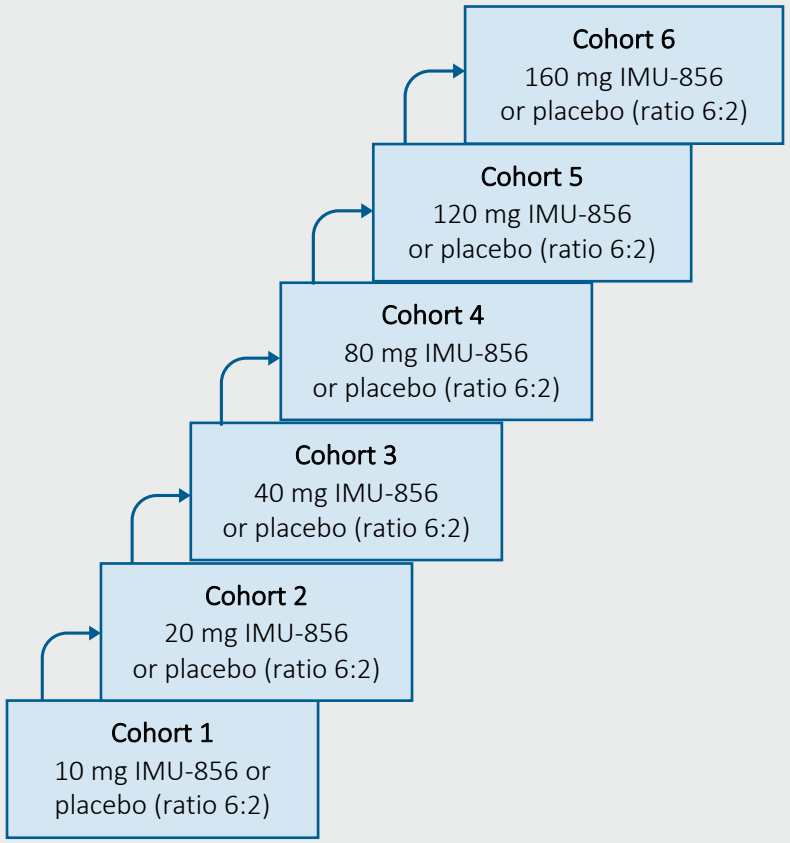
Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

Ongoing Part C in Patients with Celiac Disease

Dose Escalation Algorithm

Part A, Cohorts 1-6: Single Ascending Doses



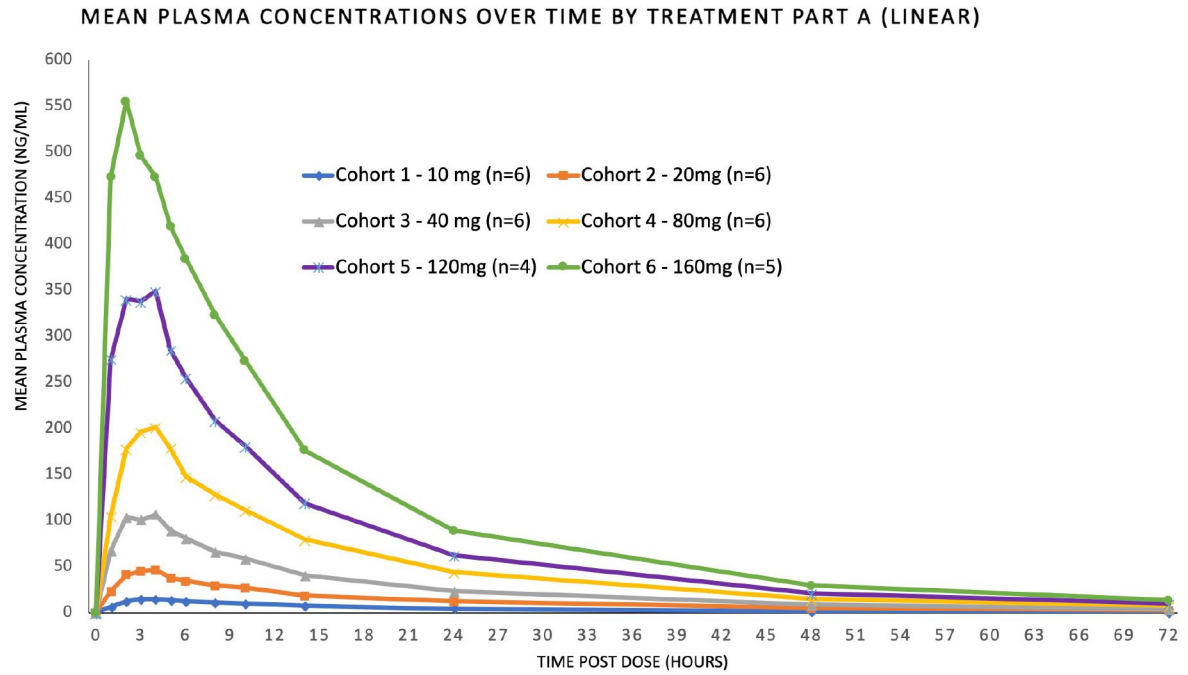
- Single oral tablet administration was performed.
- Dosing in each cohort started with two sentinel participants: one randomized to IMU-856 and one randomized to placebo.
- Remaining cohort participants were dosed after 4 days when no safety concern had arisen.
- Study completed the planned dose escalation up to highest dose of 160 mg.

Immunic THERAPEUTICS

Dose-Linear Pharmacokinetics in Single Oral Dosing

Part A, Cohorts 1-6

- Rapid absorption after oral tablet administration with peak plasma concentration reached within 2 to 4 hours
- Terminal plasma half-life of 16 to 20 hours well suited for once-daily dosing
- Dose-proportional increase in plasma C_{max} and AUC



	Median (range)	Mean (%CV)		
	T_{max} (hr)	C_{max} (ng/mL)	$T_{1/2}$ (hr)	AUC_{inf} (hr*ng/mL
Cohort 1 IMU-856 10mg (N=6)	3.00 (3.00-4.00)	16.0 (41)	18.99 (17)	320 (35)
Cohort 2 IMU-856 20mg (N=6)	3.00 (2.00-4.00)	49.0 (30)	19.45 (17)	907 (27)
Cohort 3 IMU-856 40mg (N=6)	4.00 (2.00-4.00)	116 (23)	17.93 (6)	1930 (12)
Cohort 4 IMU-856 80mg (N=6)	4.00 (2.00-5.00)	210 (29)	16.17 (9)	3590 (21)
Cohort 5 IMU-856 120mg (N=4)	3.00 (2.00-4.00)	409 (16)	16.89 (14)	5680 (19)
Cohort 6 IMU-856 160mg (N=5)	2.00 (2.00-5.00)	576 (36)	16.54 (13)	8360 (23)

CV: Coefficient of Variation; Tmax = time to maximum plasma concentration; Cmax = maximum plasma concentration; T1/2 = terminal elimination half-life; AUC= Area under the plasma concentration versus time curve; AUCinf = Area under the plasma concentration versus time curve from zero to infinity

Immunic THERAPEUTICS

Single Doses of IMU-856 in Healthy Human Subjects Found to Have a Favorable Safety and Tolerability Profile

Part A, Cohorts 1-6

- No serious adverse events
- No dose-dependency in adverse events
- No maximum tolerated dose reached
- No trends for post-dose changes in any laboratory parameter
- No related adverse events in the active treatment group regarding any laboratory parameter
- No medically relevant changes in vital signs, physical examination or 12-lead electrocardiograms as compared to placebo

Conclusions

Part A: Single Ascending Doses

- Single ascending oral doses of IMU-856 provided favorable pharmaceutical properties in Part A of this phase 1 clinical trial.
- The favorable safety and tolerability profile allowed a smooth transition from Part A (SAD) to Part B (MAD) in healthy human subjects.

01

Phase 1 Clinical Trial of IMU-856

Trial Design and Status

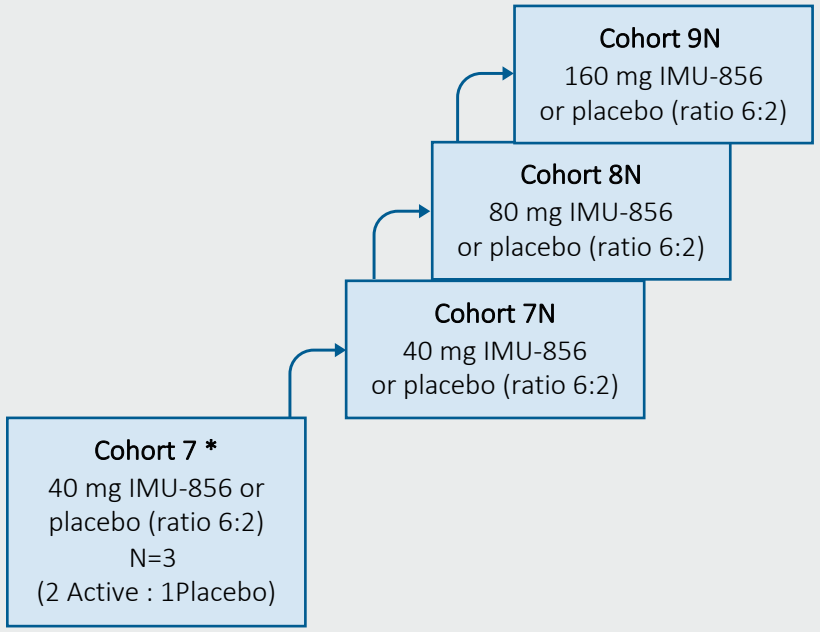
Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

Ongoing Part C in Patients with Celiac Disease

Dose Escalation Algorithm

Part B, Cohorts 7, 7N-9N: Multiple Ascending Doses



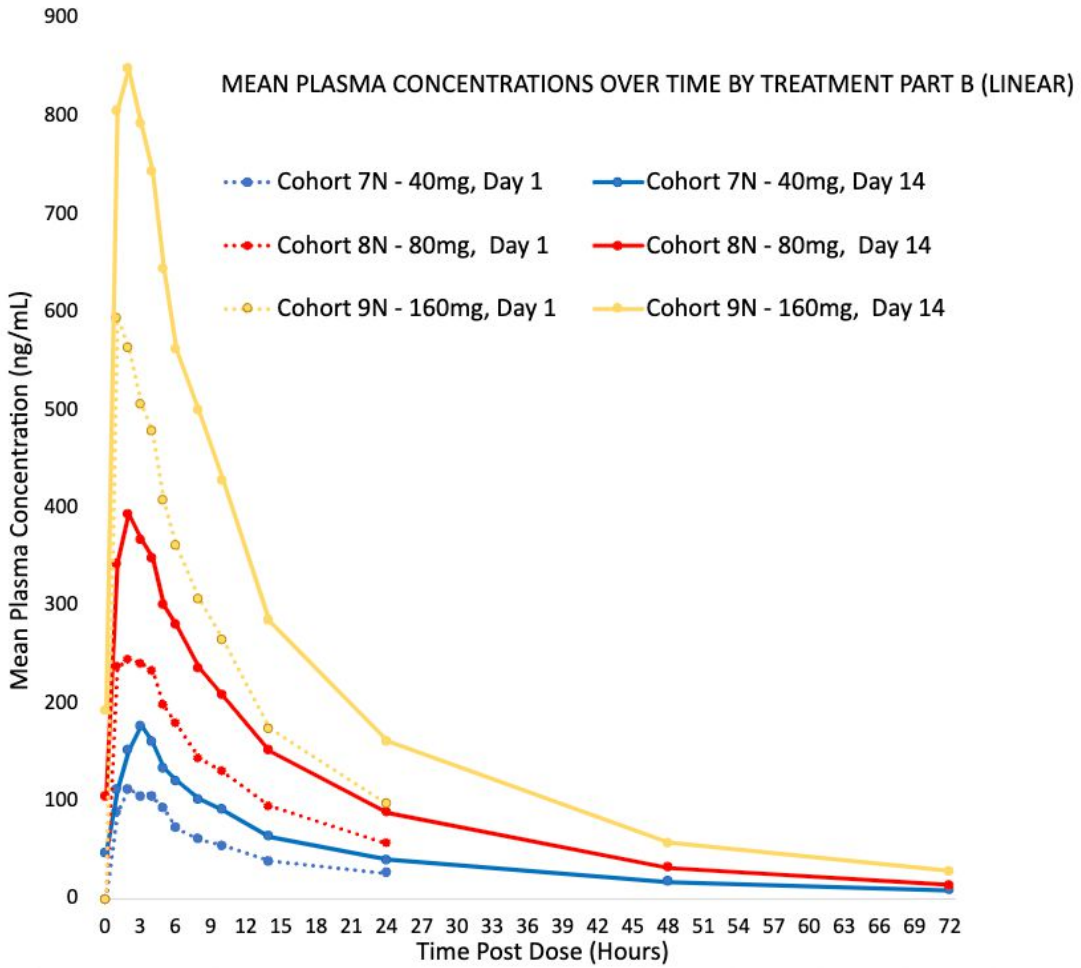
- Single daily oral tablet administration was performed over 14 days.
- Dosing in each cohort started with two sentinel participants: one randomized to IMU-856 and one randomized to placebo.
- Remaining cohort participants were dosed after one week when no safety concern had arisen.
- Study completed the planned dose escalation up to highest dose of 160 mg.

*The manufacturing process for IMU-856 tablets was optimized following Cohort 7. For any following cohorts, tablets manufactured with an optimized manufacturing process were used, however, there were no substantial changes in the tablet formulation.

Immunic THERAPEUTICS

Dose-Linear Pharmacokinetics in Multiple Dosing (Day 1 and 14)

Part B, Cohort 7N-9N



- Terminal plasma half-life at steady state (Day 14 values) 17 to 21 hours comparable to single dose
- Linear pharmacokinetics also after multiple dosing with dose-proportional increase in plasma C_{max} and AUC
- Accumulation factor of ~ 1.5 allowing predictable trough levels and drug exposure after once-daily oral administration

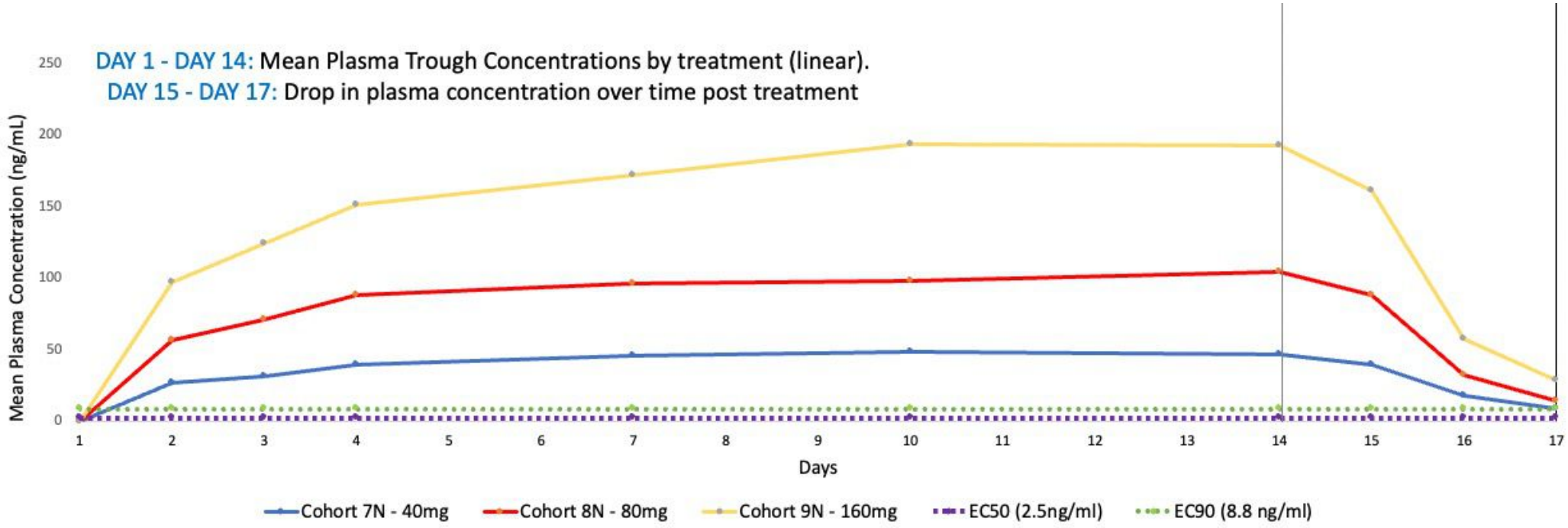
Value (mean)	Day 1			Day 14, steady state		
	Cohort 7N 40 mg	Cohort 8N 80 mg	Cohort 9N 160 mg	Cohort 7N 40 mg	Cohort 8N 80 mg	Cohort 9N 160 mg
C_{max} (ng/mL)	131	269	653	184	400	913
T_{max} (h)	2.40	2.20	1.83	3.00	2.65	2.17
$T_{1/2}$ (h)	10.8	10.5	8.9	21.5	17.7	17.4
$AUC_{0\text{-}tau}$ (h*ng/mL)	1300	3048	6190	2067	4829	9853

Cmax: maximum plasma drug concentration; h: hours; Tmax: time to reach maximum plasma concentration; T1/2 (h): terminal elimination half-life; AUC0-tau: area under the drug concentration-time curve from time zero to 24 hours

Immunic THERAPEUTICS

Pharmacokinetic Results (Trough Levels After Multiple Dosing)

Part B, Cohort 7N-9N



Favorable pharmacokinetic properties for IMU-856	▪ Fast achievement of steady-state after 4-7 days of dosing ▪ Fast drop in plasma concentration following end of treatment according to terminal plasma half-life ▪ Mean plasma trough concentrations in steady state substantially above EC_{50} and EC_{90} of target inhibition (cellular assay, readout: enzymatic function in cellular test system)

C_{max}: maximum plasma drug concentration; Accumulation factors were calculated as the relationship of $AUC_{0\text{-}tau}$ of Day 14/Day 1 (after first dosing). EC50: half-maximal effective concentration. EC90: 90% maximal effective concentration

Immunic THERAPEUTICS

Overall Summary of TEAE, SAE and AE Severity

Part B, Cohorts 7, 7N-9N

Category	Treatment					
	Cohort 7* 40 mg (N=2)	Cohort 7N 40 mg (N=5)	Cohort 8N 80 mg (N=6)	Cohort 9N 160 mg (N=6)	Active (N=19)	Placebo (N=7)
Subjects with TEAEs, n (%)	2 (100%)	4 (80%)	5 (83%)	4 (67%)	15 (79%)	5 (71%)
Subjects with mild TEAEs, n (%)	1 (50%)	3 (60%)	3 (50%)	2 (33%)	9 (47%)	4 (57%)
Subjects with moderate TEAEs, n (%)	1 (50%)	1 (20%)	1 (17%)	2 (33%)	5 (26%)	1 (14%)
Subjects with severe TEAEs, n (%)	-	-	1 (17%)	-	1 (5%)	-
Subjects with study drug related severe TEAEs, n (%)	-	-	-	-	-	-
Subjects with SAE , n (%)	-	-	1 (17%)	-	1 (5%)	-
Subjects with TEAEs leading to withdrawal, n (%)	-	-	1 (17%)	-	1 (5%)	-
Number of TEAEs	13	16	25	12	66	18
Number of mild TEAEs	12	15	21	9	57	17
Number of moderate TEAEs	1	1	3	3	8	1
Number of severe TEAEs	-	-	1	-	1	-
Number of study drug related severe TEAEs	-	-	-	-	-	-
Number of SAEs	-	-	1	-	1	-
Number of TEAEs leading to withdrawal	-	-	1	-	1	-

Once-daily 14-day dosing of IMU-856 was found to be safe and well-tolerated:

- No dose-dependency in adverse events
- No IMP-related SAEs

TEAE: Treatment-Emergent Adverse Event; SAE: Serious Adverse Event; AE: Adverse Event; IMP: Investigational Medicinal Product.
*The manufacturing process for IMU-856 tablets was optimized following Cohort 7. For any following cohorts, tablets manufactured with an optimized manufacturing process were used, however, there were no substantial changes in the tablet formulation.

Most Common Treatment-Emergent Adverse Events
Part B, Cohorts 7, 7N-9N

MedDRA Preferred Term	Number (%) of subjects with TEAEs occurring in more than 2 subjects [Number of TEAEs reported]					
	Cohort 7* 40 mg (N=2)	Cohort 7N 40 mg (N=5)	Cohort 8N 80 mg (N=6)	Cohort 9N 160 mg (N=6)	Active (N=19)	Placebo (N=7)
Catheter site pain	-	2 (40%) [2]	-	1 (17%) [1]	3 (16%) [3]	3 (43%) [3]
Headache	-	-	2 (33%) [2]	2 (33%) [2]	4 (21%) [4]	2 (29%) [2]
Diarrhea	1 (50%) [1]	1 (20%) [2]	2 (33%) [2]	1 (17%) [1]	5 (26%) [6]	-
Abdominal pain	1 (50%) [1]	1 (20%) [1]	1 (17%) [2]	-	3 (16%) [4]	1 (14%) [1]

Once-daily oral doses of IMU-856 were safe and well-tolerated with catheter site pain and headache being the most common TEAEs.

TEAE: Treatment-Emergent Adverse Event
*The manufacturing process for IMU-856 tablets was optimized following Cohort 7. For any following cohorts, tablets manufactured with an optimized manufacturing process were used, however, there were no substantial changes in the tablet formulation.

Most Common IMP-related Treatment-Emergent Adverse Events

Part B, Cohorts 7, 7N-9N

MedDRA Preferred Term	Number (%) of subjects with IMP-related TEAEs occurring in 2 and more subjects [Number of TEAEs reported]					
	Cohort 7* 40 mg (N=2)	Cohort 7N 40 mg (N=5)	Cohort 8N 80 mg (N=6)	Cohort 9N 160 mg (N=6)	Active (N=19)	Placebo (N=7)
Diarrhea	1 (50%) [1]	1 (20%) [2]	2 (33%) [2]	1 (17%) [1]	5 (26%) [6]	-
Abdominal pain	1 (50%) [1]	1 (20%) [1]	1 (17%) [1]	-	3 (16%) [3]	1 (14%) [1]
Headache	-	-	1 (17%) [1]	1 (17%) [1]	2 (11%) [2]	1 (14%) [1]
Decreased appetite	-	1 (20%) [1]	1 (17%) [1]	-	2 (11%) [2]	-
Dry mouth	1 (50%) [1]	-	-	1 (17%) [1]	2 (11%) [2]	-
Constipation	-	-	1 (17%) [1]	-	1 (5%) [1]	1 (14%) [1]

Diarrhea and abdominal pain are the most common IMP-related TEAEs, both mild in severity.

TEAE: Treatment-Emergent Adverse Event; IMP: Investigational Medicinal Product

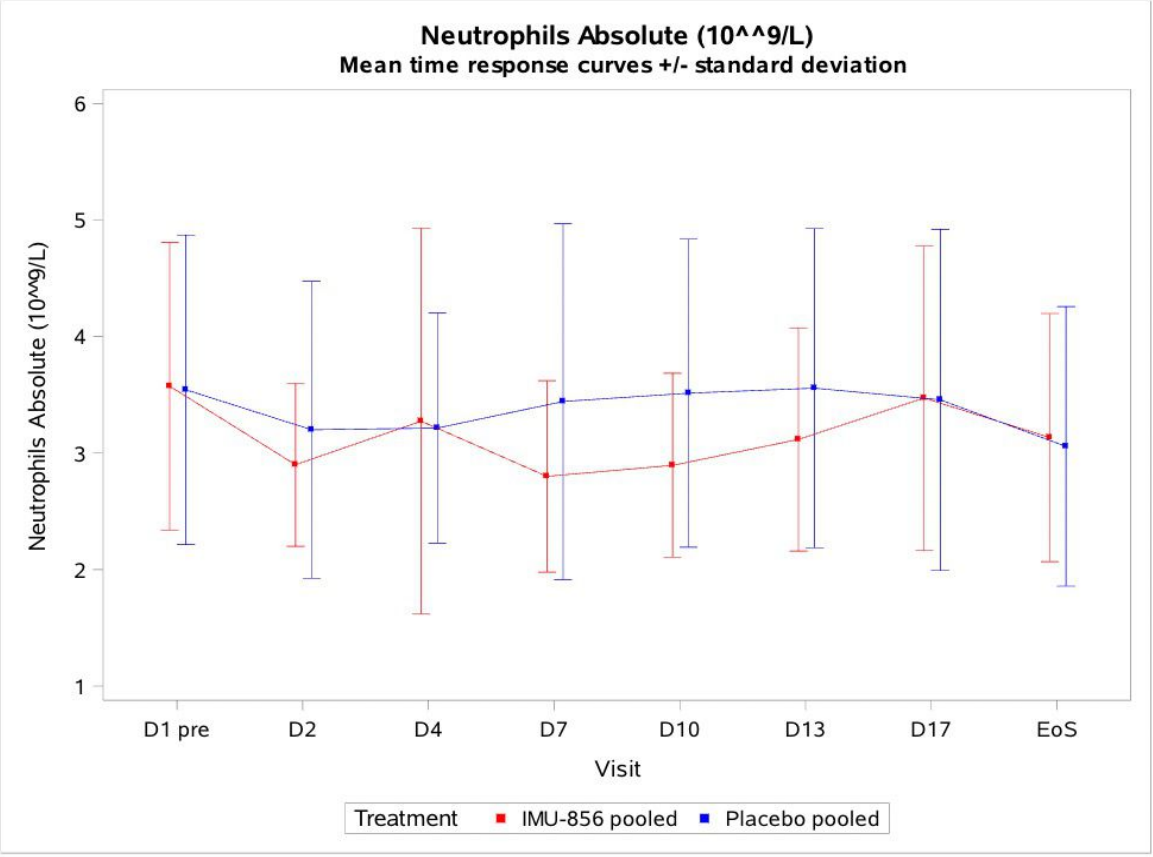
*The manufacturing process for IMU-856 tablets was optimized following Cohort 7. For any following cohorts, tablets manufactured with an optimized manufacturing process were used, however, there were no substantial changes in the tablet formulation. .

Immunic THERAPEUTICS

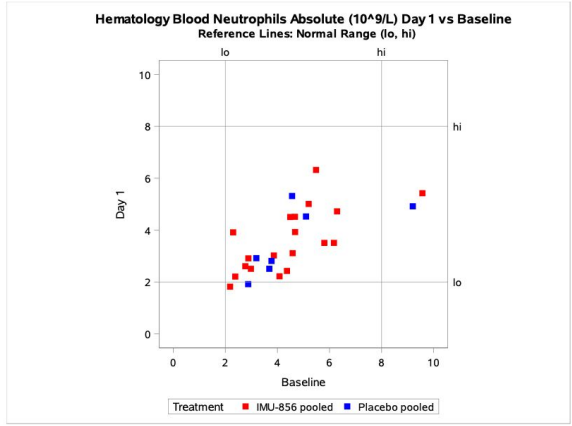
Laboratory Parameters: No Change in Neutrophils Compared to Placebo

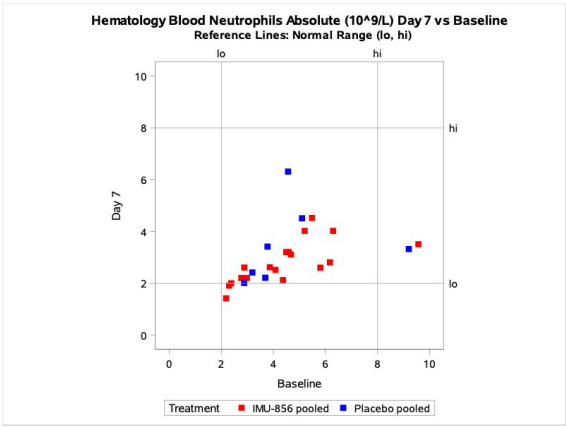
Part B, Cohorts 7, 7N-9N

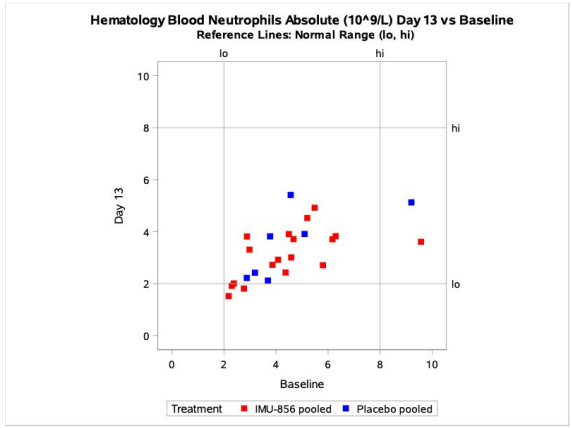
Laboratory Values Over Time
Hematology - Neutrophils

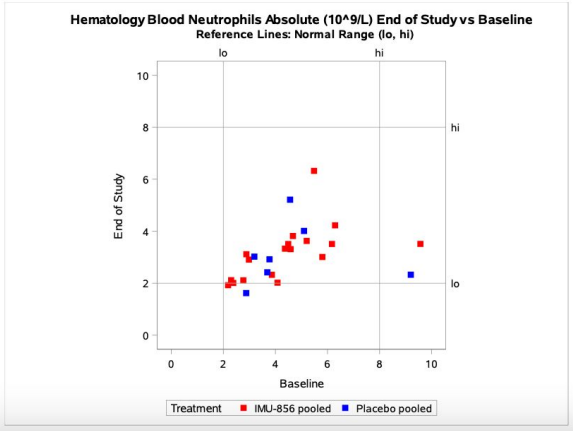


Individual Laboratory Values
Hematology - Neutrophils







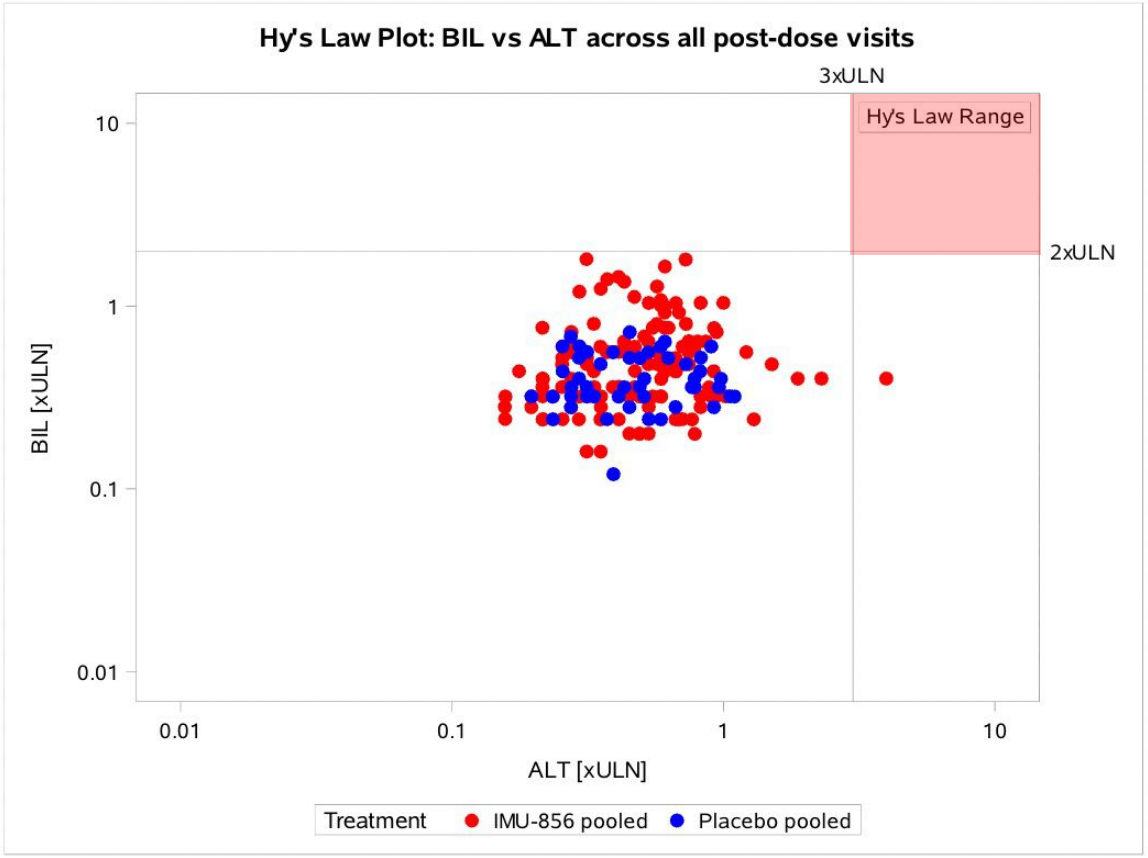


Immunic THERAPEUTICS

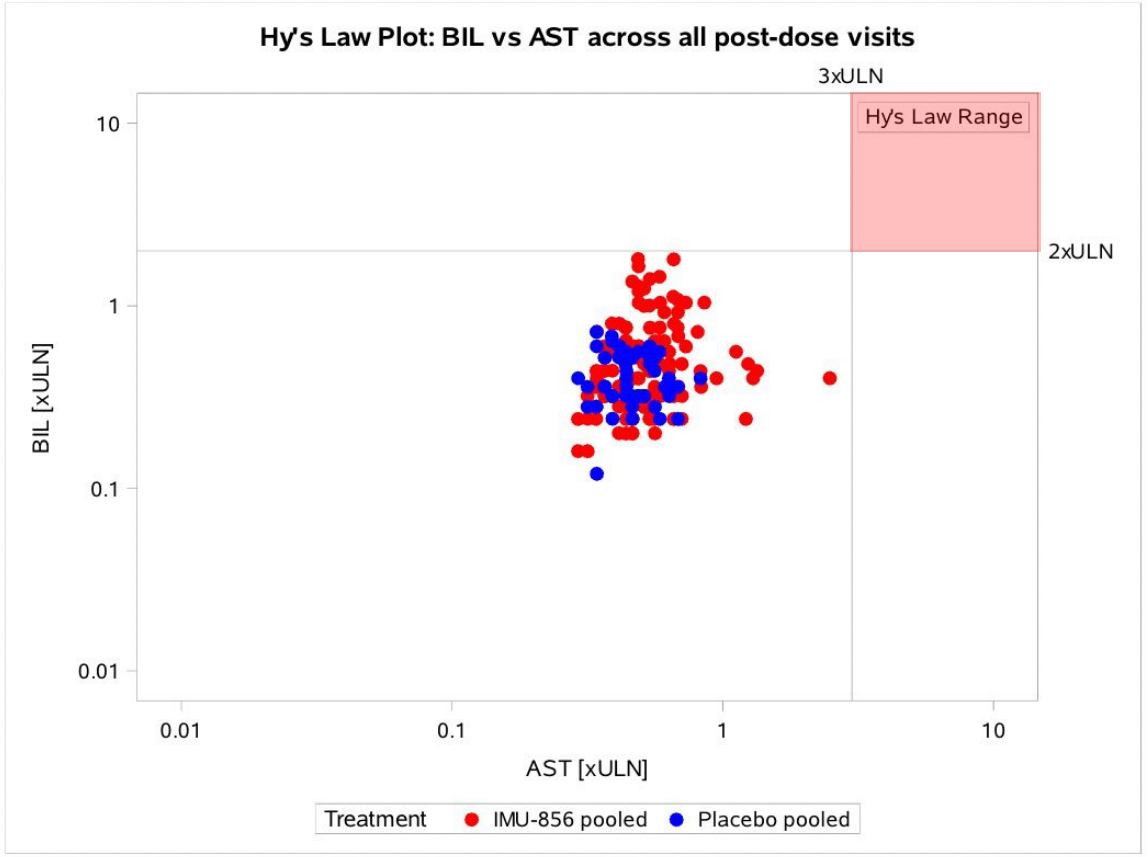
Laboratory Parameters: No Hy's Law Range Cases Observed

Part B, Cohorts 7, 7N-9N

Bilirubin vs. ALT Showed No Evidence of DILI Potential



Bilirubin vs. AST Showed No Evidence of DILI Potential



ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; DILI: drug-induced liver injury; BIL: Bilirubin; ULN: Upper Limit of Normal

Immunic THERAPEUTICS

Multiple Doses of IMU-856 in Healthy Human Subjects Found to Have a Favorable Safety and Tolerability Profile

Part B, Cohorts 7, 7N-9N

- No IMP-related serious adverse events
- No dose-dependency in adverse events
- No maximum tolerated dose reached
- No trends for post-dose changes in any laboratory parameter
- No medically relevant changes in vital signs, physical examination or 12-lead electrocardiograms as compared to placebo
- Pharmacokinetics well suited for once-daily administration and stable predictable trough levels

IMP: Investigational Medicinal Product

Immunic THERAPEUTICS

Conclusions

Part B: 14-Day Multiple Ascending Doses

- Daily oral doses of IMU-856 (up to 160 mg) demonstrated a favorable safety, tolerability and pharmacokinetic profile.
- This allowed a smooth transition from Part B (MAD) to Part C (28-day dosing in patients with celiac disease) which is currently ongoing and actively recruiting.

01

Phase 1 Clinical Trial of IMU-856

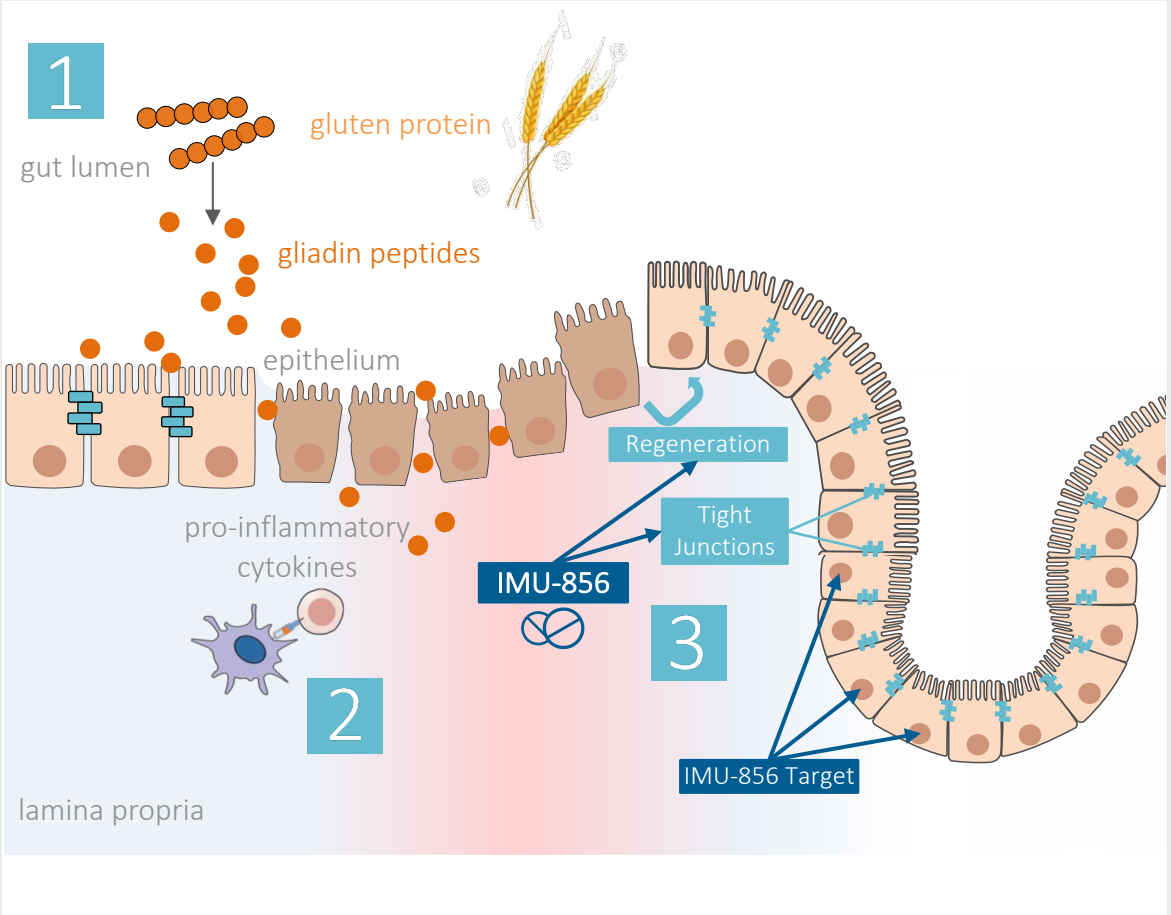
Trial Design and Status

Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

Ongoing Part C in Patients with Celiac Disease

Celiac Disease is a Serious Autoimmune Disease



Celiac disease is a multifactorial, complex autoimmune disease caused by an immune reaction against a degradation product of gluten and is strongly associated with specific HLA class II gene variants (HLA-DQ2 and -DQ8)[1]

1
- Gluten is degraded into gliadin peptides which are taken up by the bowel epithelium (trans- or paracellular)

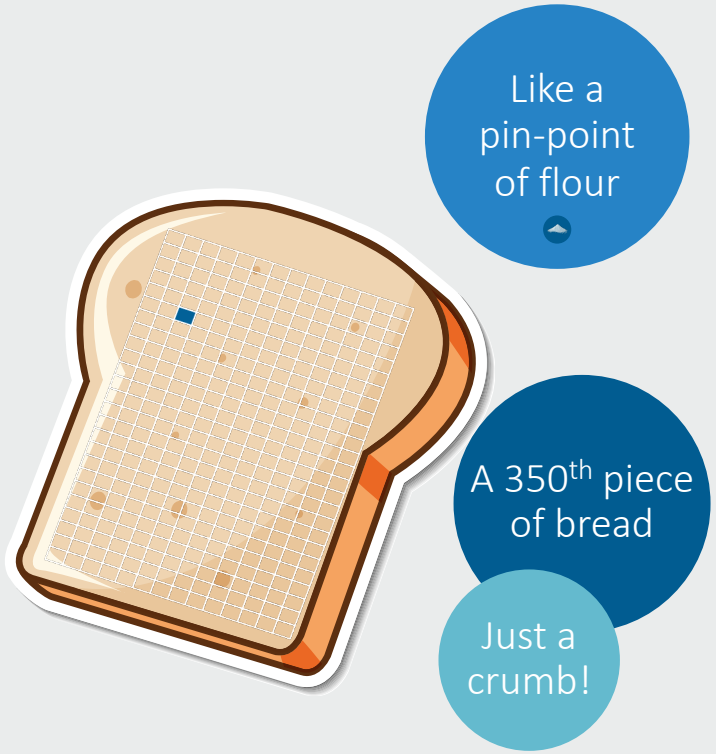
2
- In patients with a specific HLA receptor (DQ2 and DQ8) composition, deaminated gliadin (by TG2) is recognized and can trigger an immune response which leads upon continued gliadin uptake to
  - ✓ Increased intestinal permeability
  - ✓ Epithelial and mucosal damage with negative changes of the gut architecture, including villous atrophy leading to malabsorption of nutrients

3
- Hypothesis for IMU-856's mode of action:
  - Improves intestinal barrier function and restores permeability
  - Restores villous architecture by triggering regenerative processes of the epithelial lining

HLA: human leukocyte antigen; TG2: tissue transglutaminase 2
Picture: self-drawn; [1] Caio et al. BMC Medicine (2019) 17:142

Celiac Disease Currently Has No Adequate Treatment Options

How much is 10 mg of gluten?



10 mg of gluten is the total limit for all foods combined for the entire day.

The Only Option Today is a Gluten Free Diet[1]

- The only established therapeutic option is a life-long strict adherence to a gluten free diet, which involves complete avoidance of proteins from wheat, barley, and rye.
- There is a high risk of accidental and inadvertent gluten intake, often due to a wide gluten cross contamination.
- A threshold of 10 mg gluten/day[1] is considered safe for patients with celiac disease.

Symptomatic Patients Despite Gluten Free Diet

- Between 24% and 47% of patients show signs and symptoms of ongoing active celiac disease despite strict gluten free diet[2], most likely due to:
  - Continuous (inadvertent) gluten exposure
  - Slow response to gluten withdrawal
- These patients are the main target for celiac disease medications.

Picture and Ref [1]: https://nationalceliac.org/celiac-disease-questions/understanding-gluten-levels/; [2] Lebwohl et al., Aliment Pharmacol Ther. 2014 March ; 39(5): 488–495

Immunic THERAPEUTICS

Patients Across the Spectrum of Celiac Disease Need Access to a Drug Treatment to Address Persistent Disease Activity Despite GFD

Patients with celiac disease are often wrongly diagnosed in early stages, leading to poorer prognosis on gluten free diet

Active Celiac Disease

- Numerous, intense gastrointestinal symptoms
- Antibody stimulation in response to gluten / gliadin
- >12 months for antibody normalization if GFD effective
- Histologic remission possible in 1-2 years

Persistent Villous Atrophy

- Marked by enterocyte atrophy (barrier fully compromised)
- Often seen in 25-50% of patients, despite long-term GFD
- Histologic recovery rare

Refractory Disease

- Persistent malabsorption and associated comorbidities, persistent villous atrophy
- High mortality due to lymphoma

Treatments available	Gluten Free Diet (GFD)	Maintaining GFD	Immunosuppression

Benjamin Lebwohl, Sanders, and Green 2018; B. Lebwohl et al. 2014; Caio et al. 2019; Nasr et al. 2016
GFD: gluten free diet

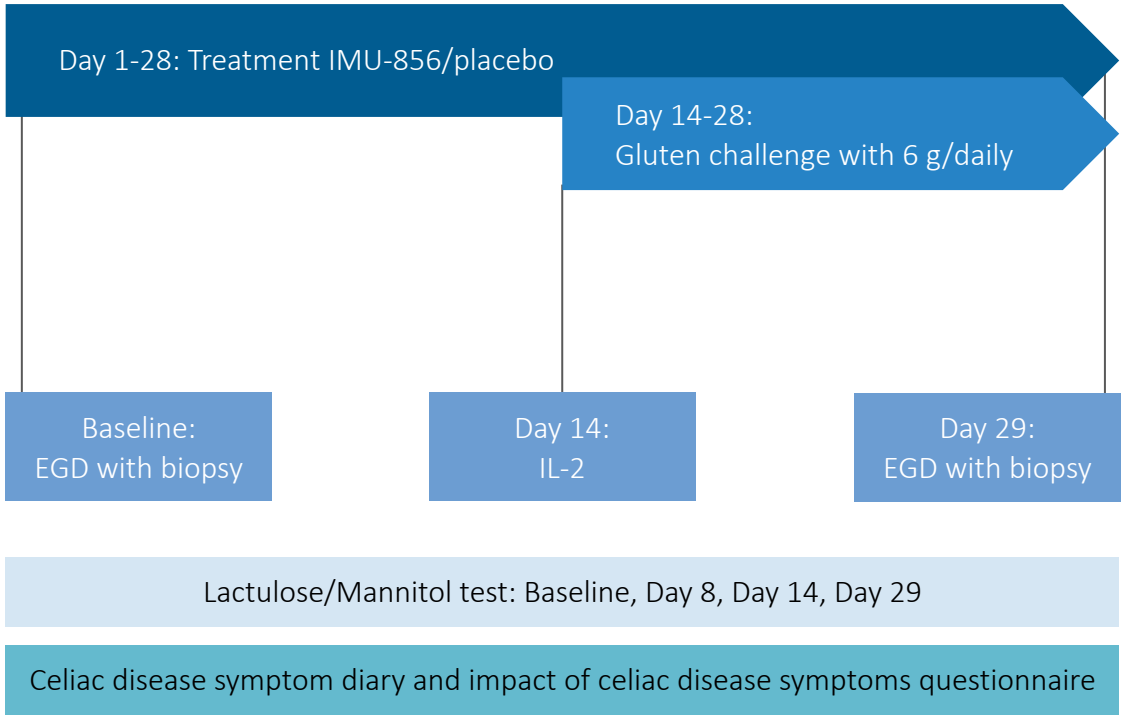
Phase 1 Clinical Trial of IMU-856
Part C in Celiac Disease Patients

Proof-of-Concept Study

- Part C includes a well-controlled celiac disease patient population, designed to assess safety and tolerability of IMU-856 as well as pharmacokinetics and acute (serum IL-2) and chronic (Vh:CrD) disease markers

- Performed at sites in Australia and New Zealand

Flow Chart of Part C in Celiac Disease



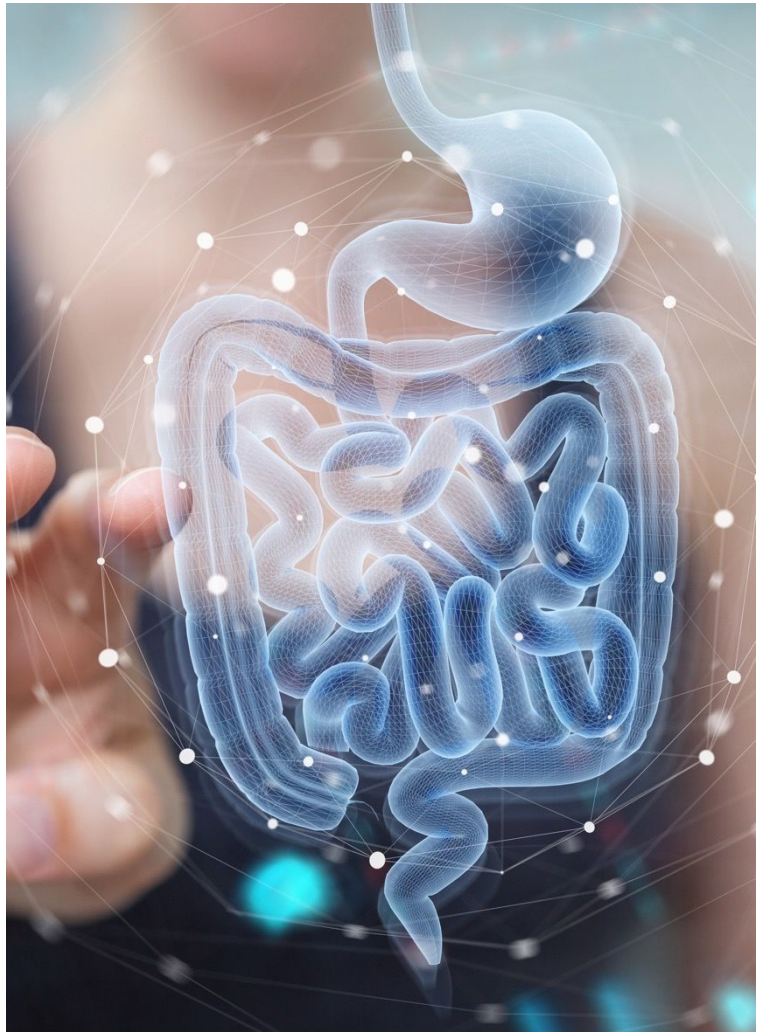
EGD: esophagogastroduodenoscopy, VH:CrD: villous hight to crypt depth ratio, one of the main histological assessments of small bowel architecture, IL-2: interleukin-2

02

IMU-856: Restoring Intestinal Barrier Function

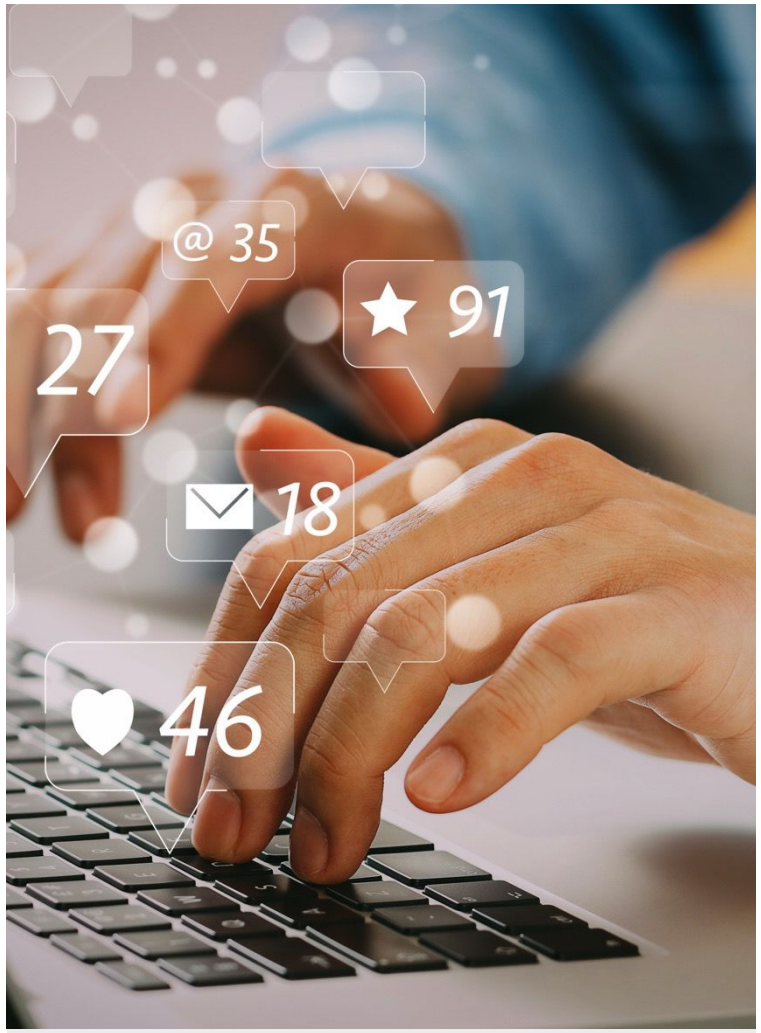
Summary and Outlook

IMU-856: Favorable Phase 1 Safety, Tolerability and Pharmacokinetic Profile



- IMU-856 showed a **favorable safety, tolerability and pharmacokinetic profile** in this phase 1 clinical trial with no IMP-related serious adverse events seen in the SAD and MAD parts.
- In particular, IMU-856 was **safe and well-tolerated** in 14-day repeated oral dosing in healthy human subjects at doses expected to exceed required therapeutic dosing.
- IMU-856 is currently being tested in a third portion of the phase 1 clinical trial in patients with celiac disease – setting the stage for a potential **first-in-class oral celiac disease** therapy.
- IMU-856 may offer **extensive potential** beyond celiac disease in other autoimmune diseases.

Outlook: Multiple Value Inflection Points Expected Across Immunic's Three Clinical-Stage Programs



Vidofludimus Calcium (IMU-838)

- Interim data of phase 2 CALLIPER trial in PMS expected in H2/2023 and top-line data expected at the end of 2024
- Read-out of the first of the phase 3 ENSURE trials in RMS targeted for end of 2025

IMU-935

- Initial phase 1b psoriasis data expected to be available in Q4/2022

IMU-856

- Initial phase 1b celiac disease data expected to be available in 2023

Immunic THERAPEUTICS

Thank You!

Jessica Breu

Head of IR & Communications

Phone: +49-89-2080477-09

Email: ir@imux.com

Web: www.imux.com

Immunic, Inc.
1200 Avenue of the Americas
New York City, NY 10036
USA

Immunic AG
Gräfelfing (Munich)
Germany

Immunic Research GmbH
Weinberg Campus
Halle (Saale)
Germany

Immunic Australia Pty. Ltd.
Melbourne
Australia

03

Phase 1 Clinical Trial of IMU-856

Extended Information Section: Part A – Single Ascending Doses

Most Common Treatment-Emergent Adverse Events
Part A, Cohorts 1-6

MedDRA Preferred Term	Number (%) of subjects with TEAEs occurring in more than 2 subjects [Number of TEAEs reported]							
	Cohort 1 10 mg (N=6)	Cohort 2 20 mg (N=6)	Cohort 3 40 mg (N=6)	Cohort 4 80mg (N=6)	Cohort 5 120 mg (N=4)	Cohort 6 160 mg (N=5)	Active (N=33)	Placebo (N=12)
Catheter site irritation	1 (17%) [1]	2 (33%) [2]	-	-	1 (25%) [1]	2 (40%) [2]	6 (18%) [6]	-
Catheter site pain	-	-	1 (17%) [1]	3 (50%) [3]	1 (25%) [1]	1 (20%) [1]	6 (18%) [6]	-
Abdominal pain	-	1 (17%) [1]	-	-	2 (50%) [2]	1 (20%) [1]	4 (12%) [4]	1 (8%) [1]
Diarrhea	-	2 (33%) [2]	-	-	1 (25%) [2]	-	3 (9%) [3]	1 (8%) [1]
Flatulence	-	1 (17%) [1]	-	-	-	2 (40%) [2]	3 (9%) [3]	-
Headache	-	-	1 (17%) [1]	-	1 (25%) [1]	-	2 (6%) [2]	1 (8%) [1]

Single doses of IMU-856 were safe and well-tolerated with catheter site irritation and catheter site pain being the most common TEAEs following oral tablet administration.

TEAE: Treatment-Emergent Adverse Event

Immunic THERAPEUTICS

Most Common IMP-related Treatment-Emergent Adverse Events

Part A, Cohorts 1-6

MedDRA Preferred Term	Number (%) of subjects with IMP-related TEAEs occurring in 2 and more subjects [Number of TEAEs reported]							
	Cohort 1 10 mg (N=6)	Cohort 2 20 mg (N=6)	Cohort 3 40 mg (N=6)	Cohort 4 80 mg (N=6)	Cohort 5 120 mg (N=4)	Cohort 6 160 mg (N=5)	Active (N=33)	Placebo (N=12)
Abdominal pain	-	1 (17%) [1]	-	-	2 (50%) [2]	-	3 (9%) [3]	1 (8%) [1]
Diarrhea	-	2 (33%) [2]	-	-	1 (25%) [1]	-	3 (9%) [3]	1 (8%) [1]
Headache	-	-	1 (17%) [1]	-	-	-	1 (3%) [1]	1 (8%) [1]
Gastrointestinal sounds abnormal	-	-	-	-	-	1 (20%) [1]	1 (3%) [1]	1 (8%) [1]

Abdominal pain and diarrhea were the most common IMP-related TEAEs, however, they occur in less than 10% of patients, were only mild in severity, and are comparable to the incidence in the placebo group.

TEAE: Treatment-Emergent Adverse Event; IMP: Investigational Medicinal Product

Immunic THERAPEUTICS

Summary of Safety and Tolerability Profile
Part A, Cohorts 1-6

Deaths, SAEs or study withdrawal due to TEAEs	None
76 TEAS in 31 participants	n = 73: mild n = 3: moderate (active treatment group) • Cohort 1 (10mg): Back pain – unrelated to study treatment • Cohort 5 (120mg): Catheter site pain – unrelated to study treatment • Cohort 5 (120mg): Abdominal distension – probably related to study treatment
28 IMP-Related TEAS in 16 participants	n = 27: mild n = 1: moderate (active treatment group) • Cohort 5 (120mg): Abdominal distension
Summary	• Total number of participants n=45 (active n=33, placebo n=12) • The most reported TEAEs in participants treated with IMU-856 (occurring in more than 10% of participants) were catheter site irritation, catheter site pain and abdominal pain • No dose related trends in incidence of TEAEs in study Part A • No clinically meaningful findings relative to safety and tolerability, as assessed by clinical laboratory tests, vital signs, physical examination and 12-lead electrocardiograms (ECGs) • Safe and well-tolerated

SAE: Serious Adverse Event; TEAE: Treatment-Emergent Adverse Event; IMP: Investigational Medicinal Product

03

Phase 1 Clinical Trial of IMU-856

Extended Information Section: Part B – Multiple Ascending Doses

Demographics
Part B

	Treatment					
	Cohort 7 40 mg (N=2)	Cohort 7N 40 mg (N=5)	Cohort 8N 80 mg (N=6)	Cohort 9N 160 mg (N=6)	Active (N=19)	Placebo (N=7)
Age (years), mean	38.5	35.0	30.5	27.3	31.5	34.6
Gender						
Male, n (%)	2 (100%)	3 (60%)	4 (67%)	4 (67%)	13 (68%)	4 (57%)
Female, n (%)	-	2 (40%)	2 (33%)	2 (33%)	6 (32%)	3 (43%)
Race/ Ethnicity						
Asian, n (%)	-	-	-	3 (50%)	3 (16%)	1 (14%)
White, n (%)	2 (100%)	5 (100%)	6 (100%)	3 (50%)	16 (84%)	6 (86%)
Height (cm), mean	181.0	172.8	174.3	172.5	174.1	172.7
Weight (kg), mean	83.30	78.26	75.20	74.87	76.75	80.49
BMI (kg/m^2), mean	25.46	26.25	24.74	25.02	25.30	26.87

In total,
26 healthy male and female subjects entered Part B multiple dose escalation.

Demographics were similar across cohorts.

Immunic THERAPEUTICS

Summary of Safety and Tolerability Profile
Part B, Cohorts 7, 7N-9N

Deaths, SAEs or study withdrawal due to TEAEs	1 Study Withdrawal due to 1 SAE unrelated to IMP (Staph. aureus bacteremia with myocarditis caused by an infected cannula with cellulitis)
84 TEAS in 20 participants	n = 74: mild (in 13 subjects) n = 9: moderate (in 6 subjects) ▪ Cohort 7: Arthralgia ▪ Cohort 7N: Decreased appetite ▪ Cohort 8N: Cellulitis, Staph. bacteremia, Headache, Upper respiratory tract infection ▪ Cohort 9N: Pyrexia, Headache, Vulva cyst n= 1: severe; unrelated to IMP (see above)
34 IMP-Related TEAS in 15 participants	n = 31: mild (in 12 subjects) n = 3: moderate (in 3 subjects) ▪ Cohort 7N: Decreased appetite ▪ Cohort 8N + 9N: Headache
Summary	▪ Total number of participants n=26 (all active n=19, Placebo n=7) ▪ The most reported TEAEs in participants treated with IMU-856 (occurring in more than 2 participants) were Headache, Diarrhoea, Abdominal Pain, Catheter site pain ▪ No dose related trends in incidence of TEAEs in study Part B ▪ There were no other clinically meaningful findings relative to safety and tolerability, as assessed by clinical laboratory tests, vital signs, and 12-lead electrocardiograms (ECGs). ▪ Safe and well-tolerated.

SAE: Serious Adverse Event; TEAE: Treatment-Emergent Adverse Event; IMP: Investigational Medicinal Product

Analysis of Laboratory Parameters
Part B

- Laboratory values over time
  - Descriptive statistics showed no trend of values over time for any parameter

- Individual changes
  - Shift tables showed no trend of individual changes beyond the normal range for any parameter

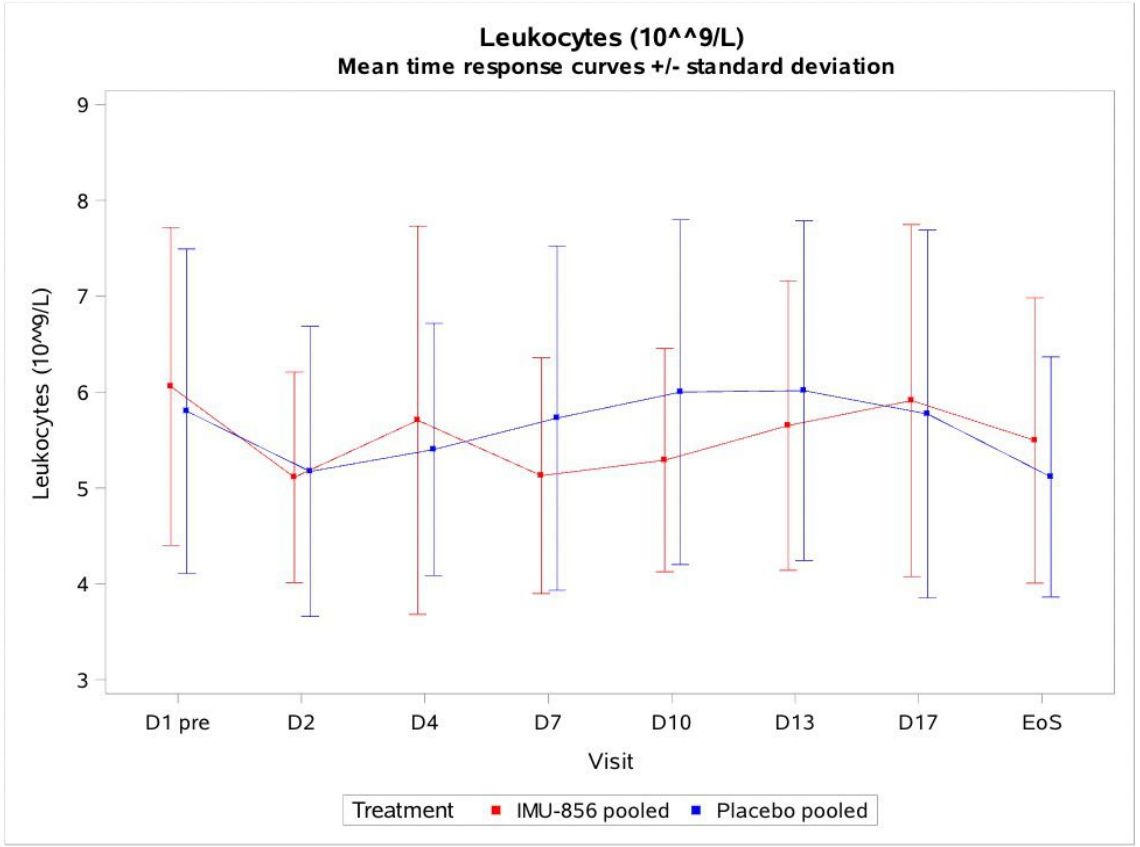
- Individual clinically significant abnormalities
  - Only 2 participants (8%) showed clinically significant abnormalities in the laboratory parameters
    - 1 participant in Cohort 8N, 80mg with Staphylococcus aureus myocarditis due to infected canula (unrelated to IMP)
    - 1 Participant (active group) in Cohort 7N, 40mg showed Transaminitis (mild in severity, possibly related): mild increase in ALT (max 4xULN) and AST (max 2.5xULN) from Day 4 on. AST back to normal at EOS, ALT dropped to 1.6xULN at EOS. Same participant reported diarrhoea from Day 1 to Day 7, mild in severity (possibly related). No other GI-related symptoms were reported for this participant.

IMP: Investigational Medicinal Product; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; EOS: End Of Study; GI: gastrointestinal

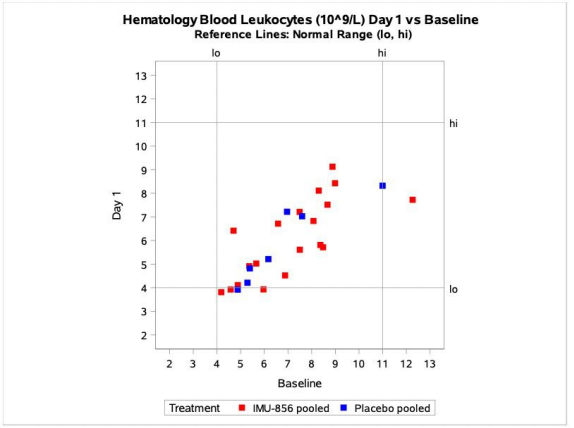
Laboratory Parameters: Leukocytes

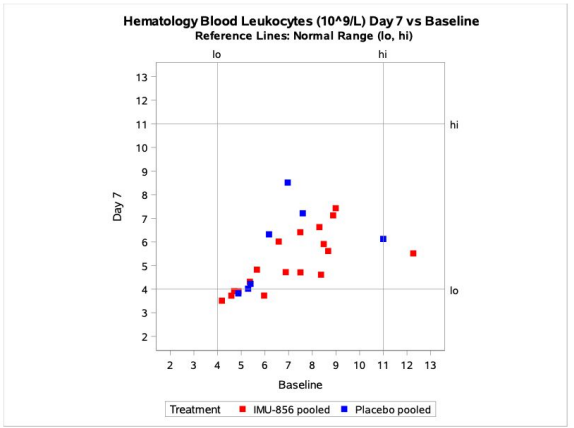
Part B, Cohorts 7, 7N-9N

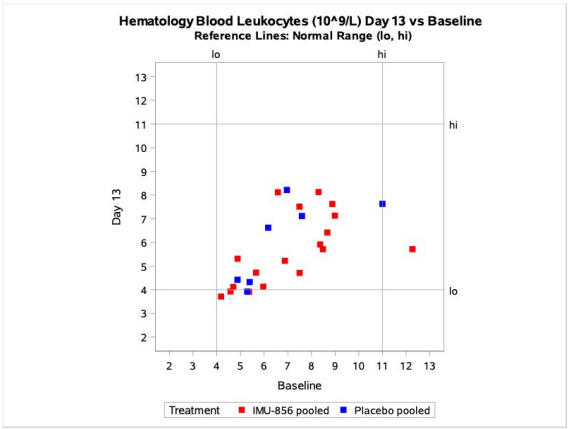
Laboratory Values Over Time
Hematology - Leukocytes

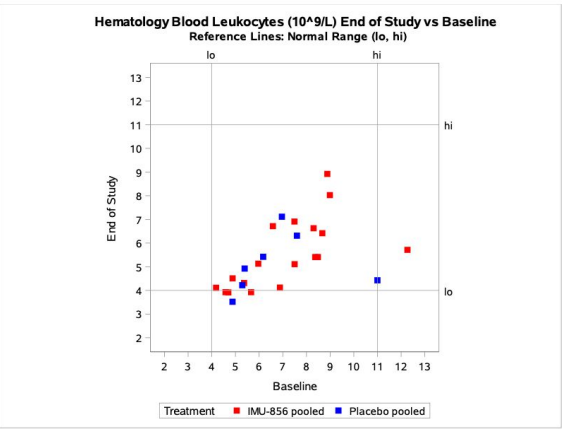


Individual Laboratory Values
Hematology - Leukocytes





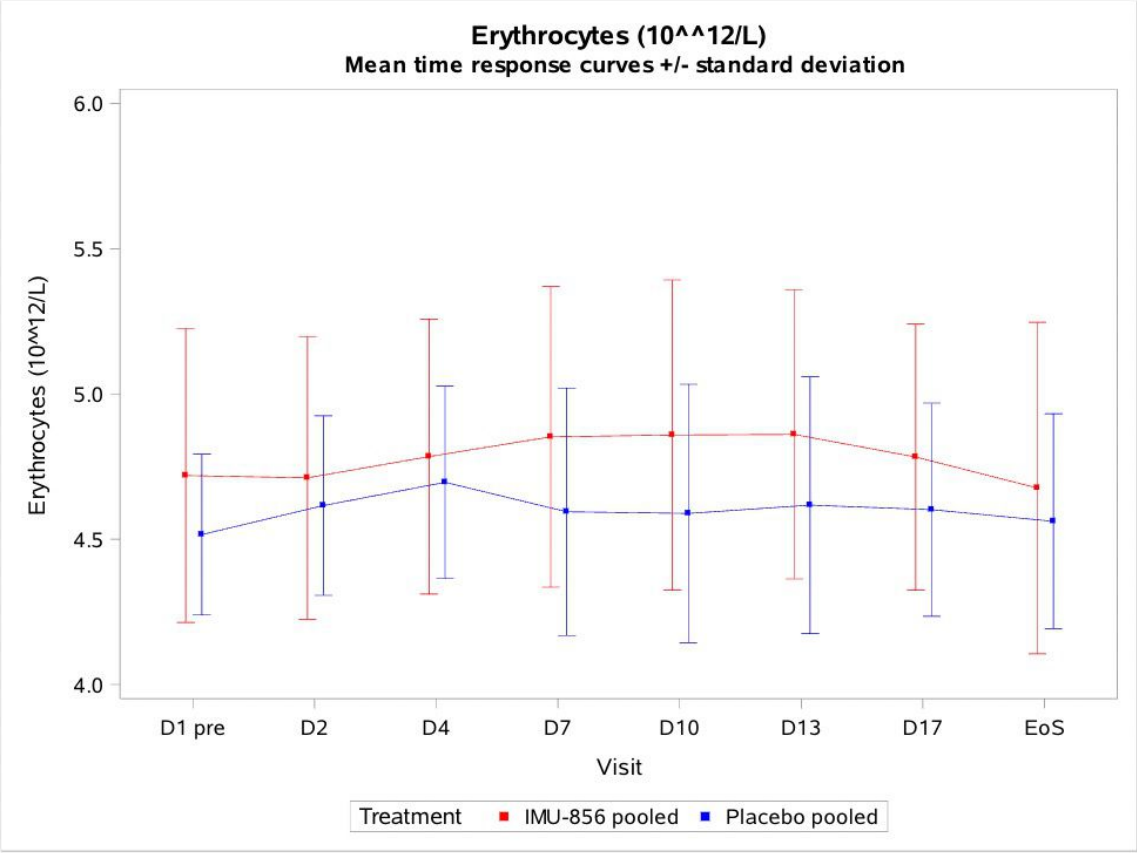




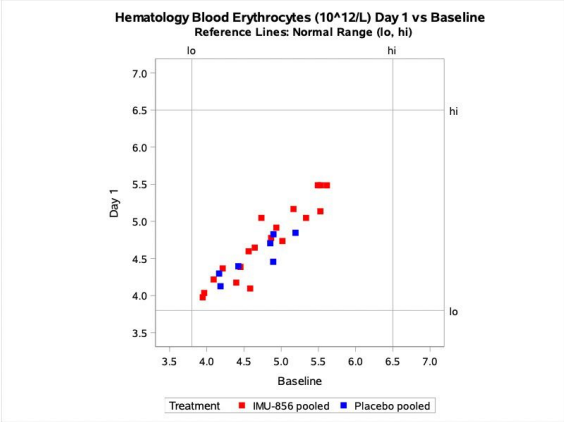
Laboratory Parameters: Erythrocytes

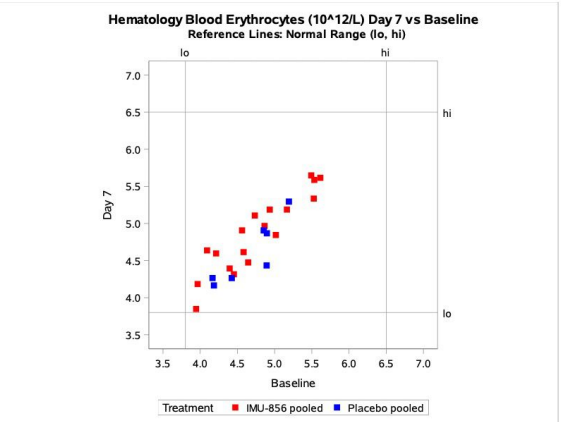
Part B, Cohorts 7, 7N-9N

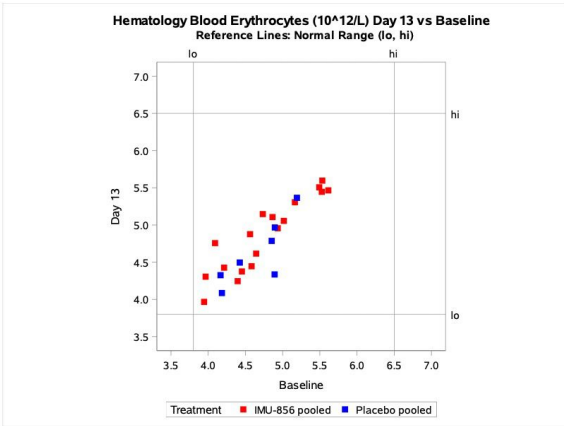
Laboratory Values Over Time
Hematology - Erythrocytes

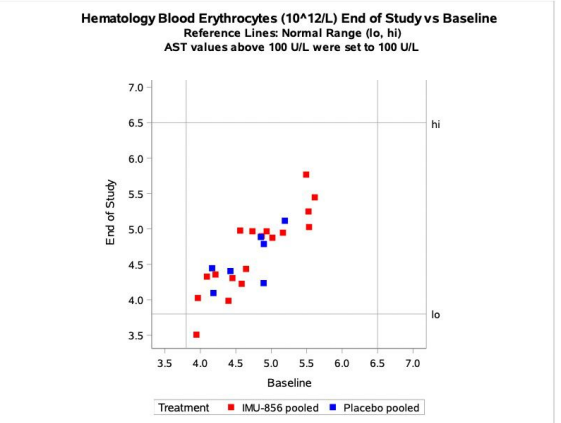


Individual Laboratory Values
Hematology - Erythrocytes







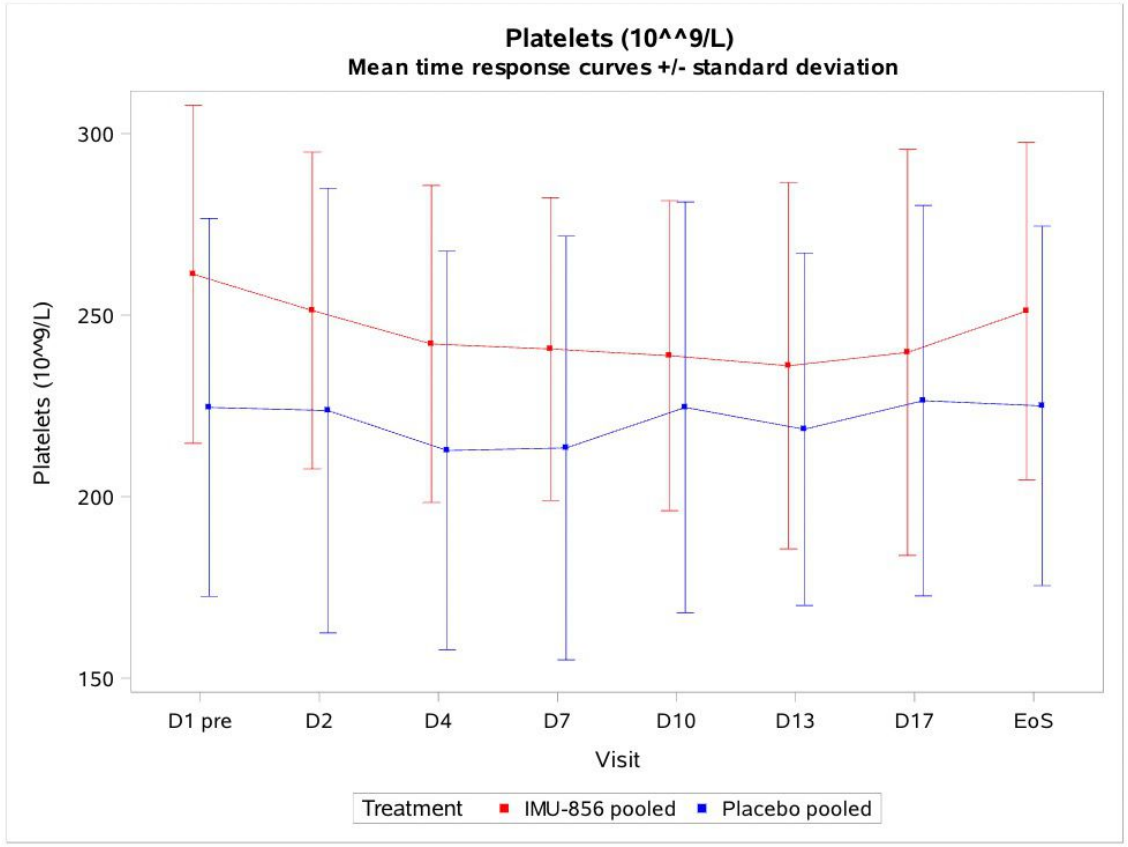


Immunic THERAPEUTICS

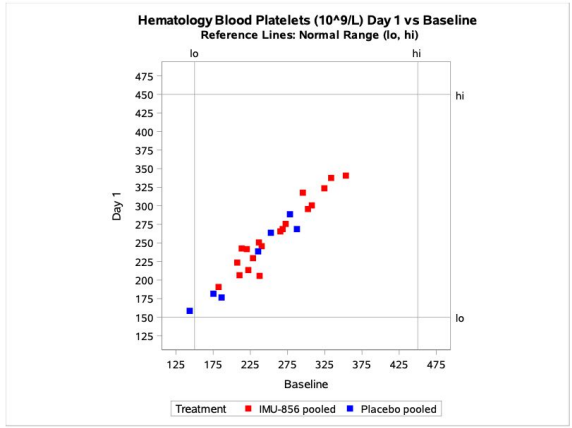
Laboratory Parameters: Platelets

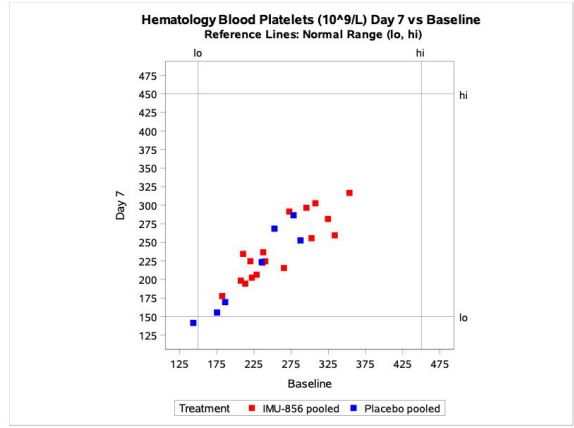
Part B, Cohorts 7, 7N-9N

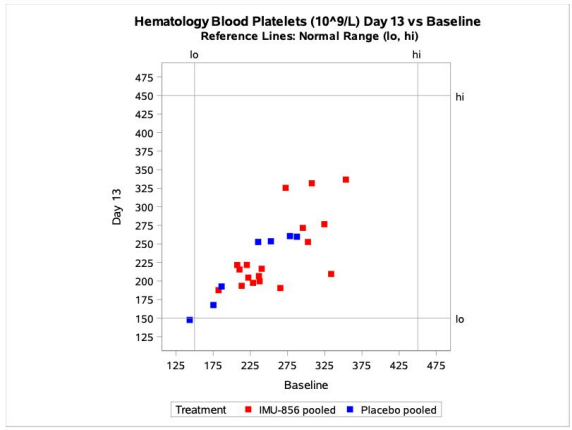
Laboratory Values Over Time
Hematology - Platelets

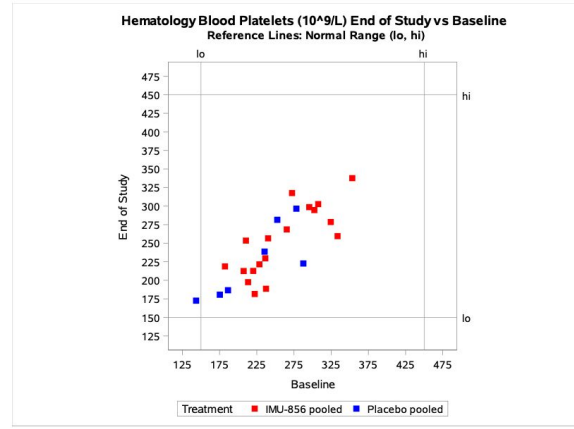


Individual Laboratory Values
Hematology - Platelets





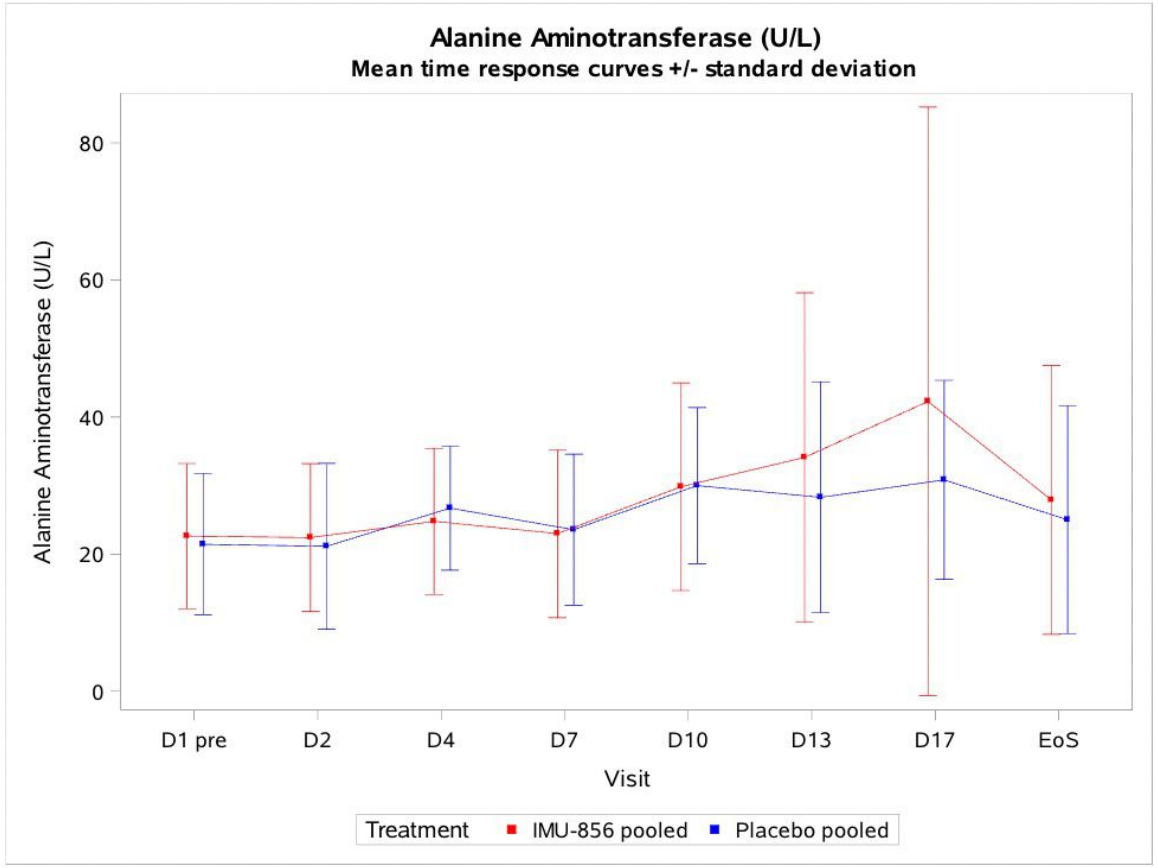




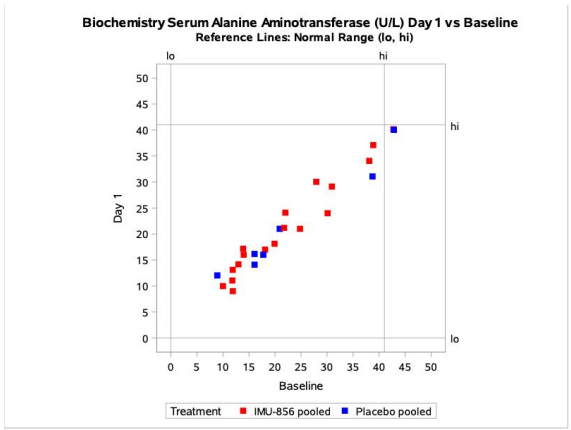
Immunic THERAPEUTICS

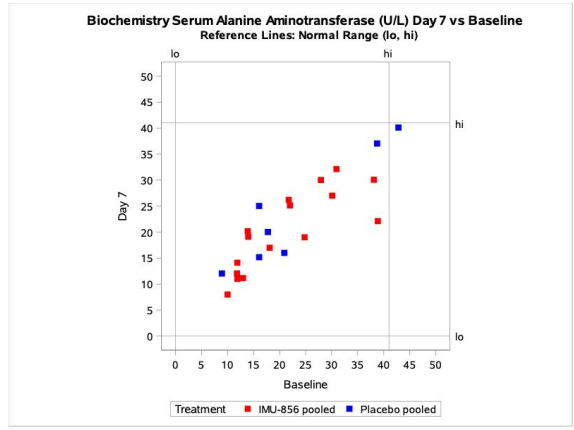
Laboratory Parameters: ALT
Part B, Cohorts 7, 7N-9N

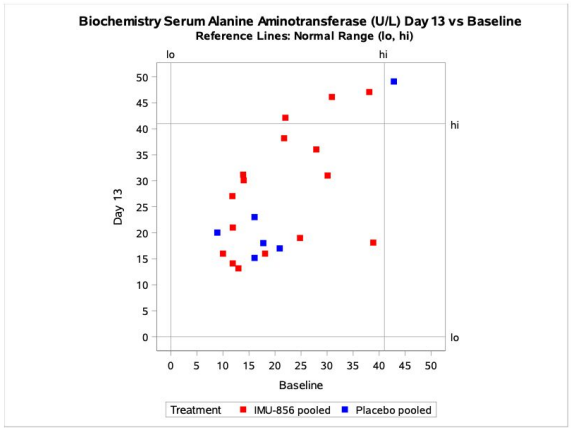
Laboratory Values Over Time
Biochemistry - ALT

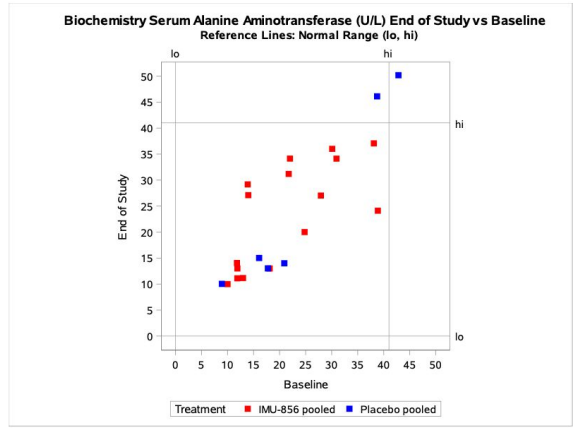


Individual Laboratory Values
Biochemistry - ALT







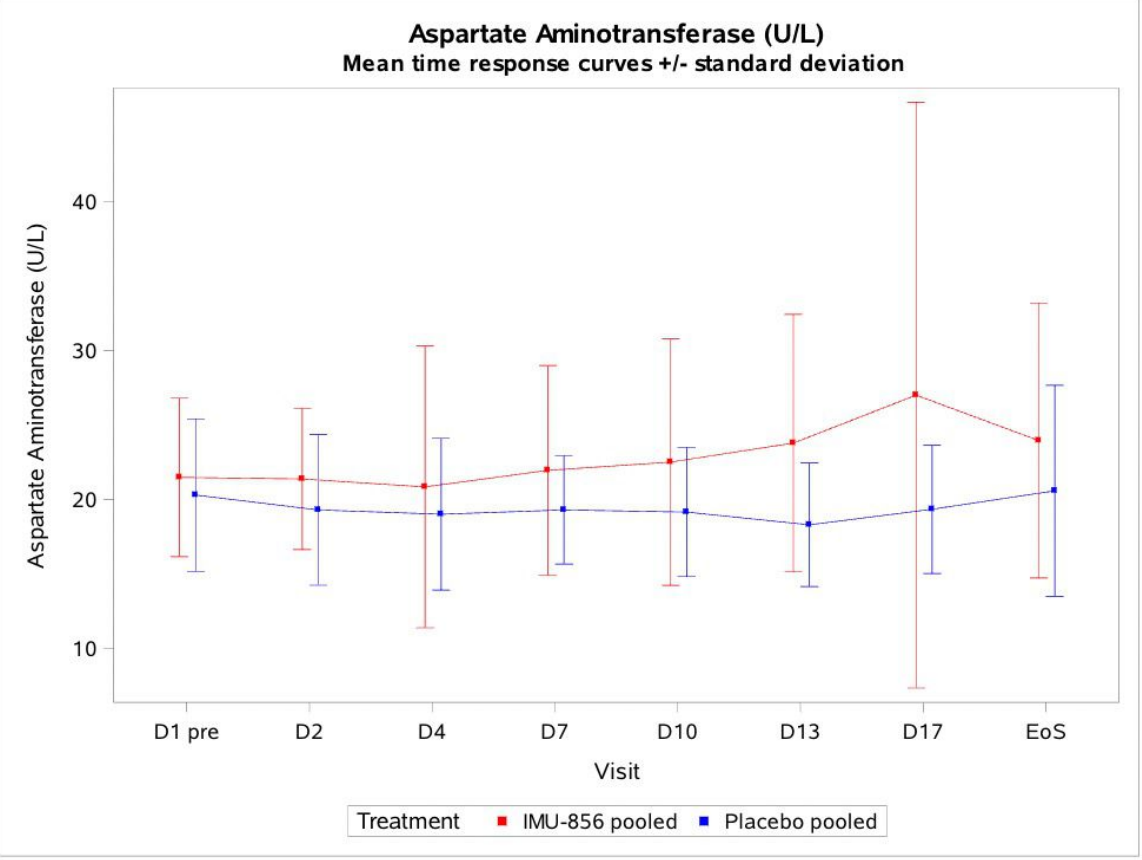


ALT: Alanine Aminotransferase

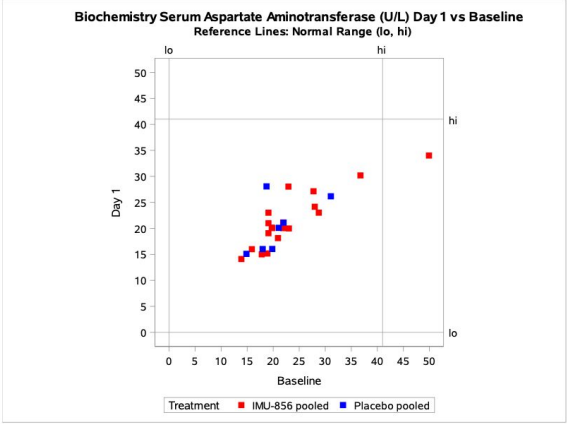
Immunic THERAPEUTICS

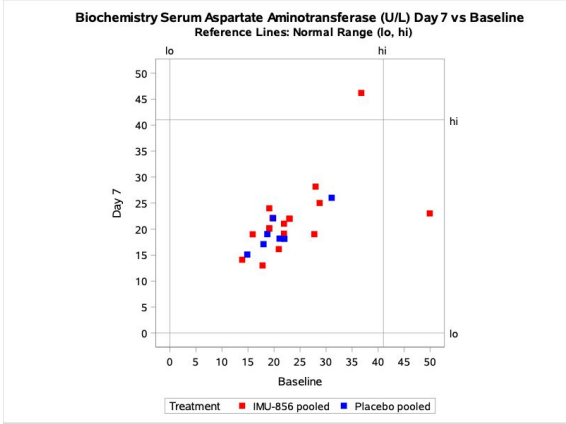
Laboratory Parameters: AST
Part B, Cohorts 7, 7N-9N

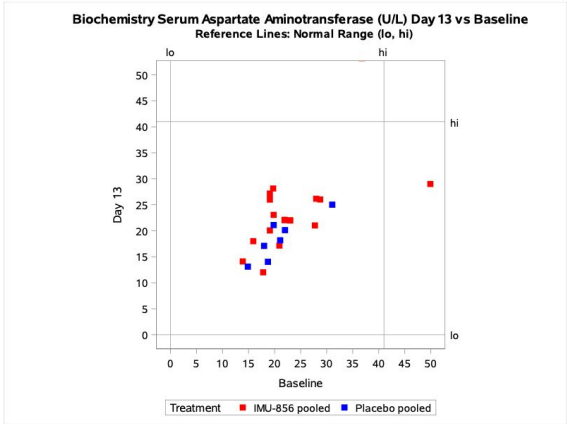
Laboratory Values Over Time
Biochemistry - AST

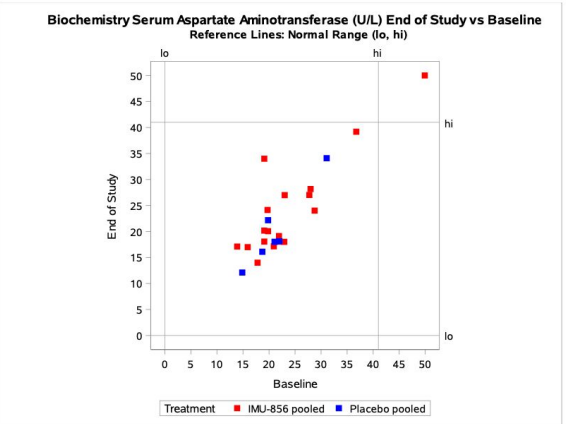


Individual Laboratory Values
Biochemistry - AST









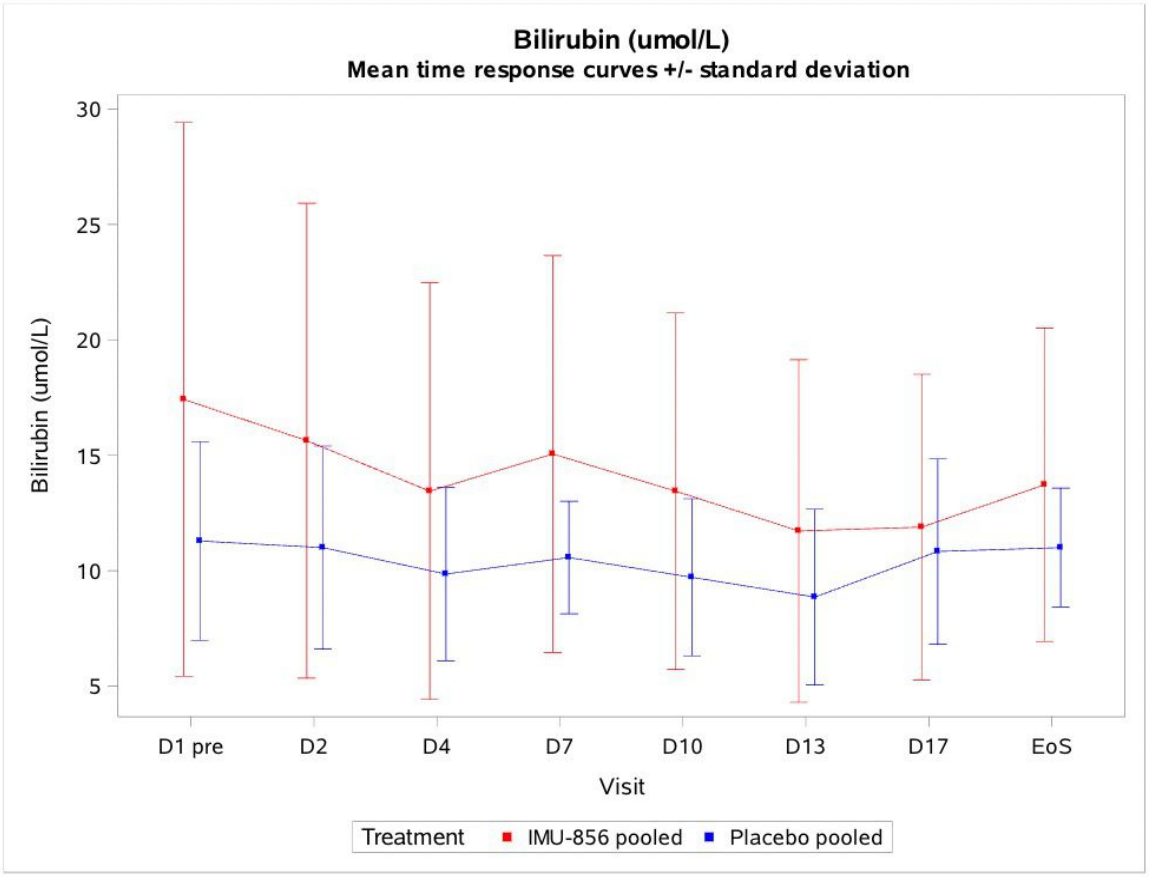
AST: Aspartate Aminotransferase

Immunic THERAPEUTICS

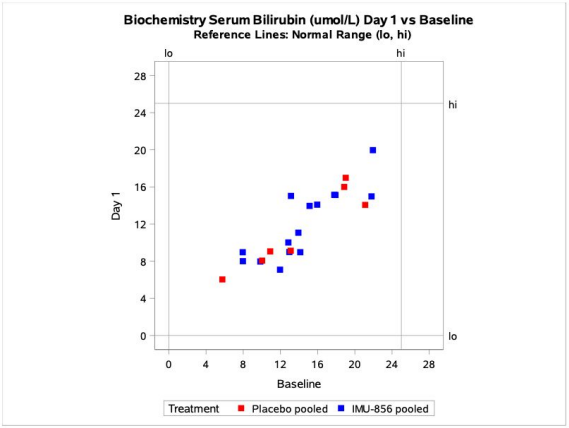
Laboratory Parameters: Bilirubin

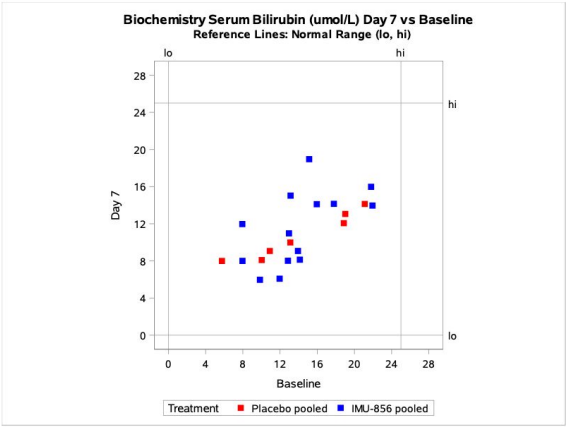
Part B, Cohorts 7, 7N-9N

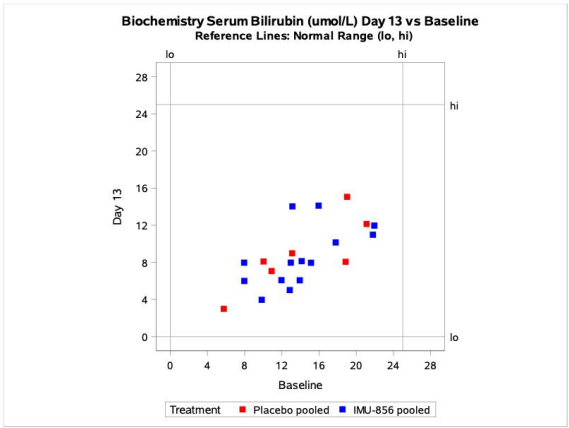
Laboratory Values Over Time
Biochemistry - Bilirubin

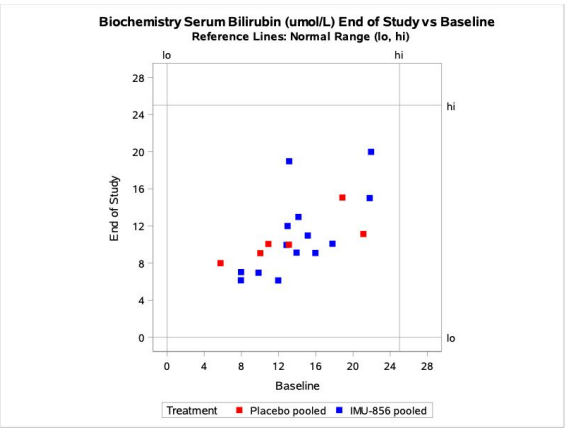


Individual Laboratory Values
Biochemistry - Bilirubin









Immunic THERAPEUTICS

Analysis of Vital Signs
Part B

- Vital signs over time
  - Descriptive statistics showed no trend of values over time for any parameter
  - No difference between active treatment and placebo group

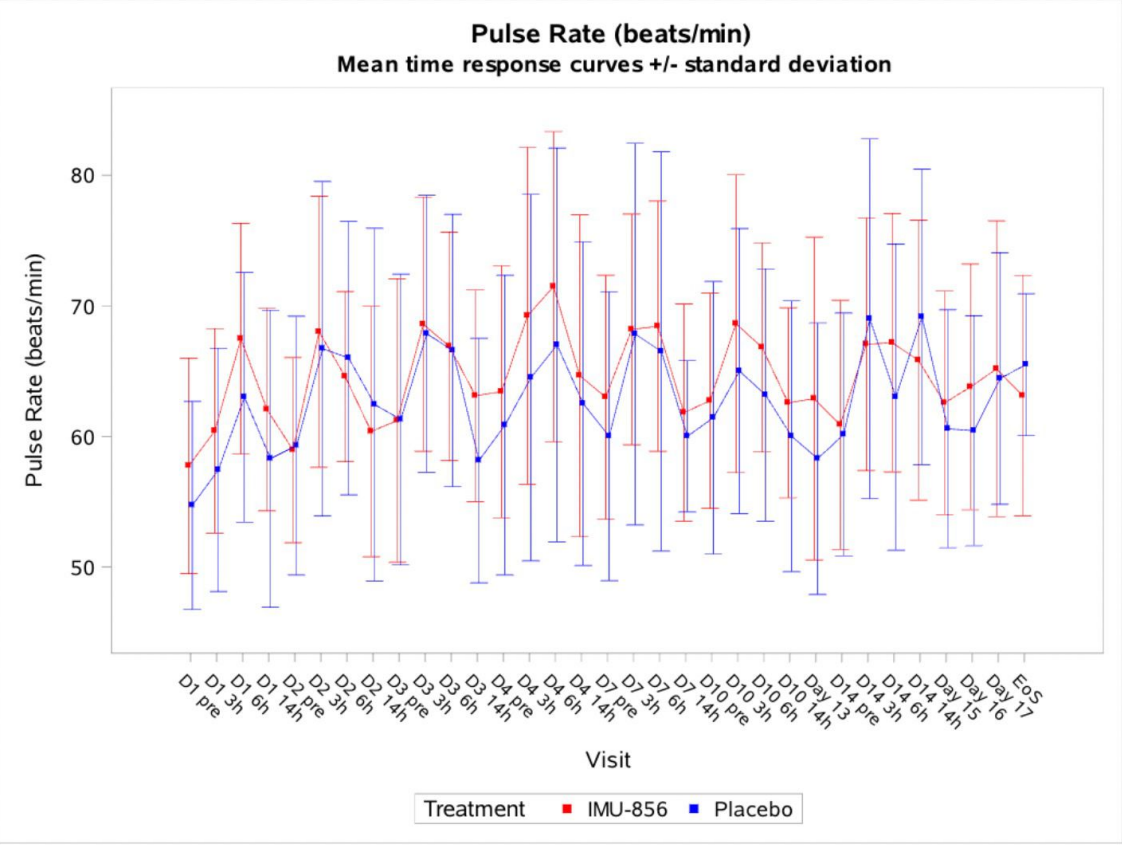
- Individual changes
  - Shift tables showed no trend of individual changes beyond the normal range for any parameter

- Individual clinically significant abnormalities
  - Abnormalities in vital signs were considered not clinically significant by the investigators
  - Thus, no TEAEs associated with vital signs have been reported

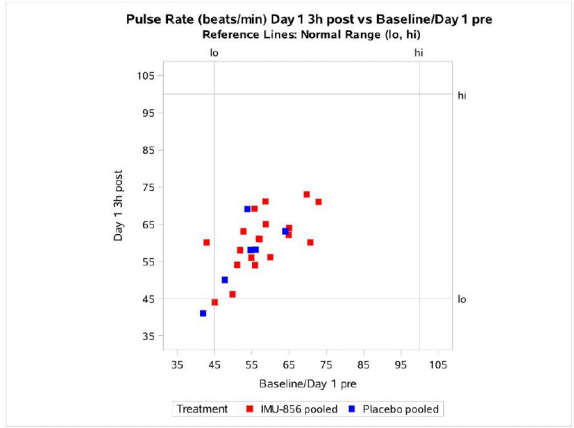
TEAE: Treatment-Emergent Adverse Event

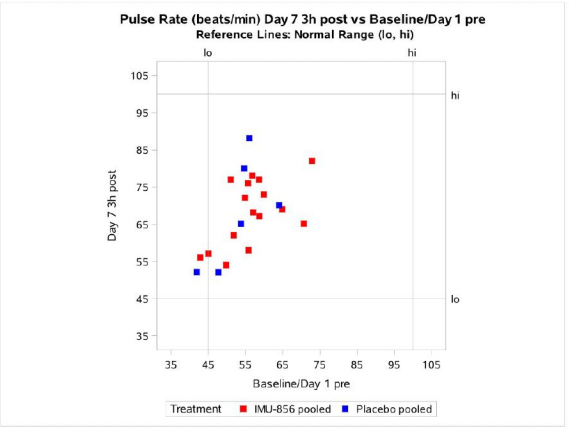
Vital Signs: Pulse Rate
Part B, Cohorts 7, 7N-9N

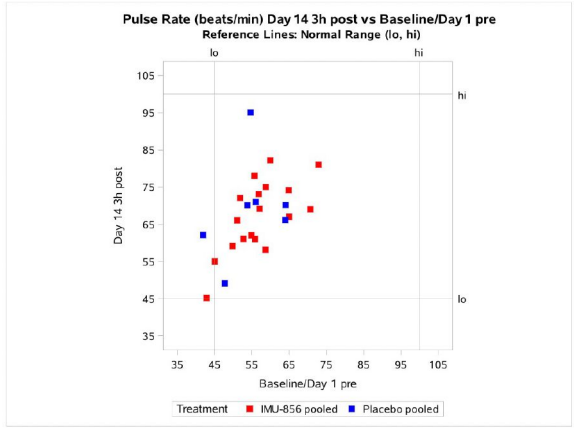
Vital Signs Over Time
Pulse Rate

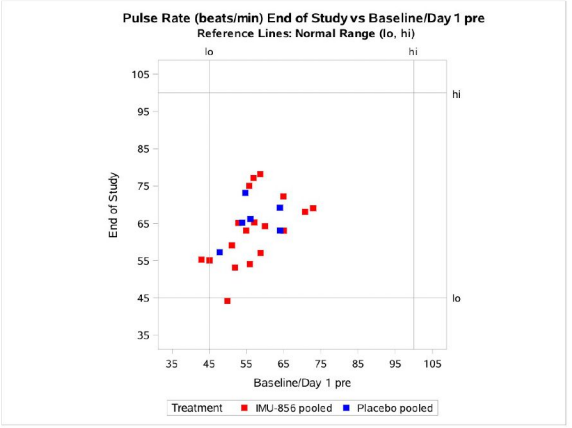


Individual Vital Signs
Pulse Rate





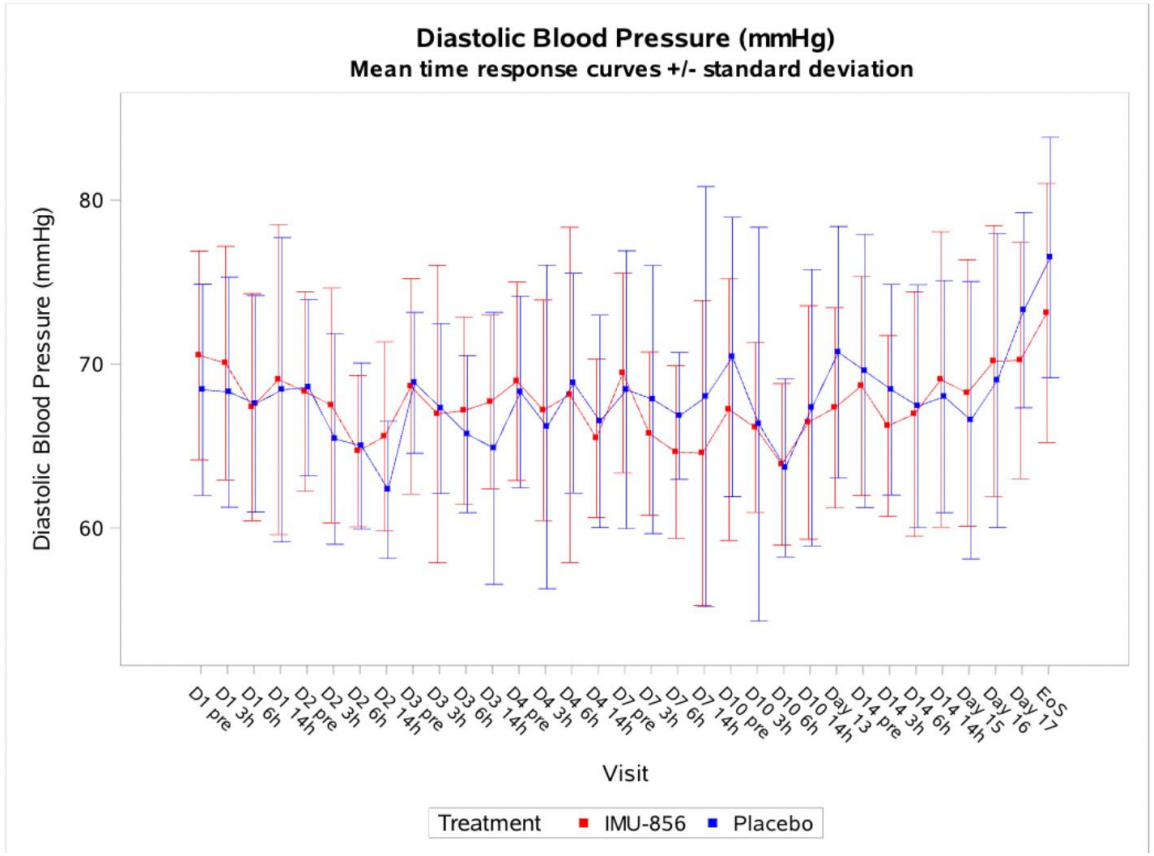




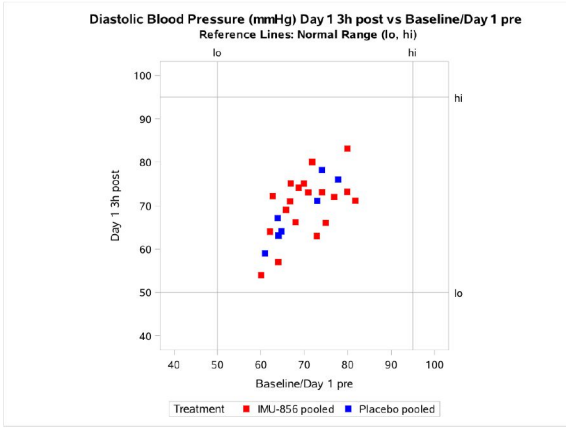
Vital Signs: Diastolic Blood Pressure

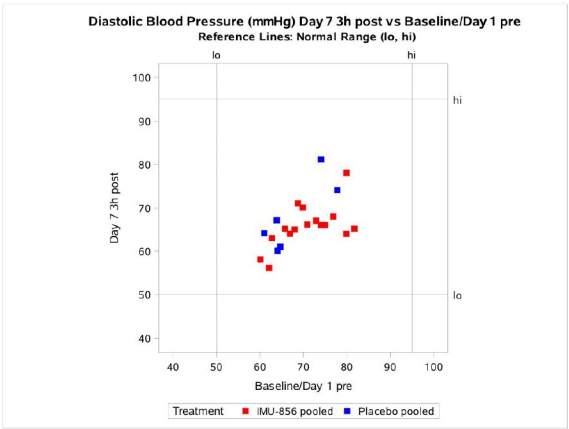
Part B, Cohorts 7, 7N-9N

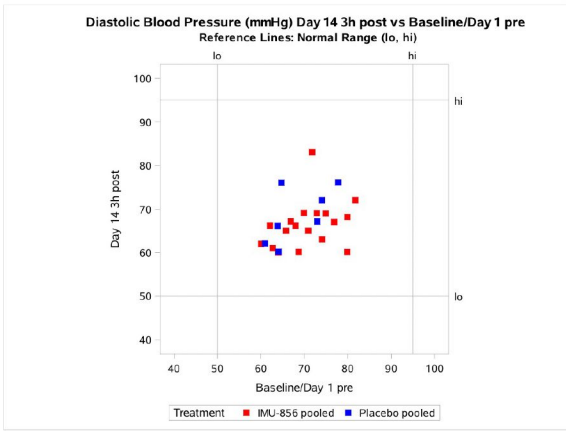
Vital Signs Over Time
Diastolic Blood Pressure

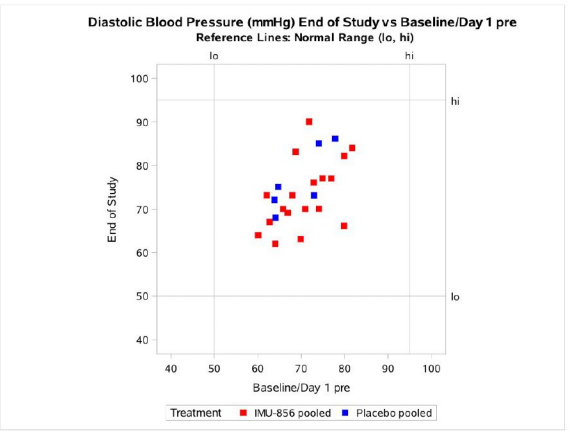


Individual Vital Signs
Diastolic Blood Pressure





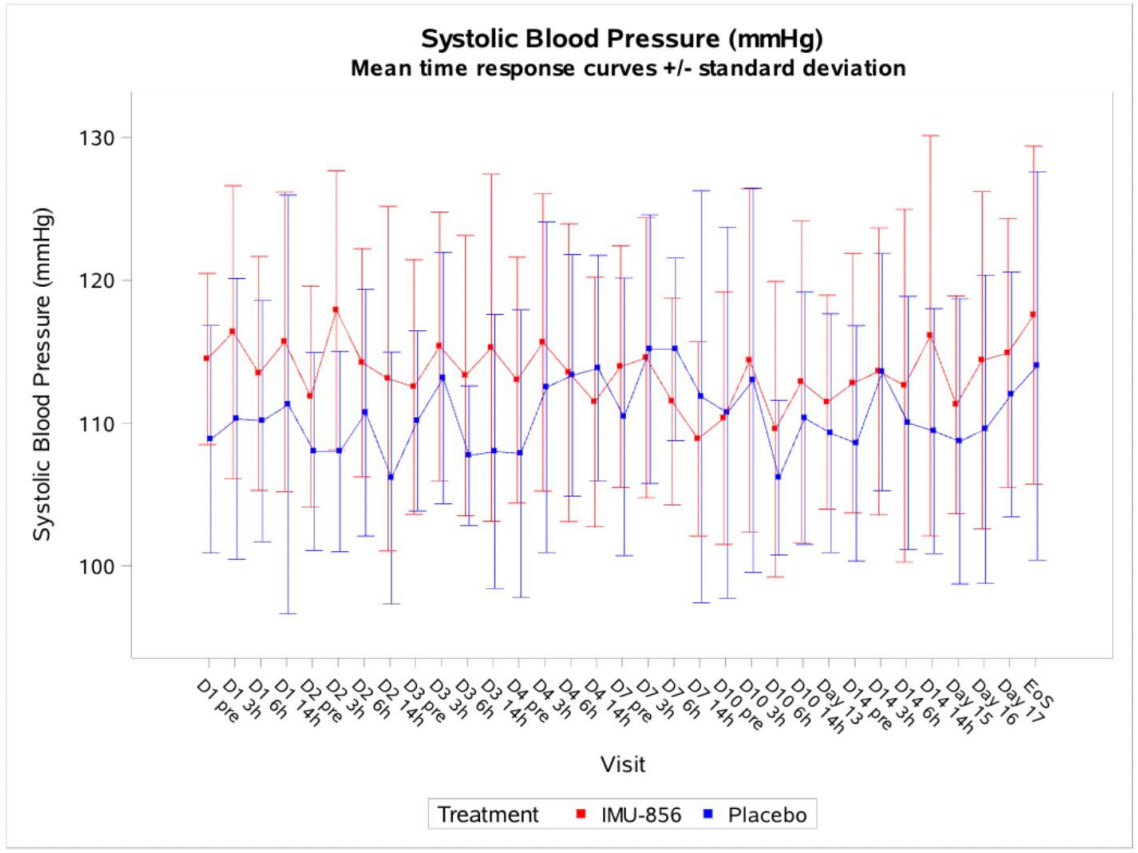




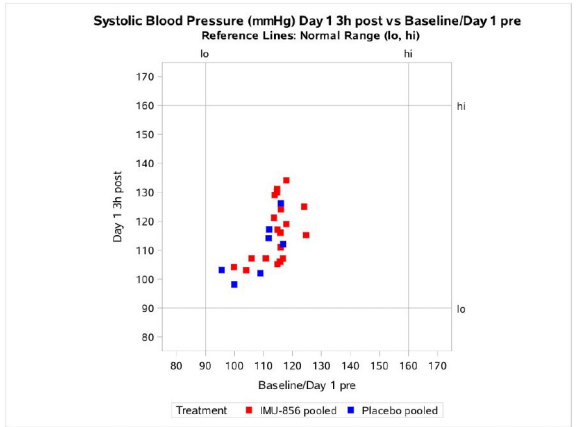
Vital Signs: Systolic Blood Pressure

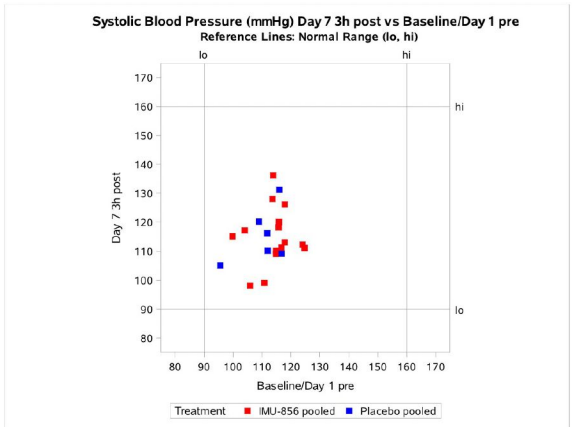
Part B, Cohorts 7, 7N-9N

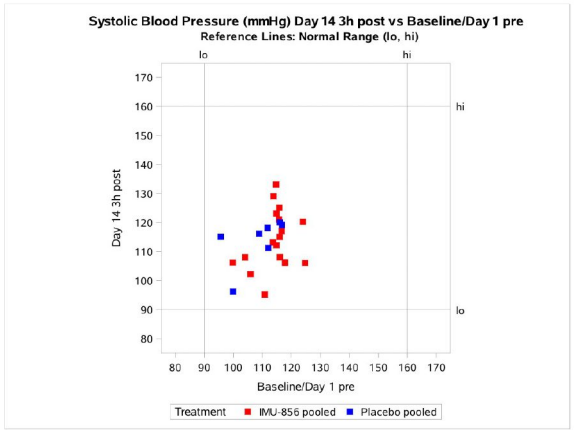
Vital Signs Over Time
Systolic Blood Pressure

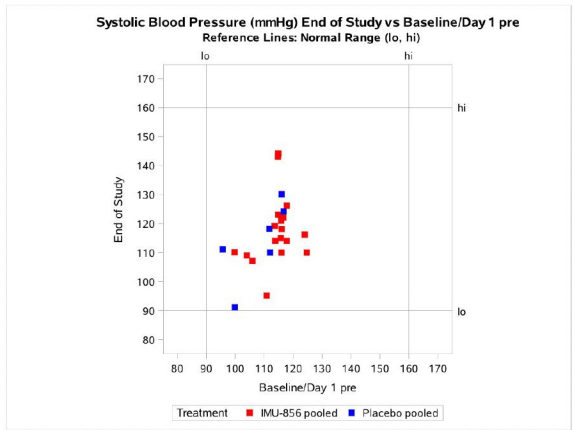


Individual Vital Signs
Systolic Blood Pressure









Immunic THERAPEUTICS

Analysis of 12-Lead Electrocardiograms
Part B

- 12-lead ECG parameters over time
  - Descriptive statistics showed no trend of values over time for any parameter
  - No difference between active treatment and placebo group

- Individual changes
  - Shift tables showed no trend of individual changes beyond the normal range for any parameter

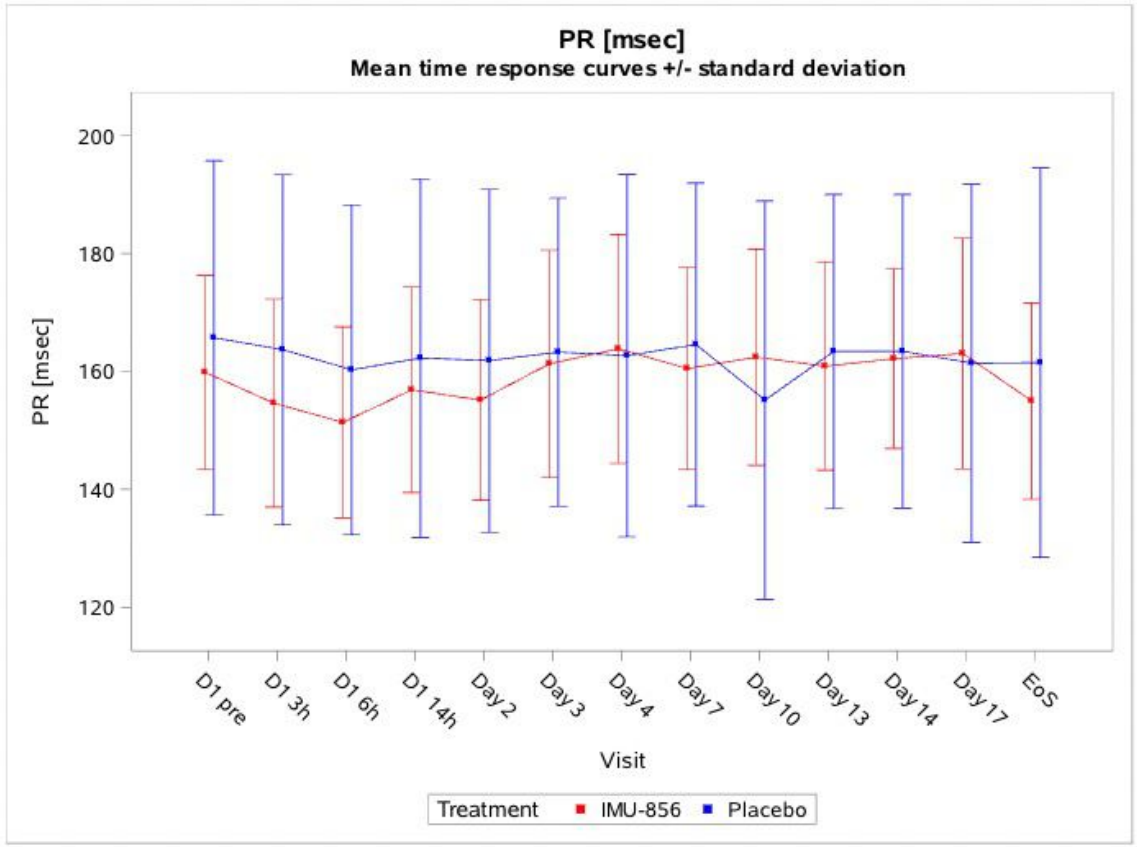
- Individual clinically significant abnormalities
  - Abnormalities in 12-lead ECG parameters were considered not clinically significant by the investigators
  - Thus, no TEAEs associated with 12-lead ECG parameters have been reported

ECG: electrocardiogram; TEAE: Treatment-Emergent Adverse Event

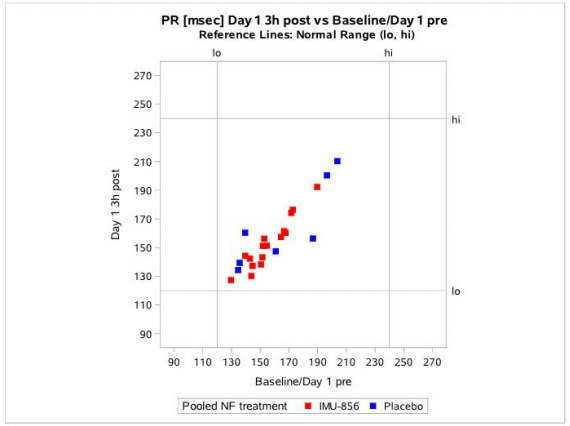
12-Lead Electrocardiograms: PR Interval

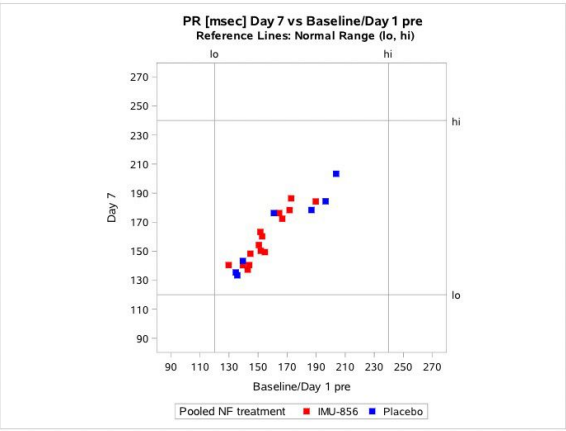
Part B, Cohorts 7, 7N-9N

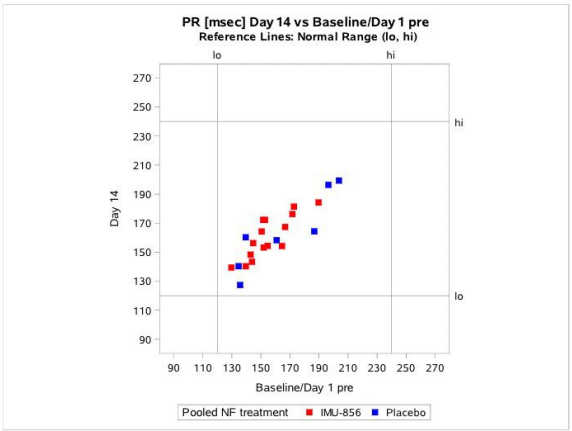
12-Lead ECGs Over Time
PR Interval

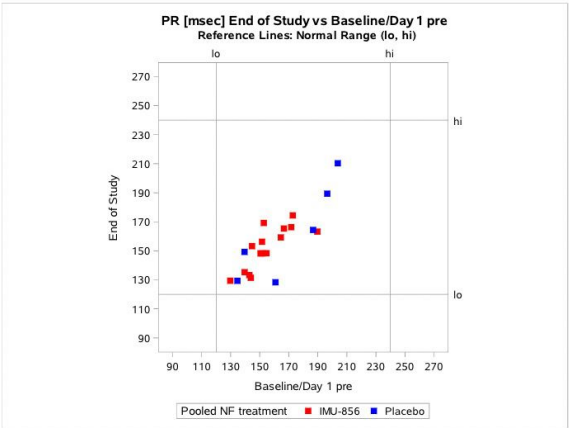


Individual 12-Lead ECGs
PR Interval







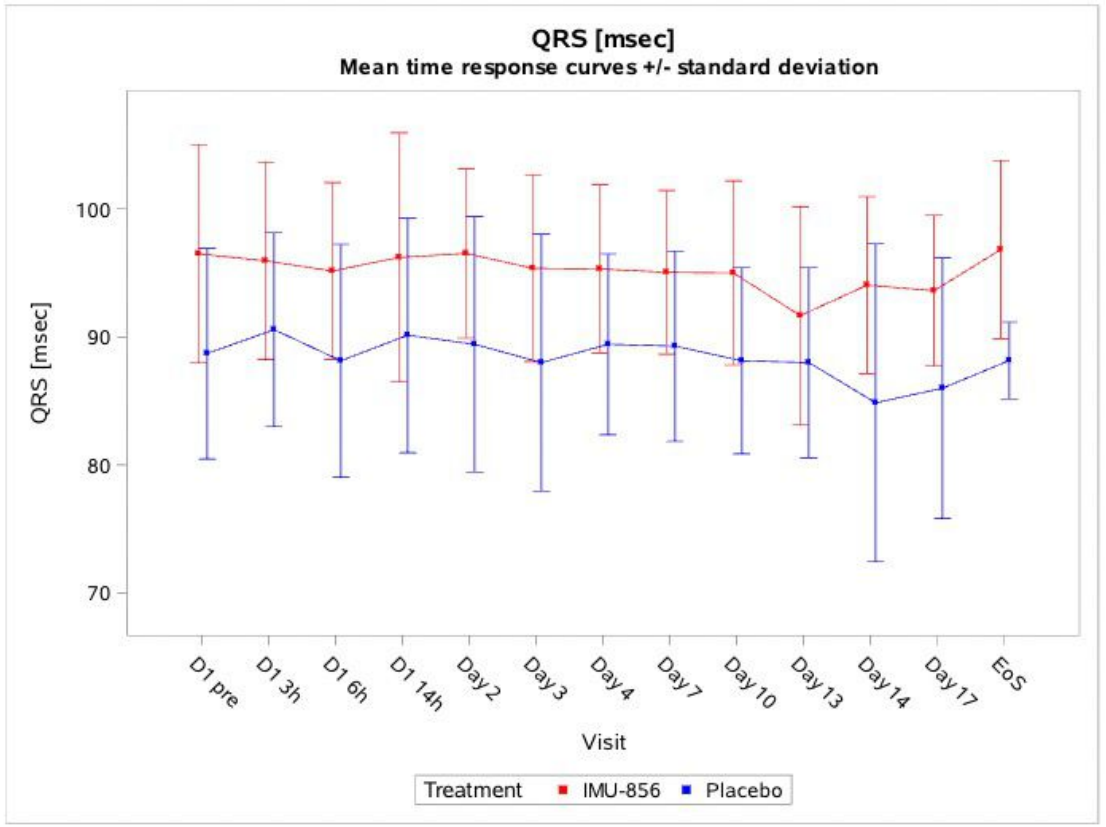


ECG: electrocardiogram

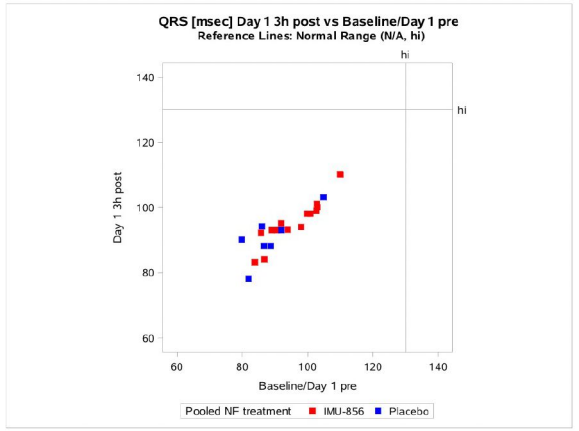
12-Lead Electrocardiograms: QRS Duration

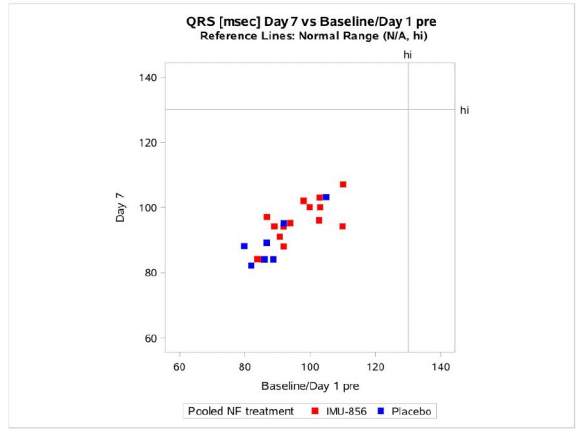
Part B, Cohorts 7, 7N-9N

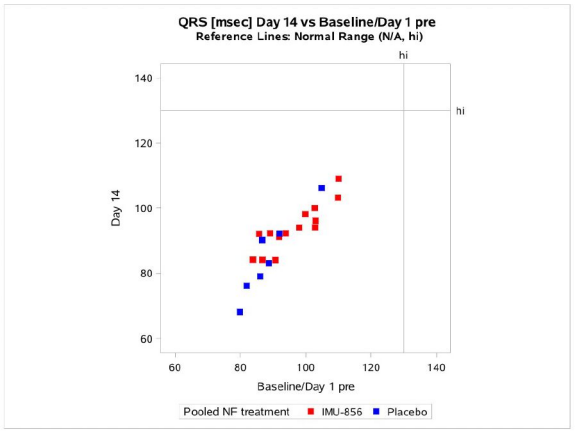
12-Lead ECGs Over Time
QRS Duration

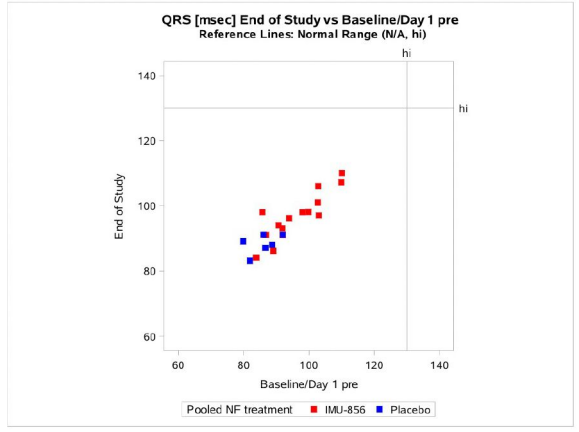


Individual 12-Lead ECGs
QRS Duration







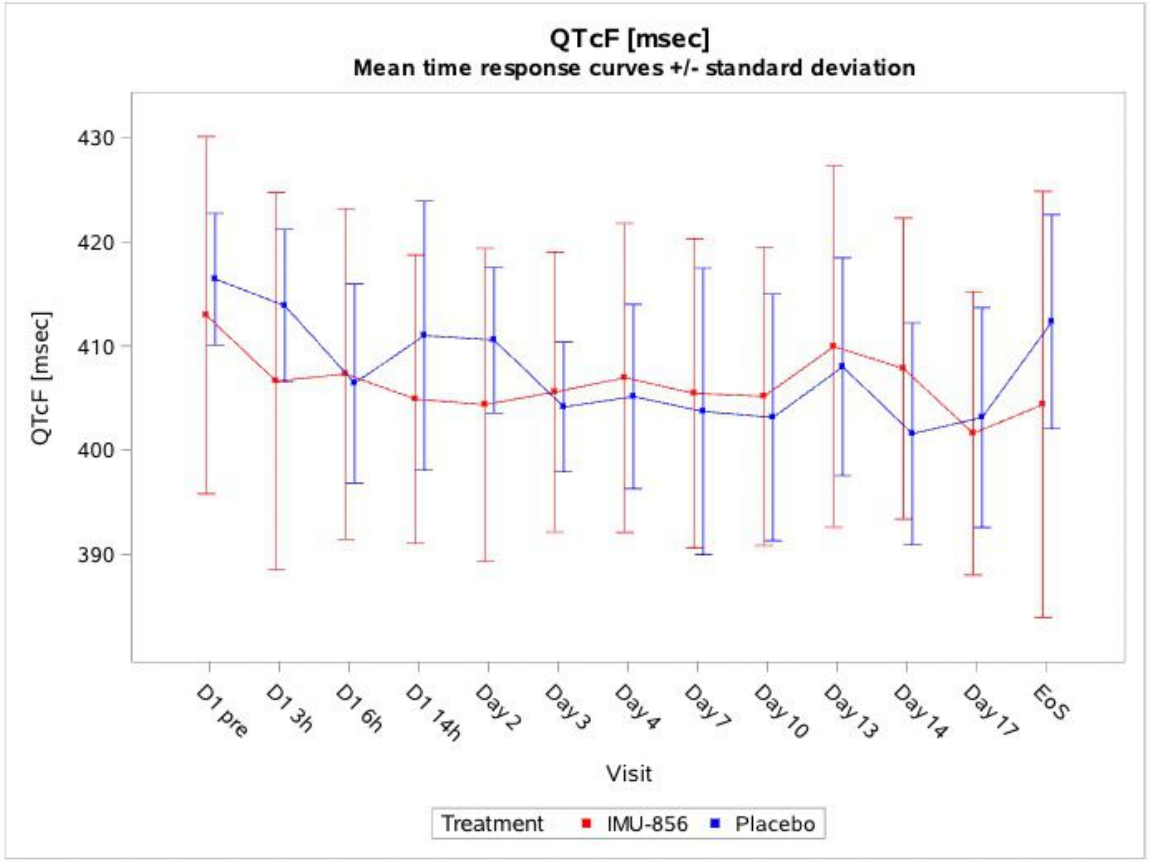


ECG: electrocardiogram

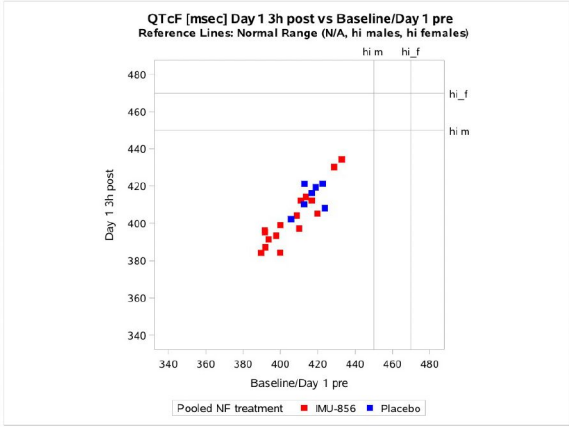
12-Lead Electrocardiograms: QTcF Interval

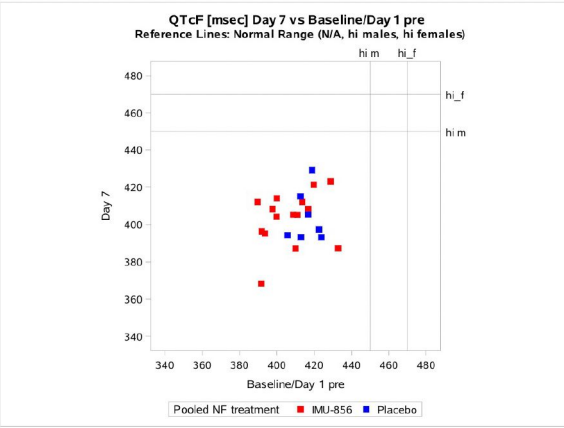
Part B, Cohorts 7, 7N-9N

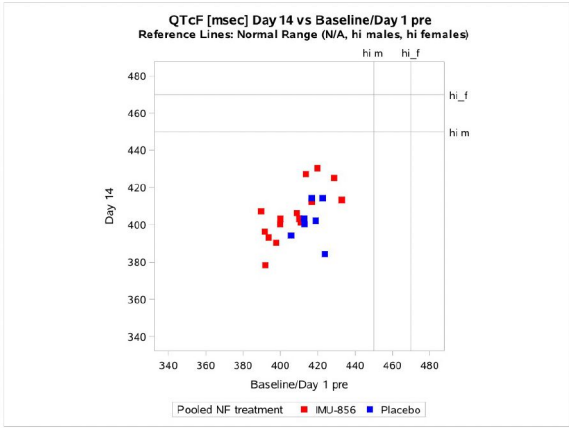
12-Lead ECGs Over Time
QTcF Interval

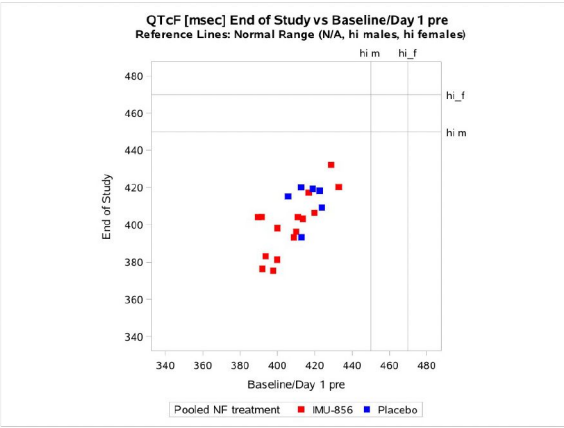


Individual 12-Lead ECGs
QTcF Interval









ECG: electrocardiogram

03

Phase 1 Clinical Trial of IMU-856

Extended Information Section: Part C – Evaluation of 28-Day Multiple Ascending Doses in Patients with Celiac Disease

Ongoing First-in-Human Study

Part C: IMU-856 in Patients with Celiac Disease During Periods of GFD and Gluten Challenge

Eligibility Criteria

- Age 18 to 65 years (inclusive)
- Biopsy proven diagnosis of Celiac Disease for at least 12 months:
  - Successful adherence to GFD for at least 12 months
  - Negative immunoglobulin A (IgA)-transglutaminase 2 (TG2) serology
  - No signs of malabsorption
  - No refractory Celiac Disease
  - No neurological/skin manifestations of Celiac Disease

Key Objectives/Endpoints

- <u>Primary:</u>
  - Safety and tolerability
- <u>Secondary:</u>
  - Trough plasma concentrations of IMU-856
  - Effects on gastrointestinal architecture and inflammation during periods of GFD and gluten challenge
- <u>Exploratory:</u>
  - Pharmacodynamic markers (non-invasive markers for epithelial damage, inflammation and intestinal permeability)
  - Patient Reported Outcomes

GFD: Gluten-free Diet

Immunic THERAPEUTICS

Phase 1 Clinical Trial of IMU-856

Part C in Celiac Disease Patients

Cohort	Planned Participants Total	Planned Participants IMU-856	Planned Participants Placebo	Study Drug Dose	Dosing Regimen
10	18	12	6	80 mg QD	28 days
11	24	16	8	160 mg QD	28 days
Total	42	28	14		

QD: quaque die = once-daily;