Immunic Therapeutics

IMU-935: Phase 1 SAD/MAD Data in Healthy Human Subjects and Preclinical Update

NASDAQ: IMUX | December 14, 2021

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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.

Development Pipeline

Program	Target	Preclinical	Phase 1	Phase 2	Phase 3	Key 2021/22 Milestones
vidofludimus calcium (IMU-838)	DHODH	Relapsing Multiple Sclerosis (RMS)				▪ Phase 2 UC: top-line data expected in Q2/2022
		Progressive Multiple Sclerosis (PMS)				
		Ulcerative Colitis (UC)				
		Crohn's Disease (CD)				
		Primary Sclerosing Cholangitis (PSC)				
IMU-935	RORγt	Psoriasis				▪ Phase 1b psoriasis: initial data expected in Q2/2022
		Castration-Resistant Prostate Cancer (CRPC)				▪ Phase 1 CRPC: initial data expected in Q3/2022
		Guillain-Barré Syndrome (GBS)				
IMU-856	Intestinal Barrier Function	Gastrointestinal Diseases				▪ Phase 1 healthy volunteers: unblinded SAD/MAD safety data expected in Q3/2022

▪ Completed or ongoing ▪ In preparation or planned

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IMU-935: Phase 1 SAD/MAD Data in Healthy Human Subjects and Preclinical Update

01 **Phase 1 Clinical Trial of IMU-935**
- Trial Design and Status
- Results Part A: Single Ascending Doses
- Results Part B: Multiple Ascending Doses
- Ongoing Part C in Psoriasis Patients

02 Newly Obtained *In Vivo* Data

03 Summary

Autoimmune Diseases and IMU-935

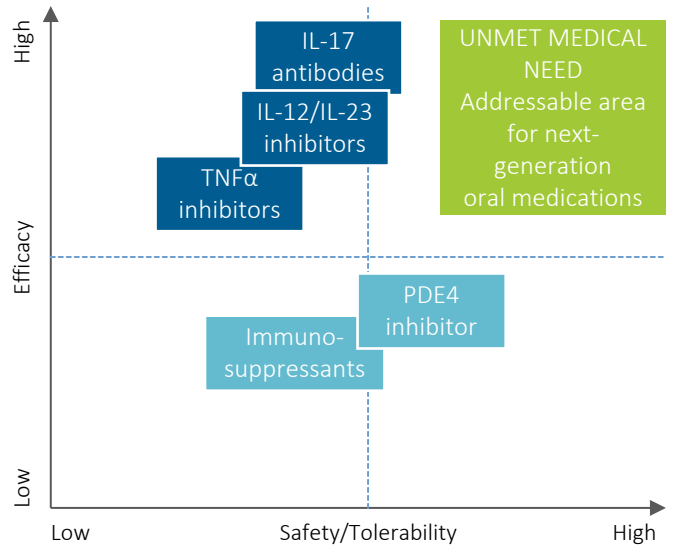
IL-17 in Autoimmune Diseases

- Autoimmune diseases affect millions of patients worldwide[1]
- Th17/IL-17/RORγt axis plays an important role in auto immunity-related diseases[2]
- Antibodies targeting this axis corroborate IL-17's role in autoimmune diseases, but are more complex, costly and less patient friendly than oral drugs[2]

Goal

- Develop an orally available and potent IL-17 inhibitor for the safe and efficacious treatment of autoimmune diseases
- Small molecule inhibitor of the pathologic functions of RORγt in autoimmune diseases without affecting physiological functions of RORγt

Unmet Need in Psoriasis Care



Strong Medical Need for Oral IL-17 Pathway Inhibitors such as IMU-935

[1] Rose, Noel R. American journal of epidemiology 2016; 183.5: 403-406 [2] Fasching, Patrizia, et al. Molecules 2017 22.1: 134
Th: T helper; IL: interleukin; TNF: tumor necrosis factor; PDE4: phosphodiesterase type 4; RORγ: retinoic acid receptor-related orphan nuclear receptor gamma

01

Phase 1 Clinical Trial of IMU-935

Trial Design and Status

Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

Ongoing Part C in Psoriasis Patients

01

Phase 1 Clinical Trial of IMU-935

Trial Design and Status

Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

Ongoing Part C in Psoriasis Patients

Clinical Trial Design Phase 1 IMU-935 and Current Status

PART A

Evaluation of single ascending doses (SAD)

—

Healthy volunteers randomized to receive single dose of either IMU-935 or placebo

- Dose escalation completed: 100, 200, 300 and 400 mg of IMU-935
- Final PK analysis ongoing
- 79 subjects enrolled
- IMU-935 was well-tolerated and showed dose-linear PK

PART B

Evaluation of multiple ascending doses (MAD)

—

Healthy volunteers randomized to receive 14-day treatment of either IMU-935 or placebo

- Dose escalation completed: 150 mg QD and 150 mg BID of IMU-935
- Final PK analysis ongoing
- 15 subjects enrolled
- IMU-935 was well-tolerated and steady-state was achieved after 3-6 days of dosing

PART C

Evaluation of moderate-to-severe psoriasis patients receiving 28-day treatment of either IMU-935 or placebo

- 150 mg QD and 150 mg BID of IMU-935
- Approximately 52 patients planned to be enrolled
- Initial data expected to be available in Q2/2022

PK: pharmacokinetic; QD: quaque die = once-daily; BID: bis in die = two times daily

01

Phase 1 Clinical Trial of IMU-935

Trial Design and Status

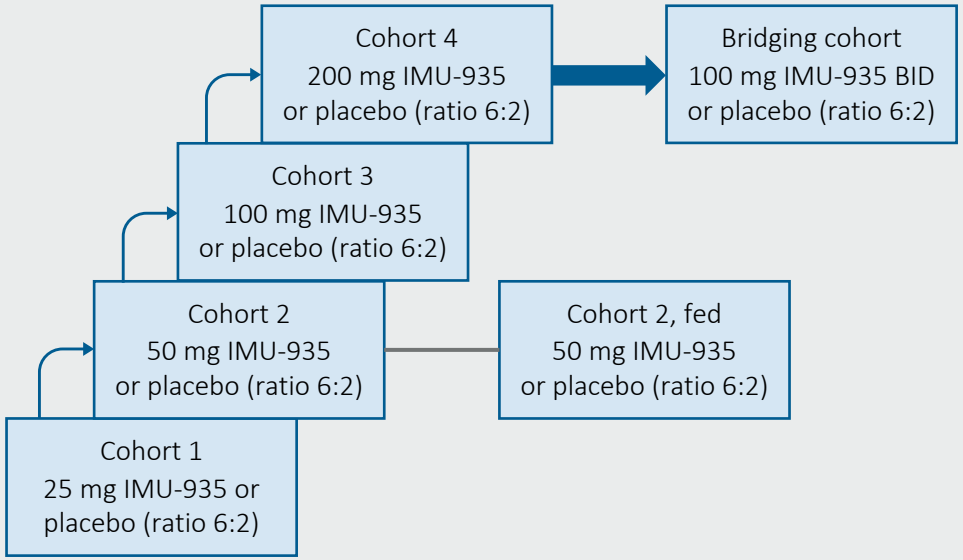
Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

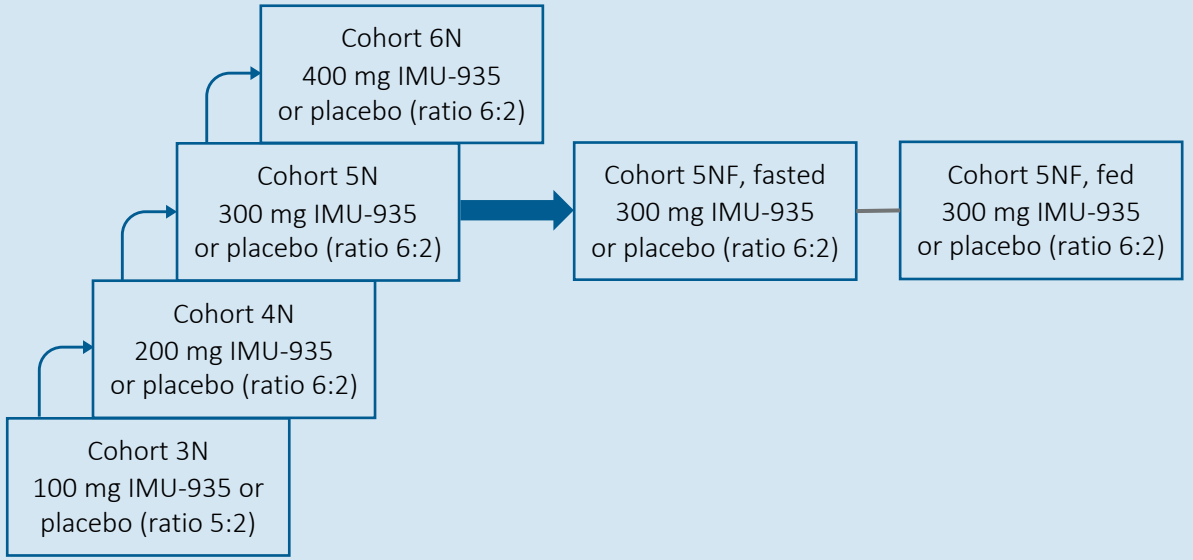
Ongoing Part C in Psoriasis Patients

Dose Escalation Scheme
Part A: Single Ascending Doses

Part A: Initial Lipid-Based Pilot Formulation



Part A-N: Powder-in-Capsule Formulation



BID: bis in die = two times daily
If no dosing regimen is specifically mentioned, then once daily administration in fasted condition was performed.
For full disclosure, data for the Part A pilot formulation can be found in the Extended Information section of this presentation, but will not be presented. The presentation will focus on the powder-in-capsule formulation (Part A-N).

Summary of Safety and Tolerability Findings
Part A-N

Single Doses of IMU-935 in Healthy Human Subjects Were Found to Have a Favorable Safety and Tolerability Profile

- 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 or 12-lead electrocardiograms as compared to placebo

Most Common Treatment-Emergent Adverse Events
Part A-N

MedDRA Preferred Term	Number (%) of subjects with TEAEs occurring in more than 2 subjects [Number of TEAEs reported]							
	100 mg (N=5)	200 mg (N=6)	300 mg (N=6)	300 mg fasted (N=6)	300 mg fed (N=6)	400 mg (N=6)	Active (N=29)	Placebo (N=10)
Headache	-	1 (17%) [1]	-	3 (50%) [5]	1 (17%) [1]	1 (17%) [1]	5 (17%) [8]	3 (30%) [4]
Dizziness	-	-	2 (33%) [2]	1 (17%) [1]	-	1 (17%) [1]	4 (14%) [4]	-
Catheter site pain	1 (20%) [1]	2 (33%) [2]	-	-	-	-	3 (10%) [3]	1 (10%) [1]
Constipation	-	1 (17%) [1]	-	-	-	2 (33%) [2]	3 (10%) [3]	-
Fatigue	-	-	-	2 (33%) [2]	-	-	2 (7%) [2]	1 (10%) [1]

Single doses of IMU-935 using the powder-in-capsule formulation were safe and well-tolerated with headache, dizziness, catheter site pain, constipation and fatigue being the most common TEAEs.

TEAE: Treatment-Emergent Adverse Event
Displayed are TEAEs that occurred in more than 2 subjects. The treatments 300 mg fasted and fed were given (in two periods) to the same subjects of cohort 5NF.

Summary of Safety and Tolerability Profile
Part A-N

- Serious AEs (SAE)
  - None (N=0)
- Treatment discontinuations due to AEs
  - None (N=0)
- Moderate TEAEs
  - Placebo (N=1/10; 10%)
    - Headache (2 events, unrelated)
  - IMU-935 (N=4/29, 14%)
    - Nausea, toothache, skin abrasion, AST increased (all unrelated)
    - Headache (related)

      Occurred after a single dose of 200 mg IMU-935 on day 2, resolved with treatment after 1 day
- Severe TEAEs
  - IMU-935 (N=1/29; 3%)
    - Blood creatine kinase increased (unrelated)

      Occurred after a single dose of 300 mg IMU-935 in the fed state, only elevated at end-of-study visit (day 14) and related to a rock climbing event

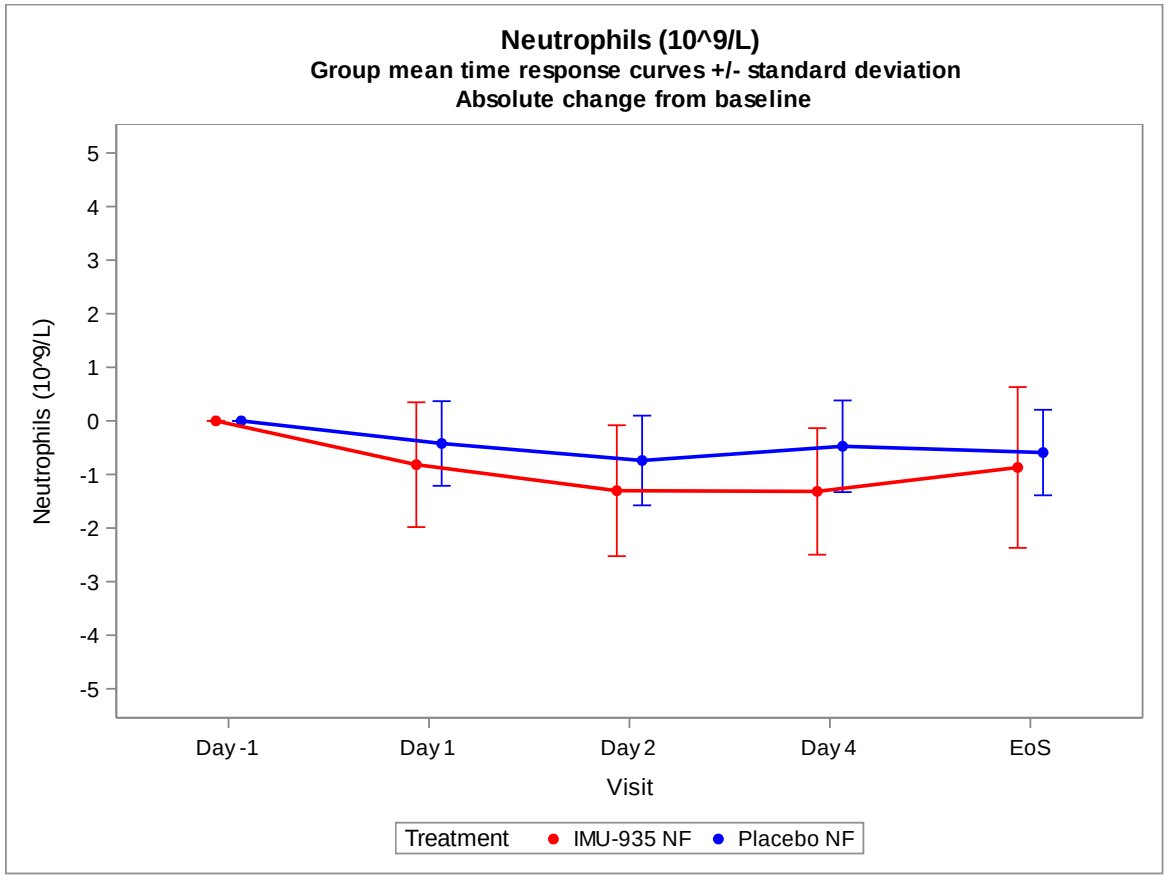
- Summary of laboratory variables
  - No trend for changes over time for any parameter
  - Shift tables showed no trend of individual changes beyond the normal range for any parameter
- TEAEs associated with laboratory abnormalities
  - Placebo (N=1/10; 10%)
    - Lipase increase (related)
  - IMU-935 (N=3/29; 10%)
    - All changes of laboratory parameters in these subjects have plausible explanations or can be clearly related to life events

      (for full disclosure, more detailed information about these events are contained in the Extended Information section of this slide deck)
- TEAEs associated with vital signs
  - None (N=0)
- TEAEs associated with 12-lead ECGs
  - None (N=0)

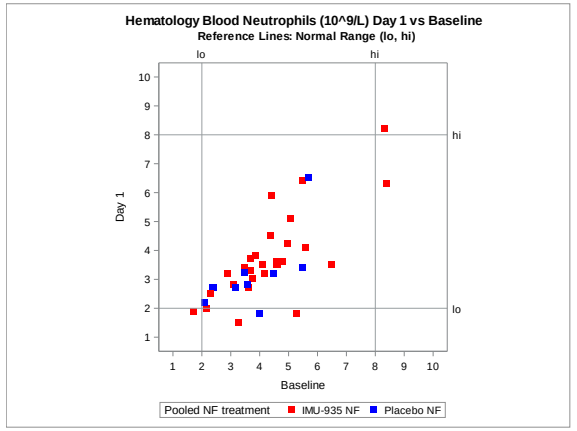
AE: Adverse Event; SAE: Serious Adverse Event; TEAE: Treatment-Emergent Adverse Event; ECG: electrocardiogram; AST: Aspartate Aminotransferase

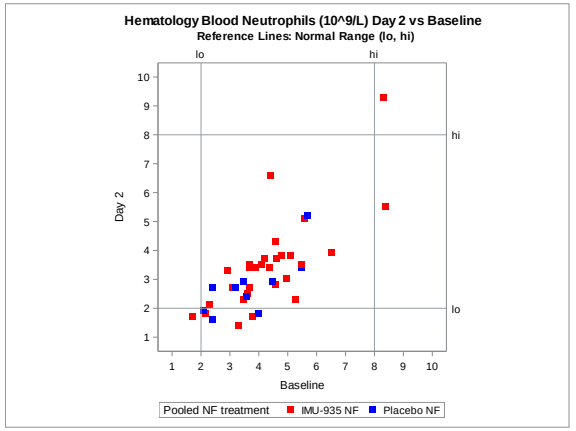
Laboratory Parameters: No Change in Neutrophils Compared to Placebo
Part A-N

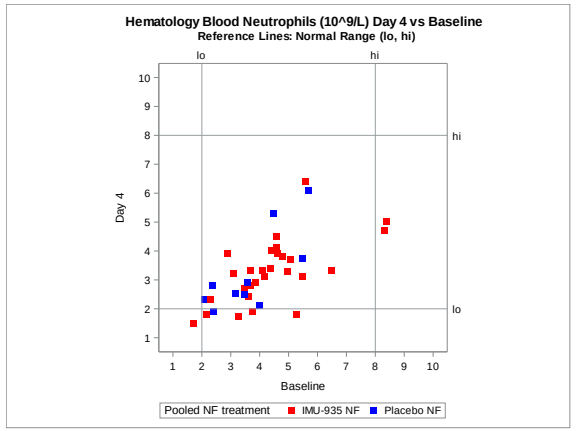
Laboratory Values Over Time
Hematology - Neutrophils

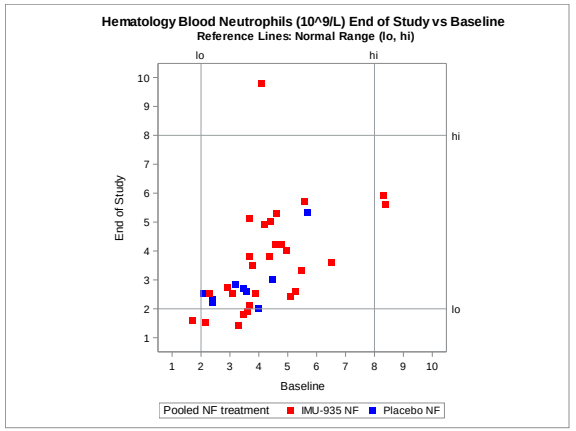


Individual Laboratory Values
Hematology - Neutrophils



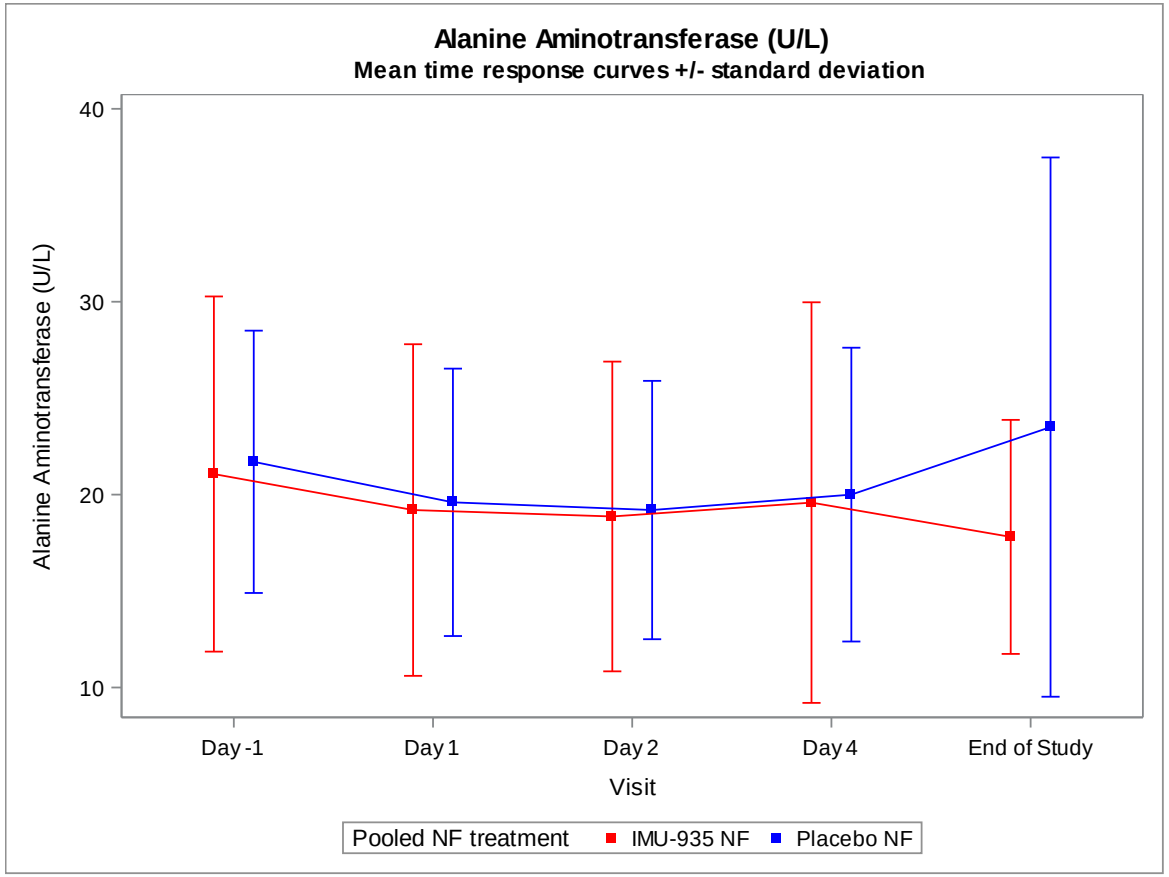




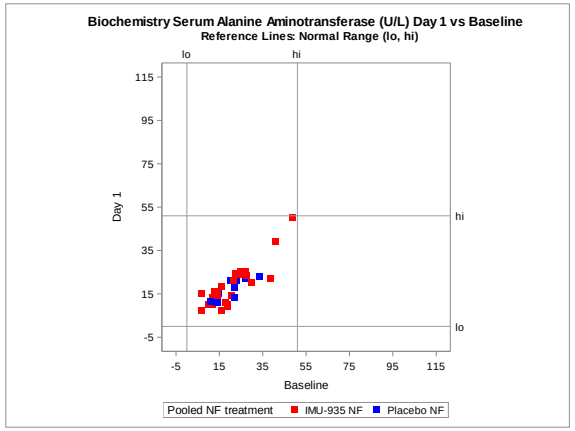


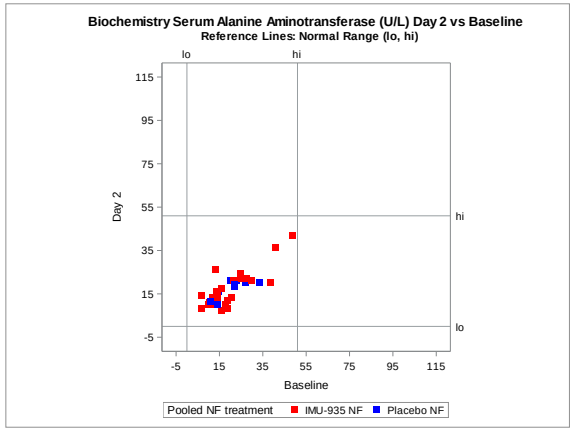
Laboratory Parameters: No Increase of ALT Compared to Placebo
Part A-N

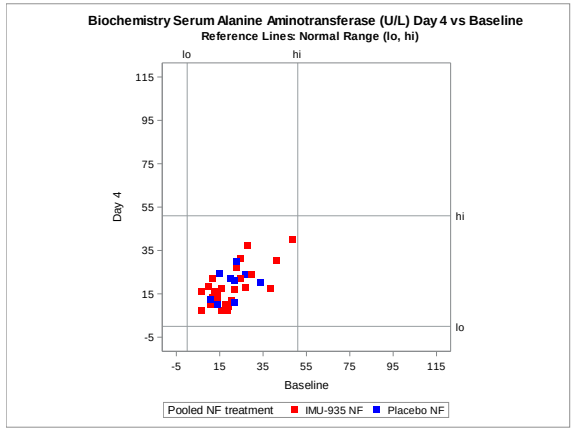
Laboratory Values Over Time
Biochemistry - ALT

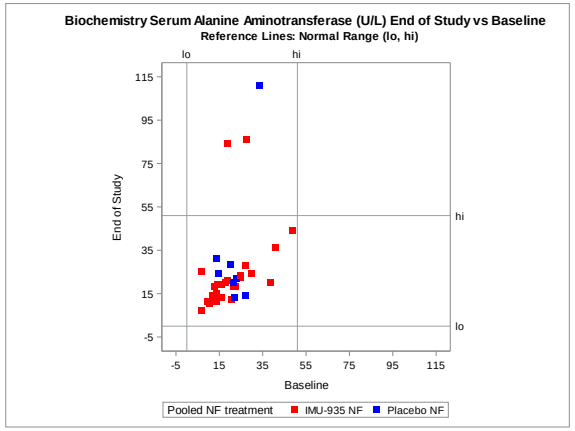


Individual Laboratory Values
Biochemistry - ALT







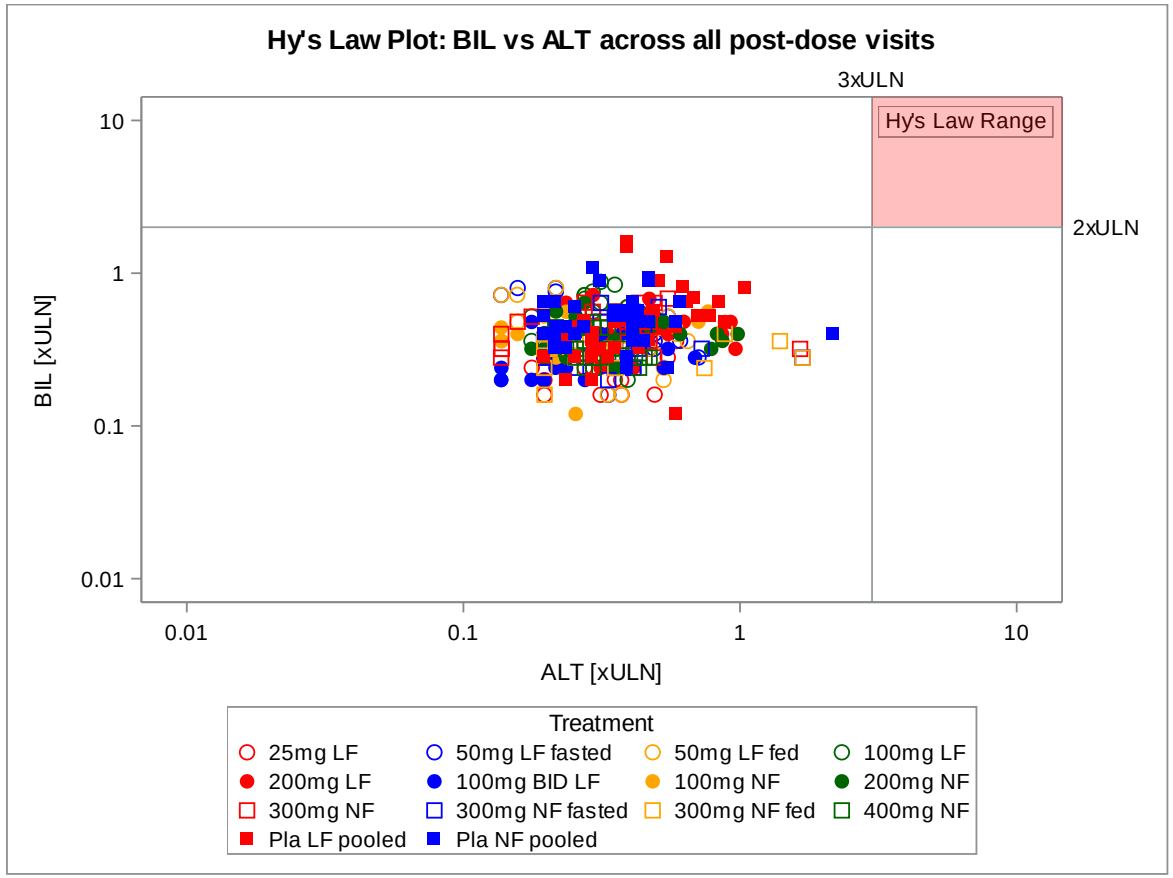


ALT: Alanine Aminotransferase

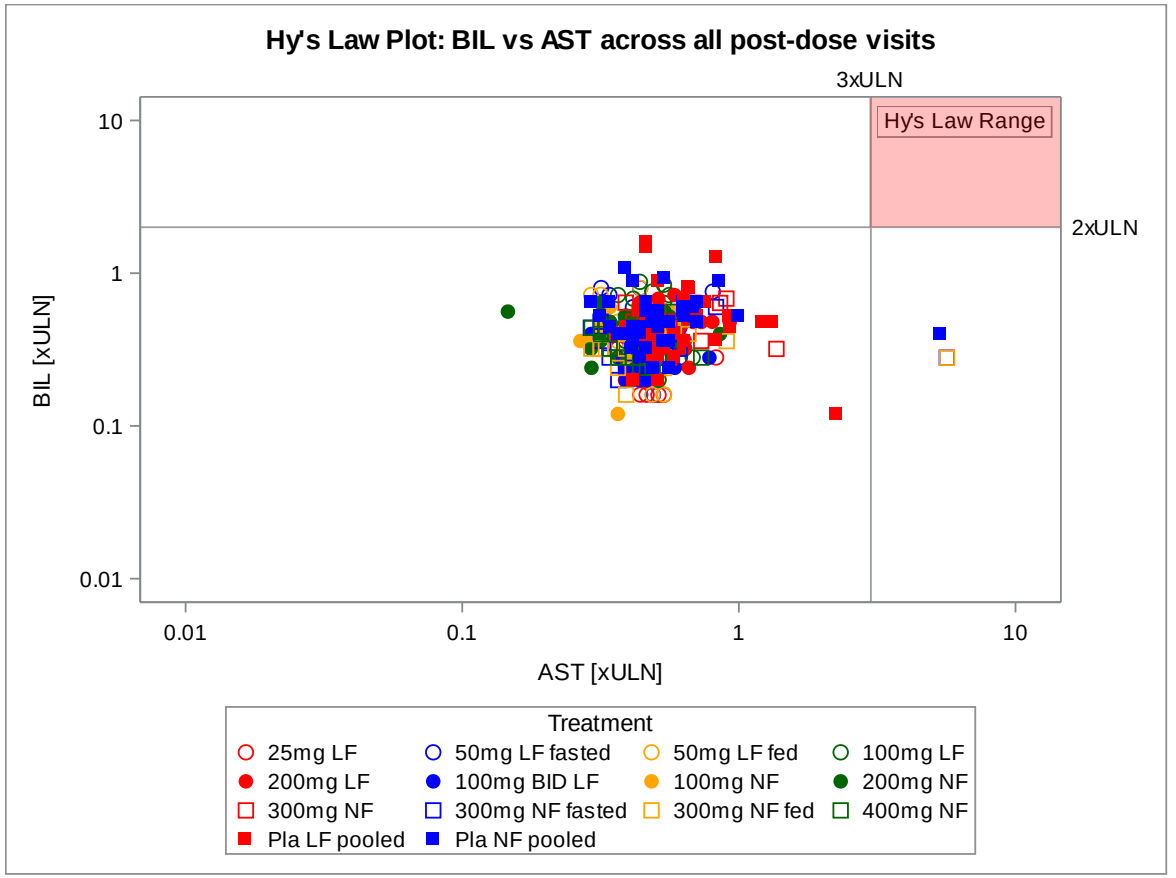
Laboratory Parameters: No Hy's Law Range Cases Observed

Part A and Part A-N Combined

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; Pla: Placebo

Conclusions

Part A-N: Single Ascending Doses

- The powder-in-capsule formulation provided favorable pharmaceutical properties in Part A-N of this clinical trial.
- Its favorable safety and tolerability allowed smooth transition from Part A (SAD) to Part B (MAD) in healthy human subjects.

01

Phase 1 Clinical Trial of IMU-935

Trial Design and Status

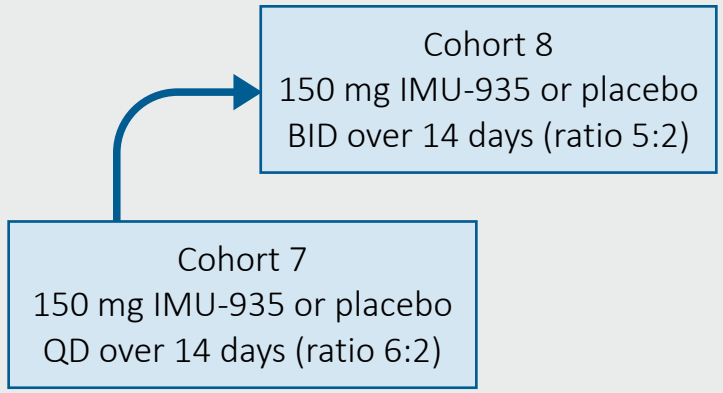
Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

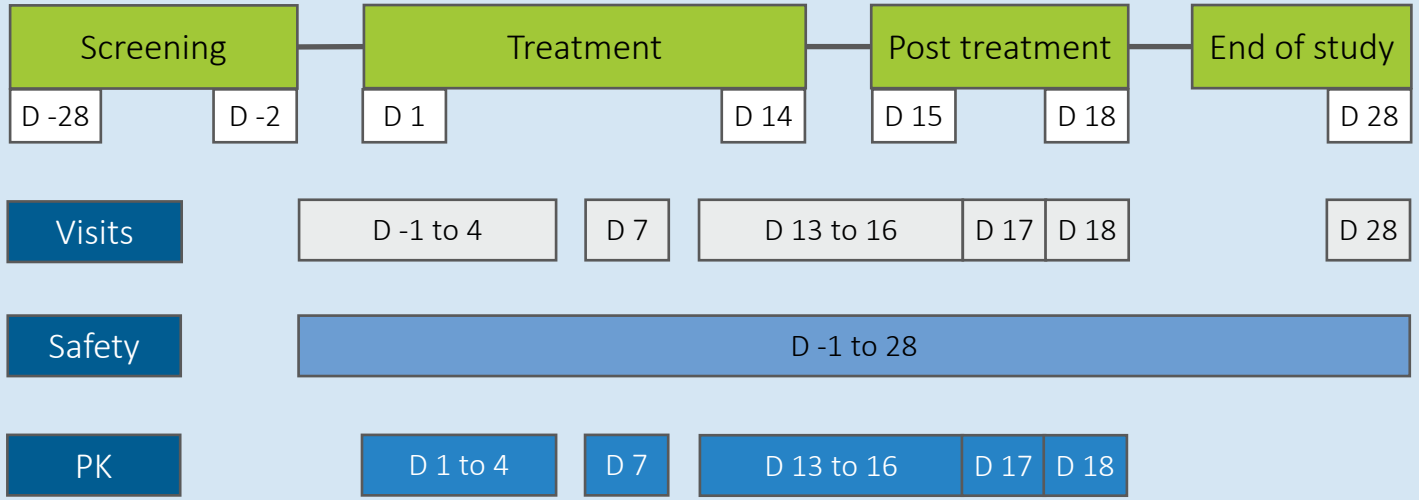
Ongoing Part C in Psoriasis Patients

Design of Part B: Multiple Ascending Doses of IMU-935

Dose Escalation Scheme



Study Period



QD: quaque die = once-daily; BID: bis in die = two times daily; D: day
Part B was performed with the powder-in-capsule formulation only.

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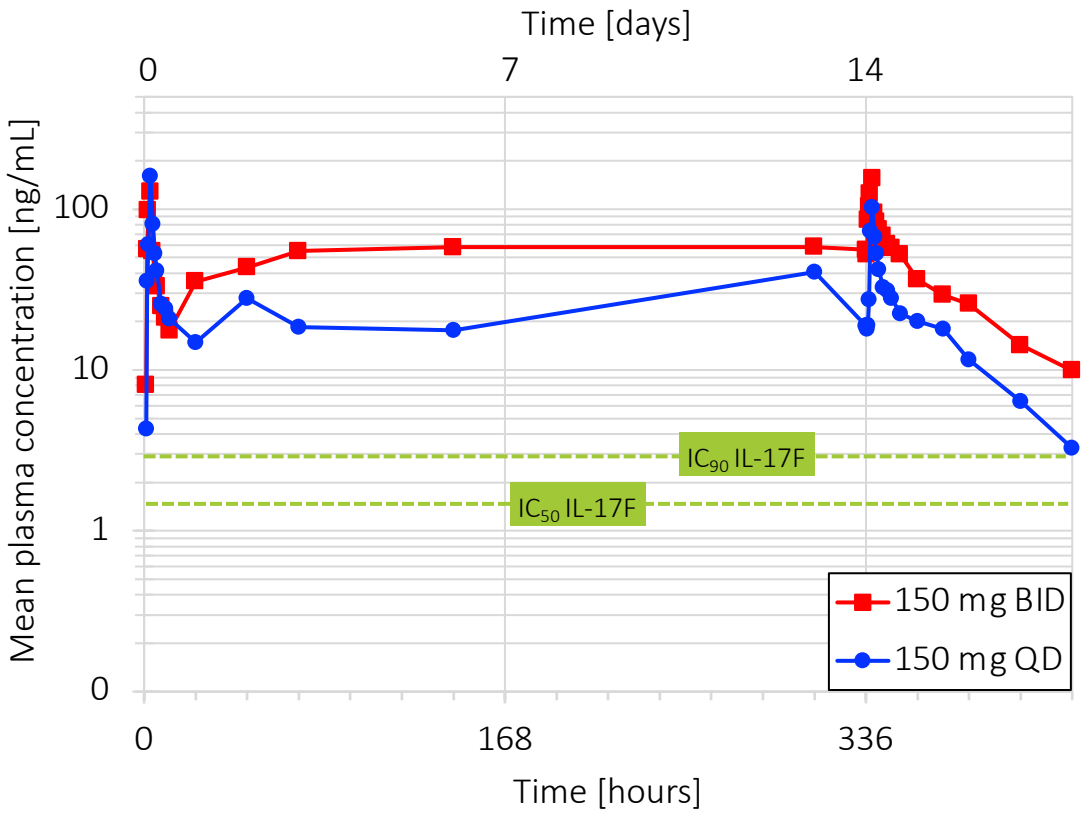
Pharmacokinetic Results

Part B: Summary of QD and BID Dosing Regimen for IMU-935

IMU-935 concentration time profiles (log-linear scale)



Favorable PK Properties for IMU-935 at Steady-State Observed

Pharmacokinetic parameters in steady-state (mean)	150 mg QD	150 mg BID
$C_{max, ss}$ (ng/mL)	124	206
$C_{min, ss}$ (ng/mL)	15.7	48.5
$T_{max, ss}$ (hr)	2.8	2.4
$t_{1/2, ss}$ (hr)	29.0	38.0
AUC_{last} (hr*ng/mL)	1540	3040

Non-compartmental analysis

- Fast achievement of steady-state within first week and stable steady-state trough levels over 14-day treatment period.
- Accumulation factors of 1.29 (150 mg QD) and 2.21 (150 mg BID) allowing predictable trough levels.

Interim data, PK analysis ongoing

QD: quaque die = once-daily; BID: bis in die = two times daily; PK: pharmacokinetic; C_{max}: maximum plasma drug concentration; T_{max}: time to reach maximum plasma concentration; hr: hours; $t_{1/2}$: half-life; AUC_{last}: area under the concentration-time curve from dosing to last measurement

Accumulation factors were calculated as the relationship of $AUC_{0\text{-}tau}$ of Day 14/Day 1 (after first dosing).

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Summary of Safety and Tolerability Findings
Part B

Daily Dosing of IMU-935 in Healthy Human Subjects Over 14 Days Was Found to Have a Favorable Safety and Tolerability Profile

- 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 adverse events regarding any laboratory parameter
- No medically relevant changes in vital signs or 12-lead electrocardiograms as compared to placebo

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Overall Summary of TEAE, SAE and AE Severity
Part B

Category	Treatment			
	150 mg QD (N=6)	150 mg BID (N=5)	Active (N=11)	Placebo (N=4)
Subjects with TEAEs, n (%)	6 (100%)	4 (80%)	10 (91%)	4 (100%)
Subjects with mild TEAEs, n (%)	6 (100%)	4 (80%)	10 (91%)	4 (100%)
Subjects with moderate TEAEs, n (%)	-	1 (20%)	1 (9%)	1 (25%)
Subjects with severe TEAEs, n (%)	-	-	-	-
Subjects with SAEs, n (%)	-	-	-	-
Subjects with TEAEs leading to withdrawal, n (%)	-	-	-	-
Number of TEAEs	15	7	22	15
Number of mild TEAEs	15	6	21	11
Number of moderate TEAEs	-	1	1	4
Number of severe TEAEs	-	-	-	-
Number of SAEs	-	-	-	-
Number of TEAEs leading to withdrawal	-	-	-	-

Daily 14-day dosing of IMU-935 using the powder-in-capsule formulation was found to be safe and well-tolerated:

- No dose-dependency in adverse events
- No SAEs
- No discontinuation due to AEs
- All mild TEAEs (except for 1 subject with moderate TEAEs in IMU-935 and placebo each)

QD: quaque die = once-daily; BID: bis in die = two times daily; TEAE: Treatment-Emergent Adverse Event; SAE: Serious Adverse Event; AE: Adverse Event

Most Common Treatment-Emergent Adverse Events
Part B

MedDRA Preferred Term	Number (%) of subjects with TEAEs occurring in more than 1 subject [Number of TEAEs reported]			
	150 mg QD (N=6)	150 mg BID (N=5)	Active (N=11)	Placebo (N=4)
Headache	2 (33%) [2]	3 (60%) [3]	5 (45%) [5]	2 (50%) [5]
Back pain	1 (17%) [1]	1 (20%) [1]	2 (18%) [2]	1 (25%) [1]
Epistaxis	2 (33%) [3]	-	2 (18%) [3]	-
Constipation	-	-	-	2 (50%) [2]
Catheter site irritation	1 (17%) [1]	-	1 (9%) [1]	1 (25%) [1]

Daily 14-day dosing of IMU-935 using the powder-in-capsule formulation was found to be safe and well-tolerated:

- Most common TEAEs were non-specific events, including headache, back pain, epistaxis, constipation and catheter site irritation

QD: quaque die = once-daily; BID: bis in die = two times daily; TEAE: Treatment-Emergent Adverse Event
Displayed are TEAEs that occurred in more than 1 subject

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Summary of Safety and Tolerability Profile
Part B

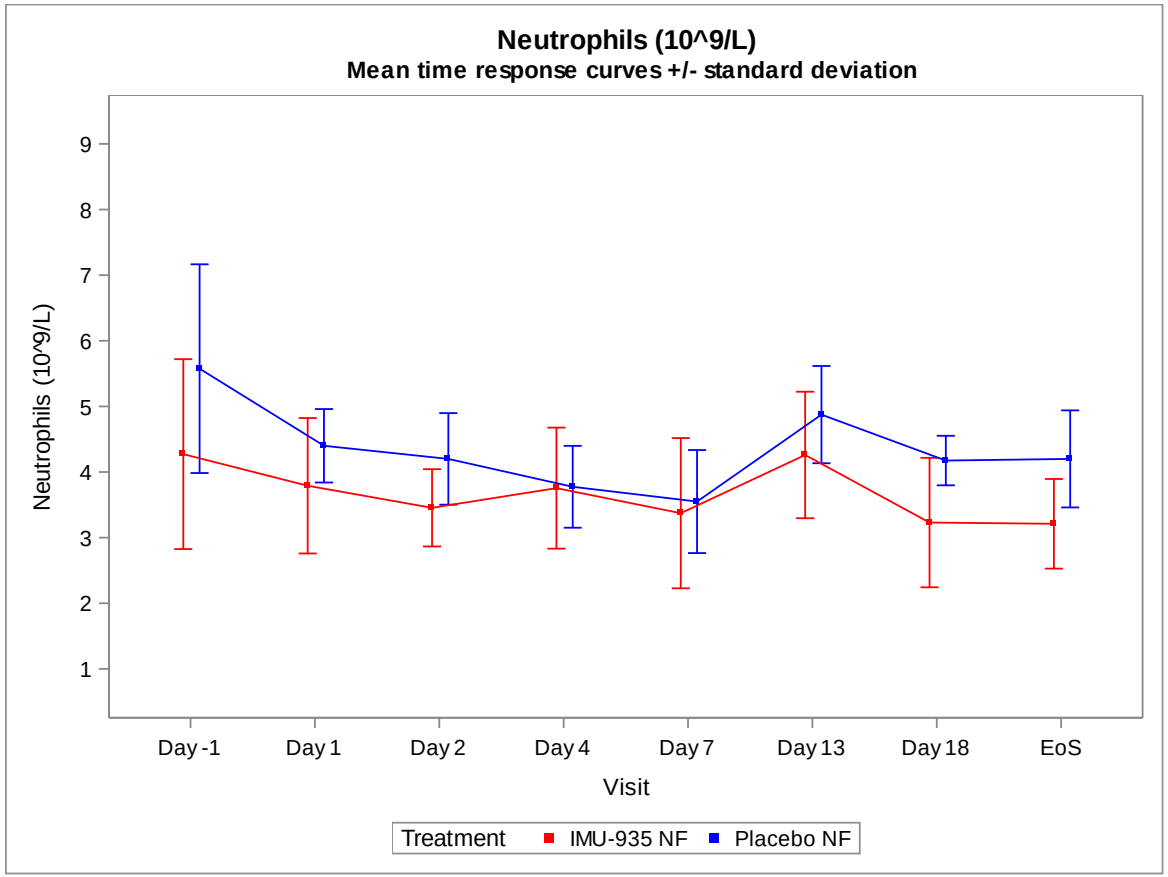
- Serious AEs (SAE)
  - None (N=0)
- Treatment discontinuations due to AEs
  - None (N=0)
- Moderate TEAEs
  - Placebo (N=1/4; 25%)
    - Constipation (related)
    - Animal bite, animal scratch and exacerbation of back pain (all unrelated)
  - 150 mg IMU-935 BID (N=1/11; 9%)
    - Catheter site reaction (unrelated)
- Severe TEAEs
  - None (N=0)
- Summary of laboratory variables
  - No trend for changes over time for any parameter
  - Shift tables showed no trend of individual changes beyond the normal range for any parameter
- TEAEs associated with laboratory abnormalities
  - None (N=0)
- TEAEs associated with vital signs
  - None (N=0)
- TEAEs associated with 12-lead ECGs
  - 150 mg IMU-935 QD (N=1)
    - PR prolongation

      Benign ECG finding in young healthy individuals
      (for full disclosure, more detailed information about this event is contained in the Extended Information section of this slide deck)

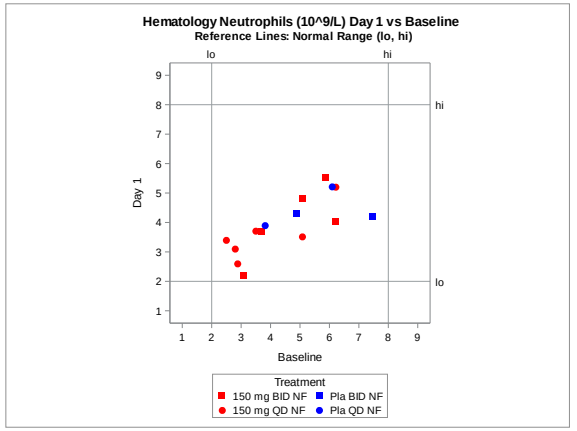
SAE: Serious Adverse Event; AE: Adverse Event; TEAE: Treatment-Emergent Adverse Event; ECG: electrocardiogram; QD: quaque die = once-daily; BID: bis in die = two times daily

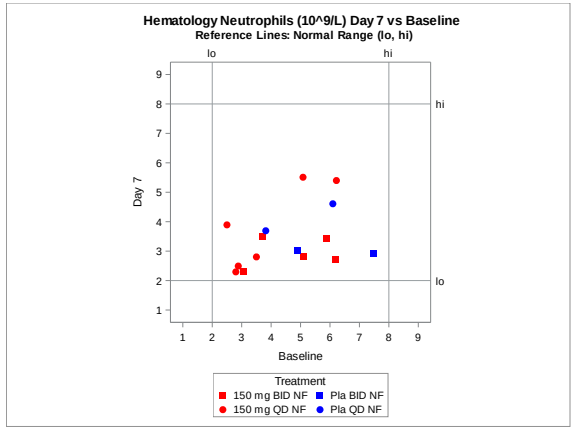
Laboratory Parameters: No Change in Neutrophils Compared to Placebo
Part B

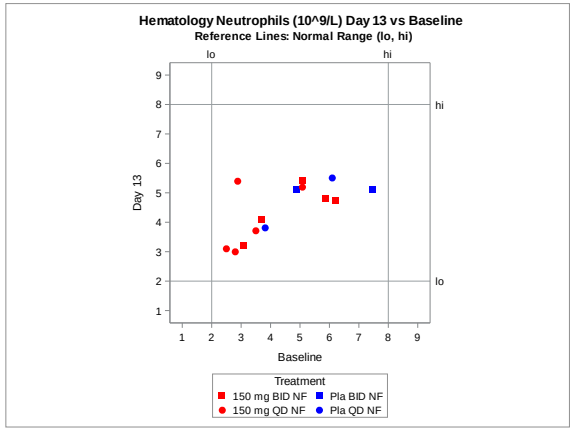
Laboratory Values Over Time
Hematology - Neutrophils

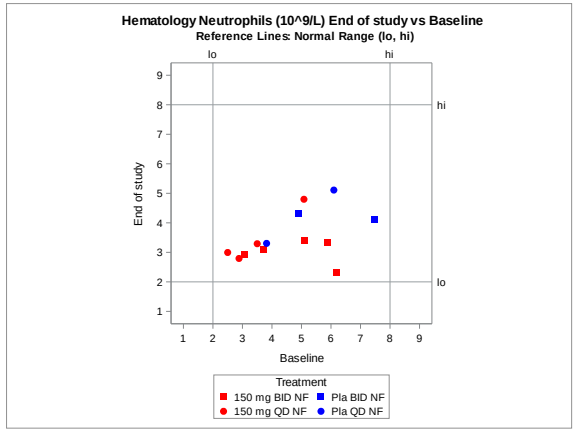


Individual Laboratory Values
Hematology - Neutrophils



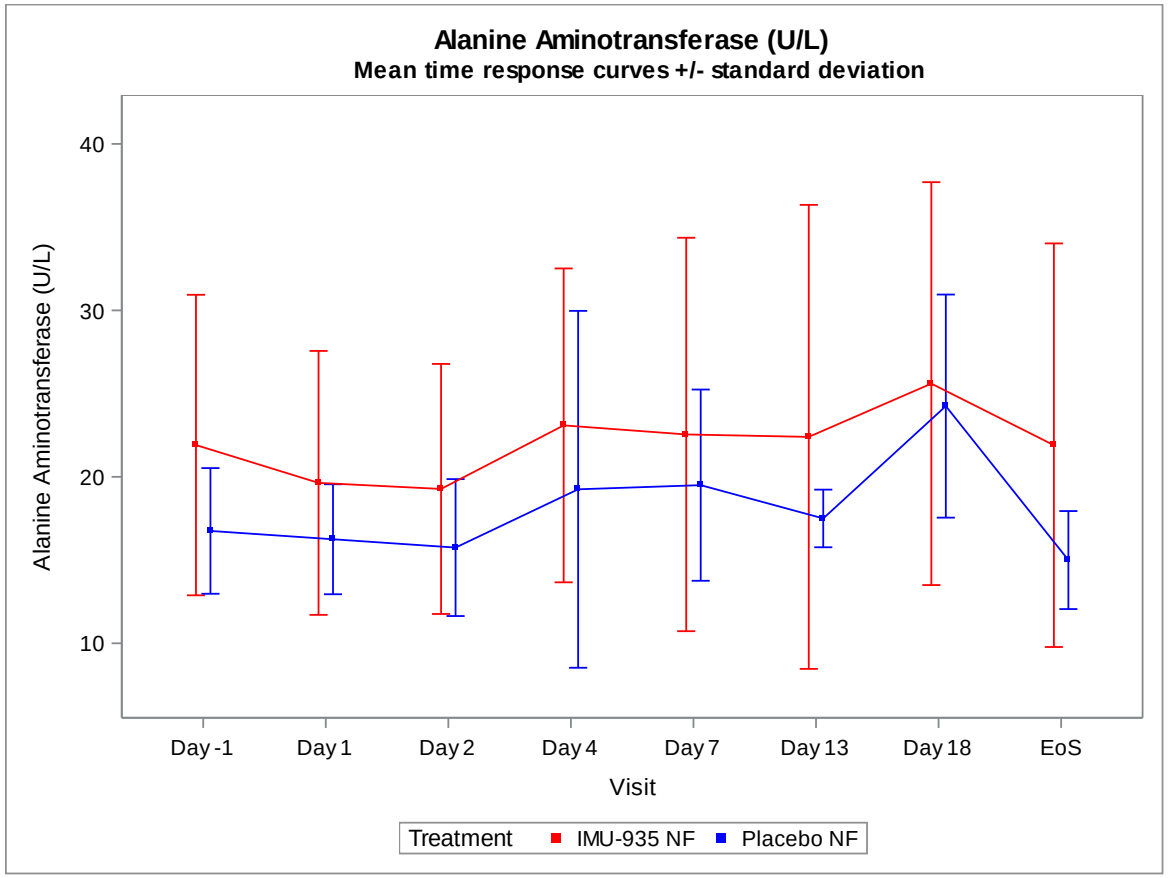




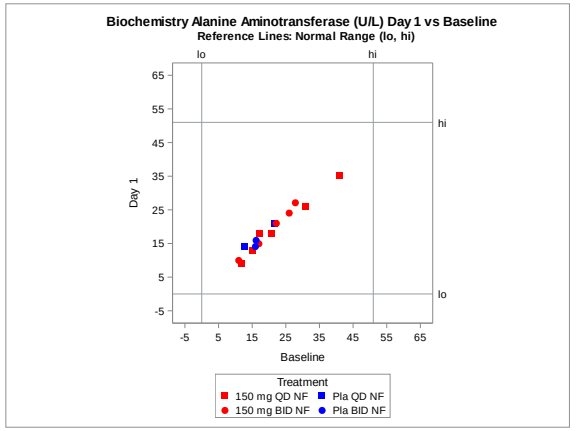


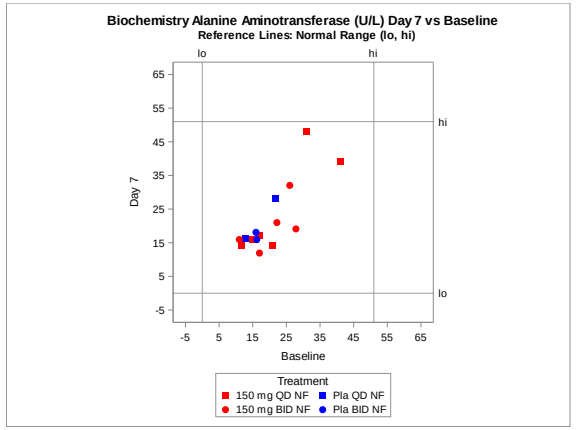
Laboratory Parameters: No Increase in ALT Compared to Placebo
Part B

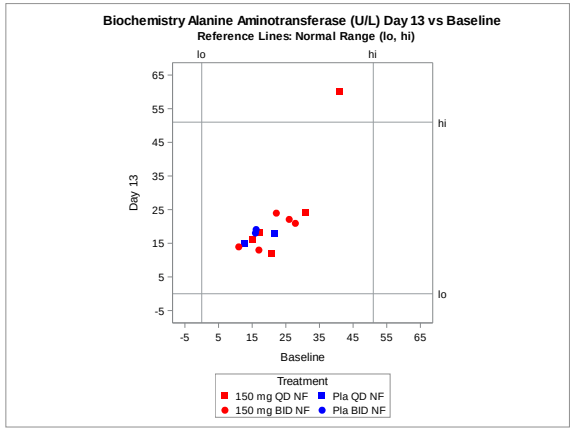
Laboratory Values Over Time
Biochemistry - ALT

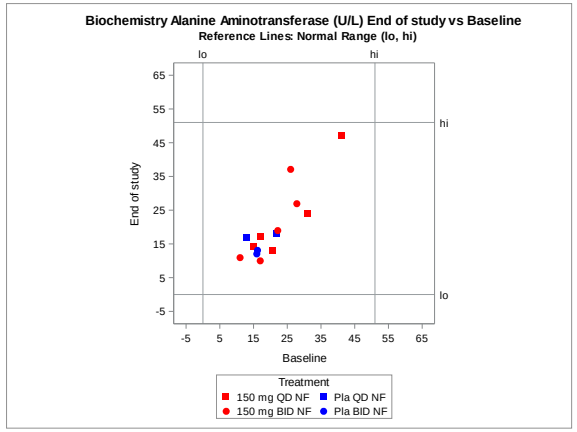


Individual Laboratory Values
Biochemistry - ALT





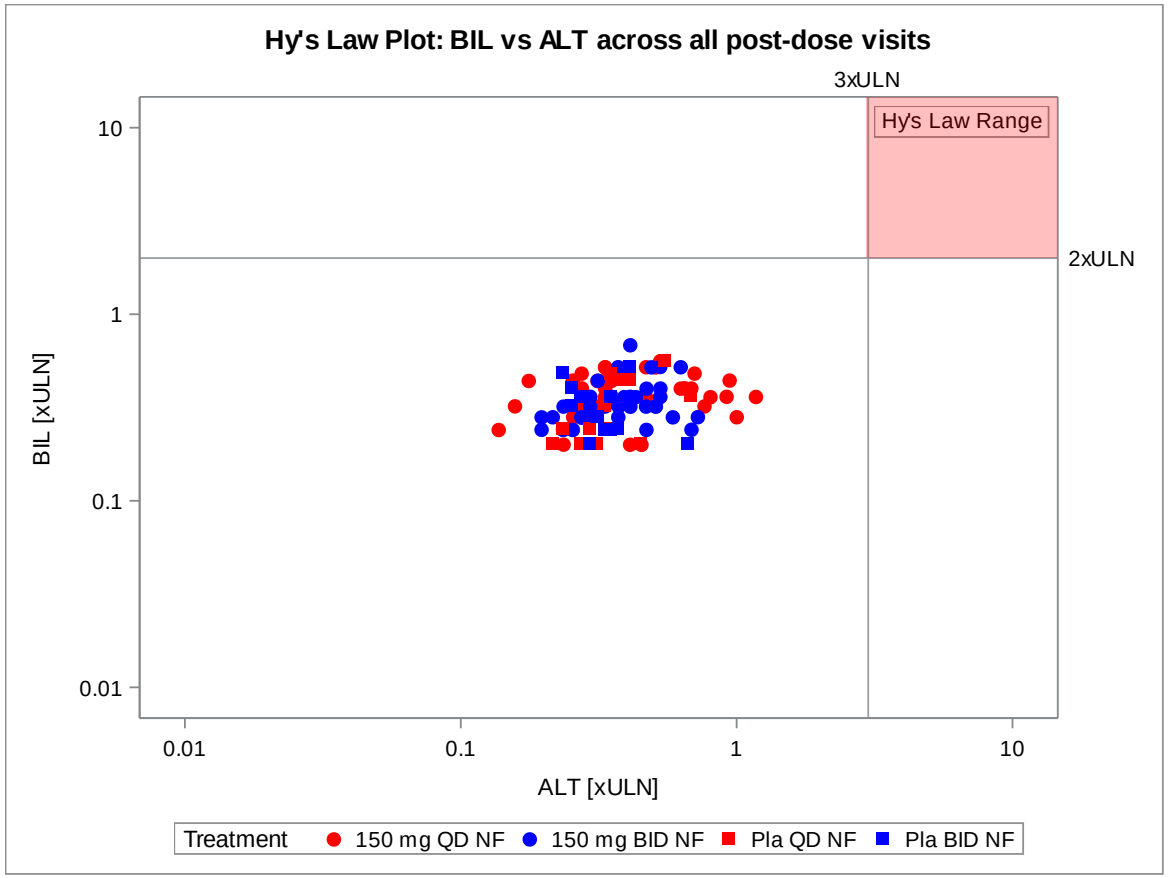




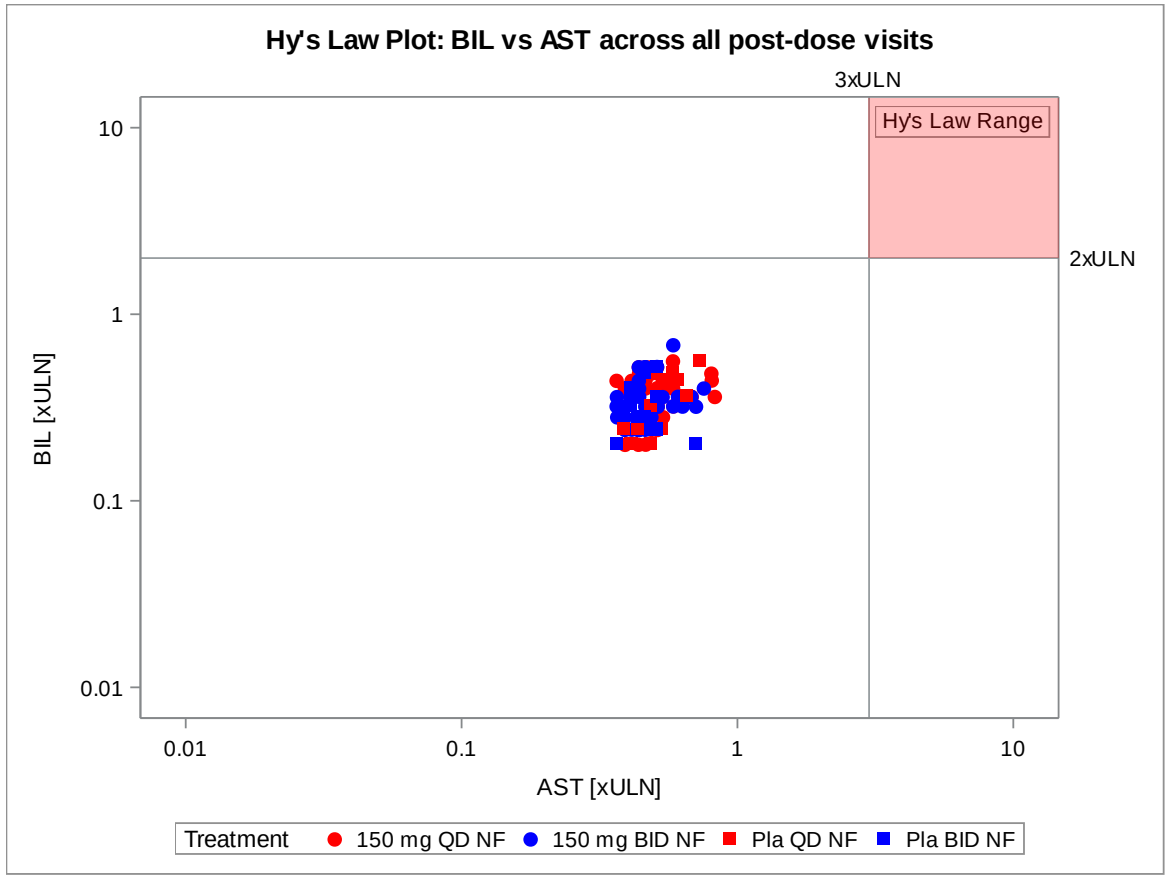
ALT: Alanine Aminotransferase

Laboratory Parameters: No Hy's Law Range Cases Observed
Part B

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; Pla: Placebo

Conclusions

Part B: 14-Days Multiple Ascending Doses

- Multiple ascending doses of IMU-935 demonstrated a favorable safety, tolerability and pharmacokinetic profile.
- This allowed smooth transition from Part B (MAD) to Part C (28-day dosing in psoriasis patients) which is currently ongoing.

01

Phase 1 Clinical Trial of IMU-935

Trial Design and Status

Results Part A: Single Ascending Doses

Results Part B: Multiple Ascending Doses

Ongoing Part C in Psoriasis Patients

Ongoing First-in-Human Study
Part C: IMU-935 in Psoriasis Patients

Study Design

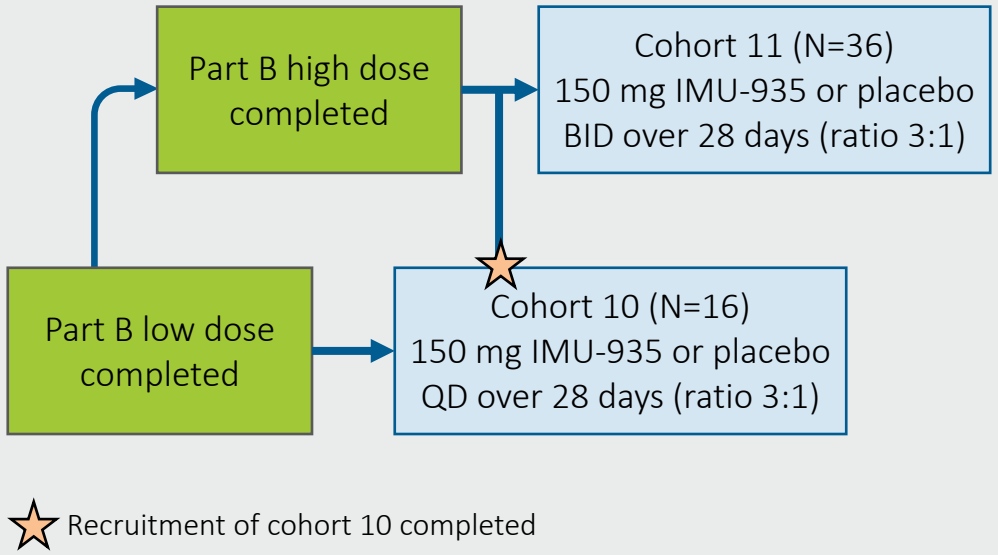
- Double-blind, placebo-controlled dose escalation study to evaluate safety, tolerability, pharmacodynamics and exploratory efficacy of IMU-935 in patients with moderate-to-severe psoriasis
- Psoriasis patients will receive 28 days of daily treatment
- Up to 52 psoriasis patients will be enrolled in 2 cohorts:
  - A cohort of 16 patients will receive a low dose of IMU-935 (150 mg QD) or placebo at a ratio of 3:1
  - A cohort of 36 patients will receive a high dose of IMU-935 (150 mg BID) or placebo at a ratio of 3:1
- Enrollment started on October 27, 2021

QD: quaque die = once-daily; BID: bis in die = two times daily

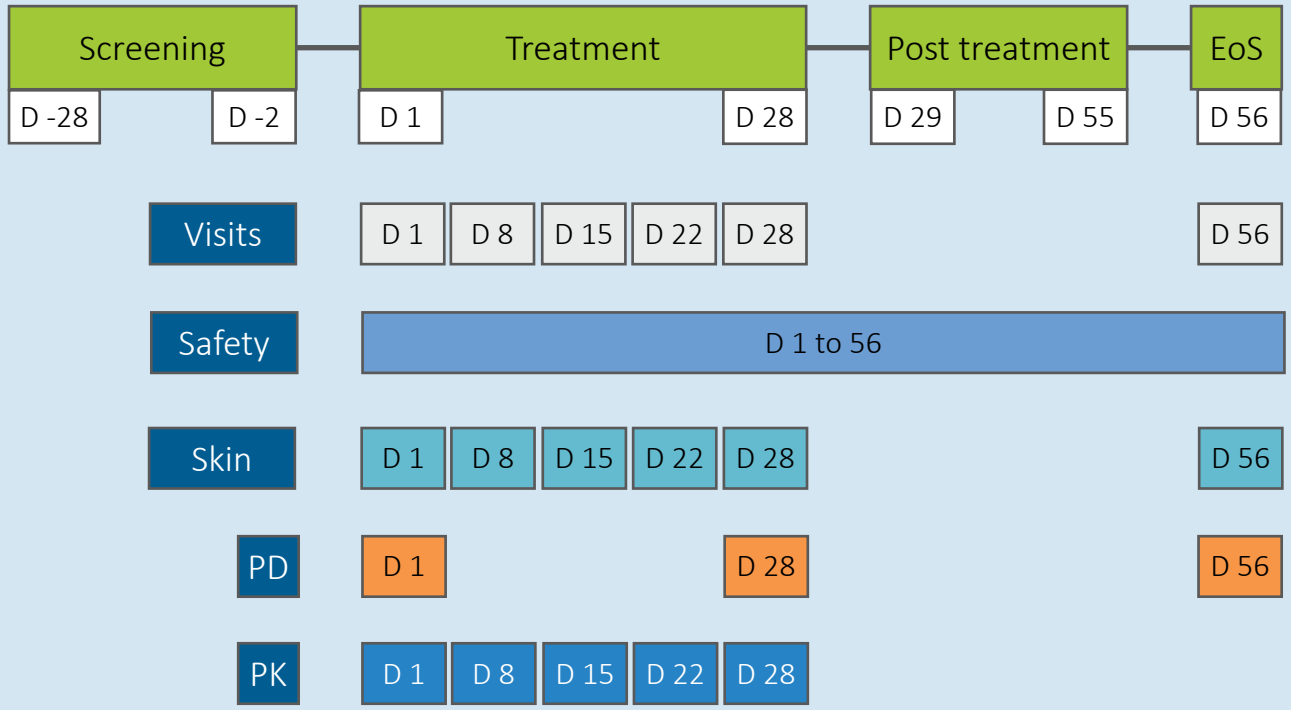
Ongoing First-in-Human Study

Part C: IMU-935 in Psoriasis Patients

Dose Escalation Scheme



Study Period



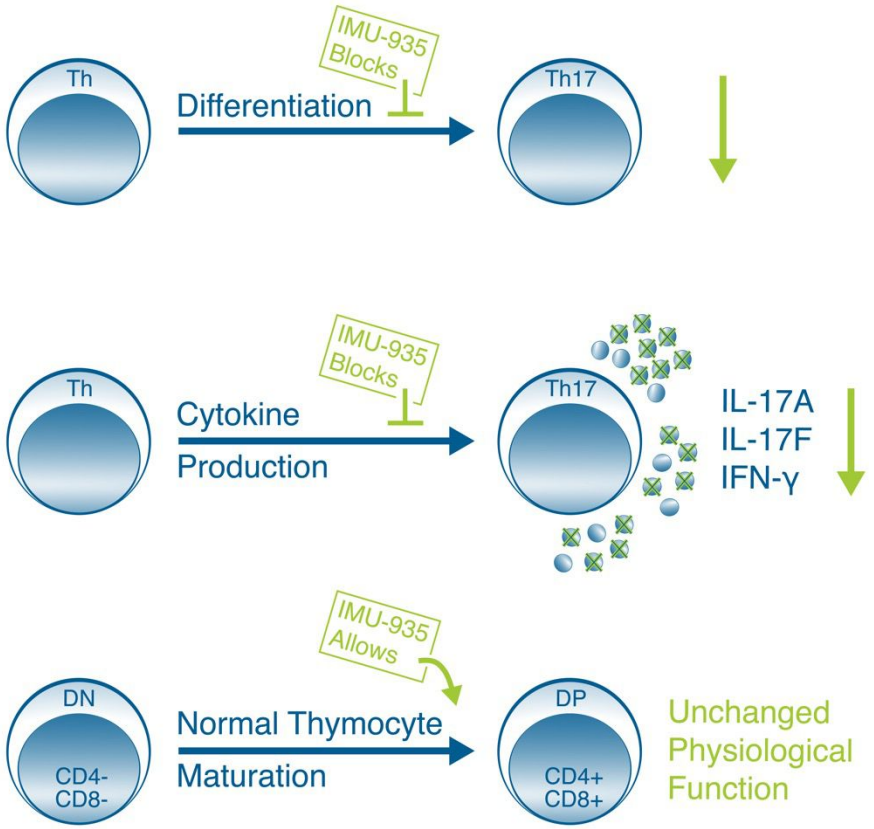
QD: quaque die = once-daily; BID: bis in die = two times daily; EoS: End of Study

02

IMU-935: An Oral IL-17 Inhibitor

Newly Obtained *In Vivo* Data

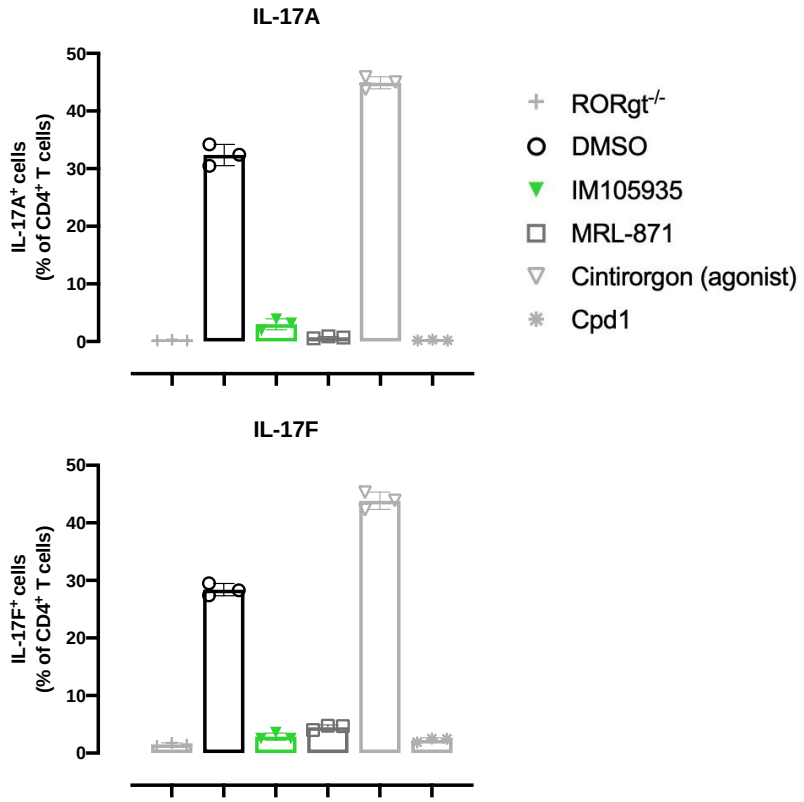
IMU-935 Selectively Inhibits Th17 Differentiation and IL-17 Secretion



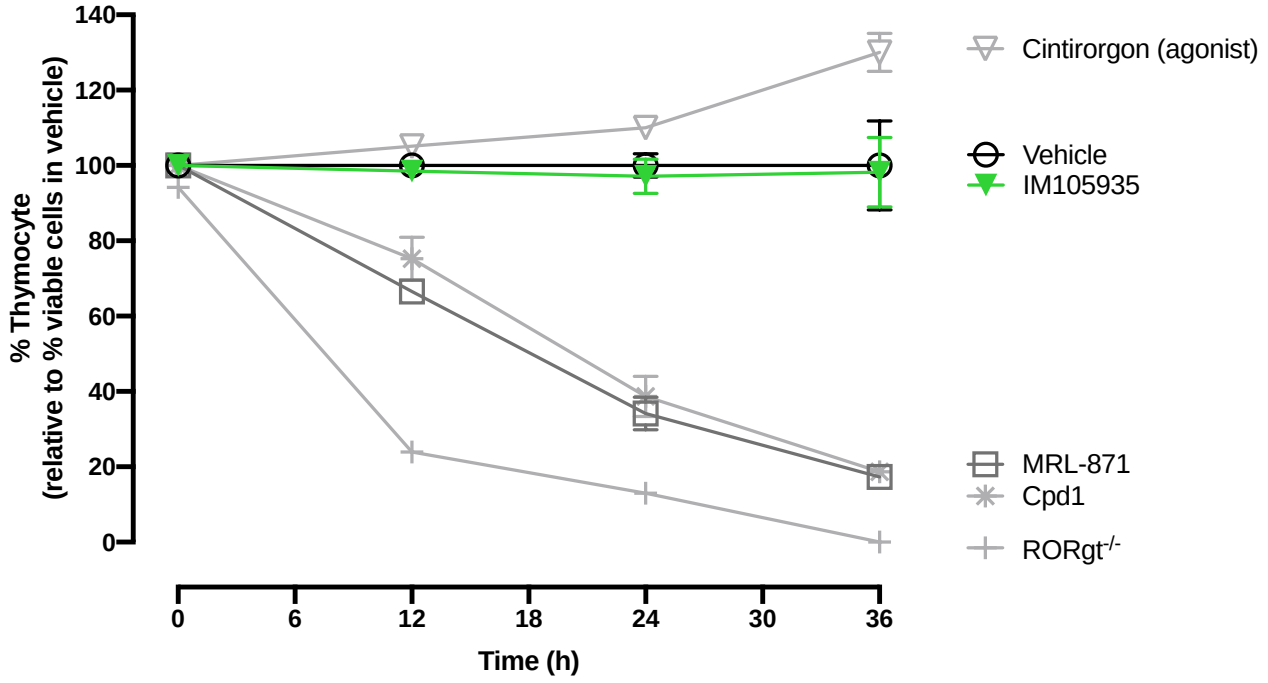
- The differentiation towards Th17 cells is inhibited by IMU-935
- The production of IL-17A and IL-17F is inhibited by IMU-935
- The physiological maturation of T cells within the thymus is **not affected by IMU-935**

Th: T helper; IL: interleukin; IFN: interferon; DN: double-negative; DP: double-positive; CD: cluster of differentiation

IMU-935's *in vitro* Selectivity on Th17 Suppression Confirmed, Well Differentiated to Other RORγt Inhibitors



Impact on Th17 differentiation at 500 nM



Impact on thymocyte viability at 1000 nM

Guo et al., 2016, Cell Reports (MRL-871), Guntermann et al., 2017, JCI Insight (Cpd1), Mahalingam et al., 2019, Clin Cancer Res. (Cintirorgon)

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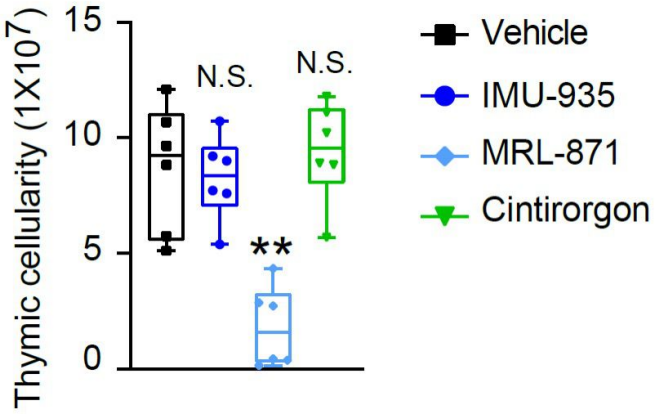
IMU-935 Allows Normal Thymocyte Maturation *in vivo*

Acute Model, 3 Days of Treatment



- IMU-935 (100 mg/kg BID), MRL-871 (100 mg/kg BID) and Cintirorgon (30 mg/kg BID) were tested for 3 days in C57BL/6j mice

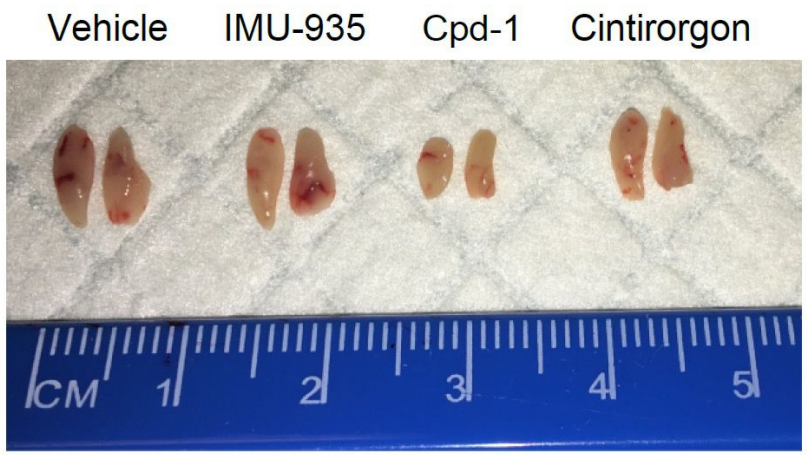
In contrast to MRL-871, **IMU-935 does not impact thymus size, thymocyte cell numbers or thymocyte maturation** in an acute mouse model.

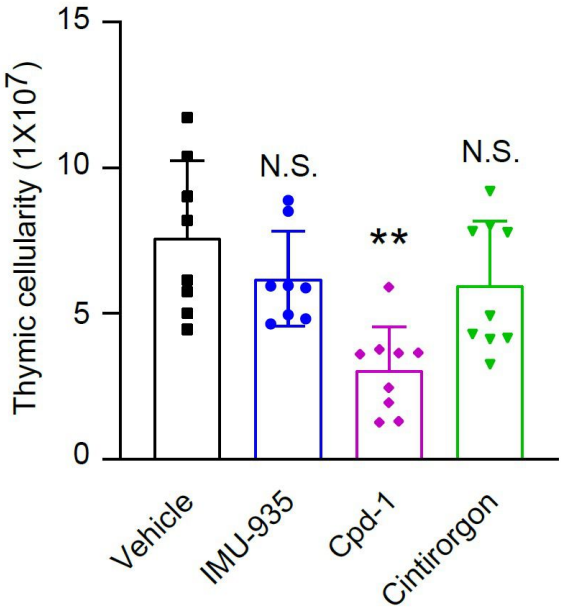
Guo et al., 2016, Cell Reports (MRL-871), Guntermann et al., 2017, JCI Insight (Cpd1), Mahalingam et al., 2019, Clin Cancer Res. (Cintirorgon)

Immunic THERAPEUTICS

IMU-935 Allows Normal Thymocyte Maturation *in vivo*

Chronic Model, 28 Days of Treatment





- C57BL/6j mice (male, 9wks, n=8-9 per group) were administrated with IMU-935 (100 mg/kg), Cpd1 (40 mg/kg), or Cintirorgon (30 mg/kg) for 4 weeks (BID)

In contrast to Cpd1, **IMU-935 does not impact thymus size, thymocyte cell numbers or thymocyte maturation** in a chronic mouse model.

Guo et al., 2016, Cell Reports (MRL-871), Guntermann et al., 2017, JCI Insight (Cpd1), Mahalingam et al., 2019, Clin Cancer Res. (Cintirorgon)

Immunic THERAPEUTICS

IMU-935 Has Shown a Favorable Safety Profile in Preclinical Studies

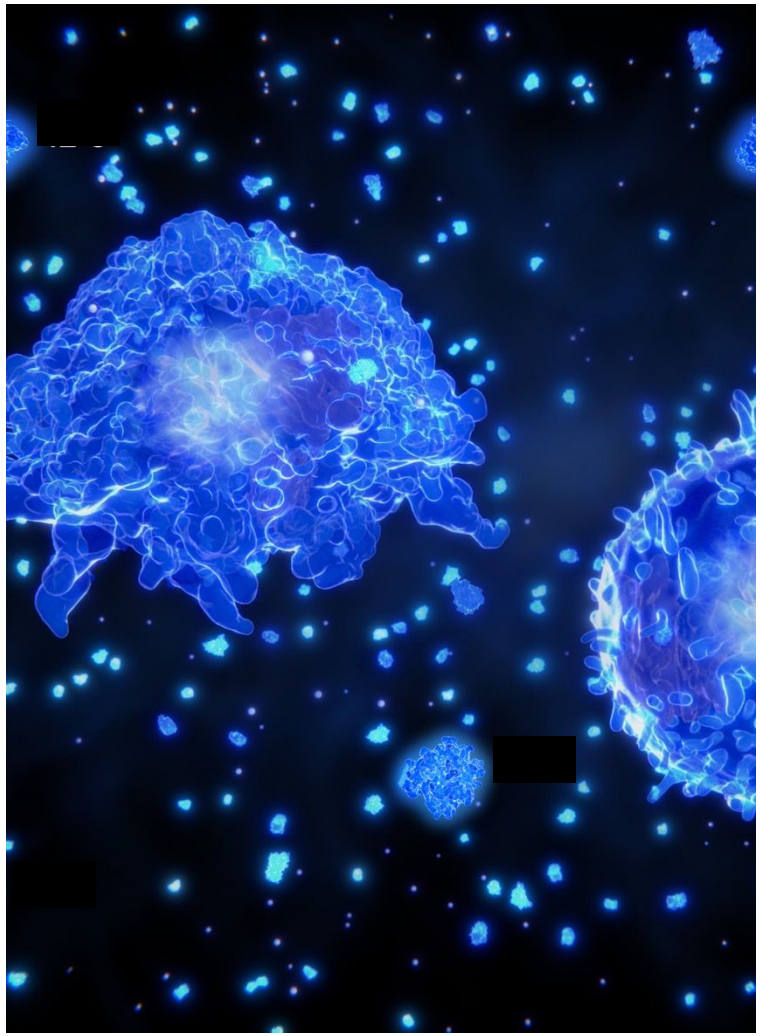
- **3-months tox studies** confirmed NOAEL seen in 28-day studies:
  - There were no IMU-935-related clinical observations, changes in body weight, food or water consumption, neurobehavioral exams, and clinical pathology parameters (urinalysis, hematology, coagulation, serum chemistry).
  - There were no drug-related observations in the gross pathological evaluation at scheduled termination or after recovery.
- **No changes in liver parameters or thymus have been observed.**
- **Data from preclinical safety studies and *in vivo* models for thymocyte maturation pave the way for IMU-935 to be a best-in-class oral IL-17 inhibitor.**

03

IMU-935: An Oral IL-17 Inhibitor

Summary

IMU-935: A Potentially Best-in-Class Oral IL-17 Inhibitor



- IMU-935 showed a very **favorable safety, tolerability and PK profile** in this phase 1 clinical trial with no serious adverse events seen in the SAD and MAD parts.
- In particular, IMU-935 was **safe and well-tolerated** in 14-day repeated oral dosing in healthy human subjects at doses expected to exceed required therapeutic dosing.
- IMU-935's outstanding **selectivity profile on Th17 over thymocyte development** was confirmed in an impressive fashion in a mouse model.
- IMU-935 is currently being tested in psoriasis patients with initial data expected in Q2/2022 – setting the stage for a potential **best-in-class oral** psoriasis therapy.
- IMU-935 may offer **extensive potential** beyond psoriasis in other autoimmune diseases.

Outlook: Multiple Value Inflection Points Expected in 2022

vidofludimus calcium (IMU-838)

- Phase 2 top-line data in ulcerative colitis expected to be available in Q2/2022

IMU-935

- Initial phase 1b psoriasis data expected to be available in Q2/2022
- Initial phase 1 CRPC data expected to be available in Q3/2022

IMU-856

- Unblinded SAD/MAD safety data in healthy volunteers expected to be available in Q3/2022

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Thank You!

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Phase 1 Clinical Trial of IMU-935

Extended Information Section

Initial Lipid-Based Pilot Formulation

Part A: Evaluation of Single Ascending Doses

Demographics
Part A: Lipid-Based Formulation

	Treatment						
	25 mg (N=6)	50 mg food effect (N=6)	100 mg (N=6)	200 mg (N=6)	100 mg BID (N=6)	Active (N=30)	Placebo (N=10)
Age (years), mean	27.0	37.8	32.3	23.8	30.5	30.3	31.4
Gender							
Male, n (%)	2 (33%)	6 (100%)	3 (50%)	5 (83%)	-	16 (53%)	7 (70%)
Female, n (%)	4 (67%)	-	3 (50%)	1 (17%)	6 (100%)	14 (47%)	3 (30%)
Race							
Asian, n (%)	1 (17%)	1 (17%)	1 (17%)	4 (67%)	-	7 (23%)	-
Black or African American, n (%)	-	-	1 (17%)	-	-	1 (3%)	2 (20%)
White, n (%)	5 (83%)	5 (83%)	4 (67%)	2 (33%)	6 (100%)	22 (73%)	8 (80%)
More than one race, n (%)	-	-	-	-	-	-	-
Height (cm), mean	170.7	183.3	173.0	170.8	163.0	172.2	174.3
Weight (kg), mean	73.90	87.45	68.52	71.52	69.00	74.08	77.82
BMI (kg/m^2), mean	25.23	26.08	22.74	24.56	26.05	24.93	25.52

In total, 40 healthy male and female subjects entered Part A single dose escalation with the lipid-based formulation.

Demographics were similar across cohorts.

BID: bis in die = two times daily

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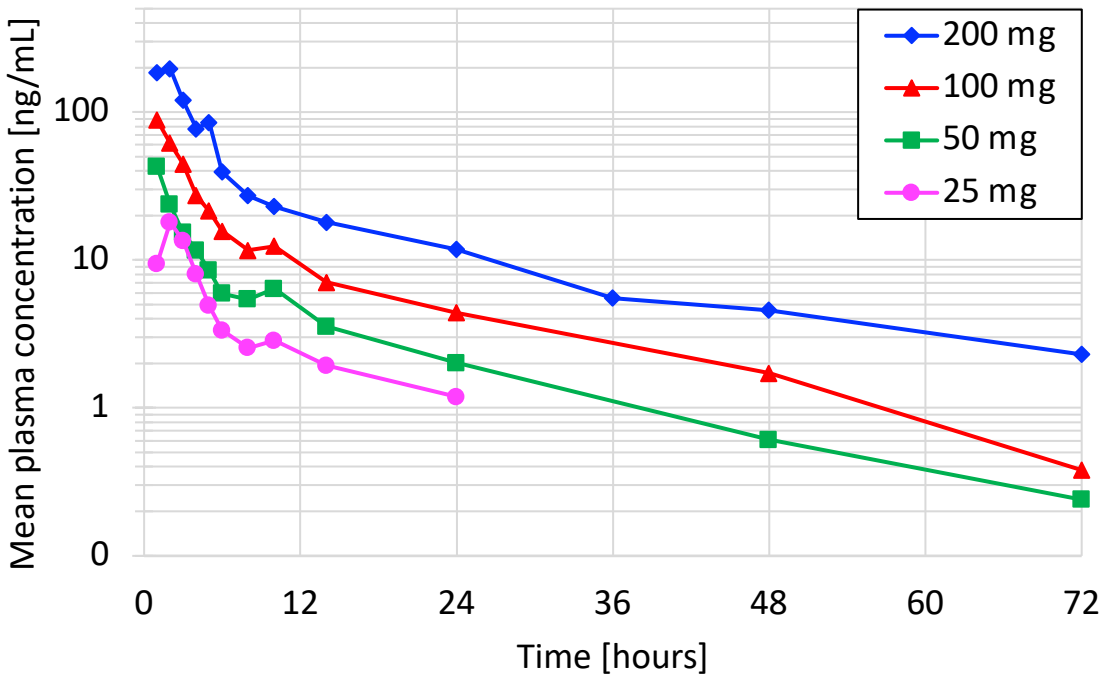
Pharmacokinetic Results

Part A: Pharmacokinetic Properties of Lipid-Based Formulation

IMU-935 concentration time profiles (log-linear scale)



Dose-Proportional Pharmacokinetics of Lipid-Based Formulation of IMU-935

Pharmacokinetic parameters (mean)	25 mg	50 mg	100 mg	200 mg
C_{max} (ng/mL)	22.8	49.6	95.7	199
T_{max} (hr)	2.0	1.5	1.3	1.8
$t_{1/2}$ (hr)	n.c.	30.5	16.9	24.1
$AUC_{0\text{-}inf}$ (hr*ng/mL)	n.c.	438	515	1360

Non-compartmental analysis

Lipid-based formulation showed T_{max} between 1 to 2 hours post-dose, half-life ranging from 16.9 to 30.5 hours and dose proportional increases of C_{max} and AUC across the investigated dose range.

Interim data, PK analysis ongoing

C_{max}: maximum plasma drug concentration; T_{max}: time to reach maximum plasma concentration; hr: hours; $t_{1/2}$: half-life; $AUC_{0\text{-}inf}$: area under the concentration-time curve from zero to infinity; n.c.: not calculated

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Overall Summary of TEAEs

Part A: Lipid-Based Formulation

Category	Treatment							
	25 mg (N=6)	50 mg fasted (N=6)	50 mg fed (N=6)	100 mg (N=6)	200 mg (N=6)	100 mg BID (N=6)	Active (N=30)	Placebo (N=10)
Subjects with TEAEs, n (%)	6 (100%)	4 (67%)	5 (83%)	5 (83%)	5 (83%)	6 (100%)	28 (93%)	9 (90%)
Subjects with mild TEAEs, n (%)	6 (100%)	4 (67%)	5 (83%)	5 (83%)	5 (83%)	5 (83%)	27 (90%)	9 (90%)
Subjects with moderate TEAEs, n (%)	1 (17%)	1 (17%)	-	3 (50%)	1 (17%)	2 (33%)	8 (27%)	1 (10%)
Subjects with severe TEAEs, n (%)	-	-	-	-	-	-	-	1 (10%)
Subjects with SAEs, n (%)	-	-	-	-	-	-	-	-
Subject with TEAEs leading to withdrawal, n (%)	-	-	-	-	-	-	-	-
Number of TEAEs	7	10	9	17	11	17	71	17
Number of mild TEAEs	6	9	9	12	10	14	60	15
Number of moderate TEAEs	1	1	-	5	1	3	11	1
Number of severe TEAEs	-	-	-	-	-	-	-	1
Number of SAEs	-	-	-	-	-	-	-	-
Number of TEAEs leading to withdrawal	-	-	-	-	-	-	-	-

TEAE: Treatment-Emergent Adverse Event; SAE: Serious Adverse Event; BID: bis in die = two times daily
The treatments 50 mg fasted and fed were given (in two periods) to the same subjects of cohort 2.

Dose-Dependent Increase of Some Local Gastrointestinal Events

Part A: Lipid-Based Formulation

MedDRA Preferred Term	Number (%) of subjects with related TEAEs [Number of related TEAEs reported]													
	Active Treatment IMU-935							Placebo Treatment						
	25 mg (N=6)	50 mg fasted (N=6)	50 mg fed (N=6)	100 mg (N=6)	200 mg (N=6)	100 mg BID (N=6)	Total Active (N=30)	25 mg (N=2)	50 mg fasted (N=2)	50 mg fed (N=2)	100 mg (N=2)	200 mg (N=2)	100 mg BID (N=6)	Total Placebo (N=10)
Diarrhea	-	-	1 (17%) [1]	2 (33%) [2]	1 (17%) [1]	1 (17%) [1]	5 (17%) [5]	-	-	-	-	-	-	-
Gastroesophageal reflux	-	-	-	-	1 (17%) [1]	1 (17%) [1]	2 (7%) [2]	-	-	-	-	1 (17%) [1]	1 (17%) [1]	2 (20%) [2]
Flatulence	-	-	-	1 (17%) [1]	-	1 (17%) [1]	2 (7%) [2]	-	-	-	-	-	-	-
Any selected local GI event							9 (30%) [9]							2 (20%) [2]

Dose-dependent increase in some local gastrointestinal events for active and placebo treatment groups (with increase in number of capsules given):

- Presumed to be an effect of amphiphilic inactive ingredients still present in this initial pilot formulation.
- The high solubility of IMU-935 in lipids may have caused high local concentrations at the gastrointestinal mucosa leading to symptoms of local intolerability.
- Higher doses of IMU-935 in a new solid formulation showed no such effects, hence all further phase 1 cohorts were performed with a new powder-in-capsule formulation.

Analysis of TEAEs
Part A: Lipid-Based Formulation

- SAEs
  - None
- Severe TEAEs
  - Headache

    After a single dose of placebo, subject R0101-001 reported 40 minutes post-dose an episode of severe headache. The TEAE lasted 3.5 hours, was unrelated to study treatment and recovered without sequelae.
- Moderate related TEAEs
  - Hot flush

    After a single dose of 100 mg IMU-935, subject R0103-006 reported 1-hour post-dose nausea, bloating, reflux symptoms and hot flush in arms and legs. Symptoms lasted a few seconds and recovered without sequelae.
- TEAEs associated with liver function tests or urinalysis
  - None
- TEAEs associated with vital signs or 12-lead ECGs
  - None

TEAE: Treatment-Emergent Adverse Event; SAE: Serious Adverse Event; ECG: electrocardiogram

Analysis of Laboratory Parameters
Part A: Lipid-Based Formulation

- 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
  - Almost all abnormalities in laboratory parameters were considered not clinically significant by the investigators
  - A single TEAE associated with laboratory parameters was reported:
    - Blood creatine kinase increased (see following slide for details)

TEAE: Treatment-Emergent Adverse Event

Laboratory Parameters
Part A: Lipid-Based Formulation

- Narratives of TEAEs associated with laboratory parameters
  - Blood creatine kinase increased

    After a single dose of placebo, subject R0101-008 had elevated CK (mild, unrelated) at the end-of-study visit (day 14). All other post-dose values of creatine kinase were in the normal range.

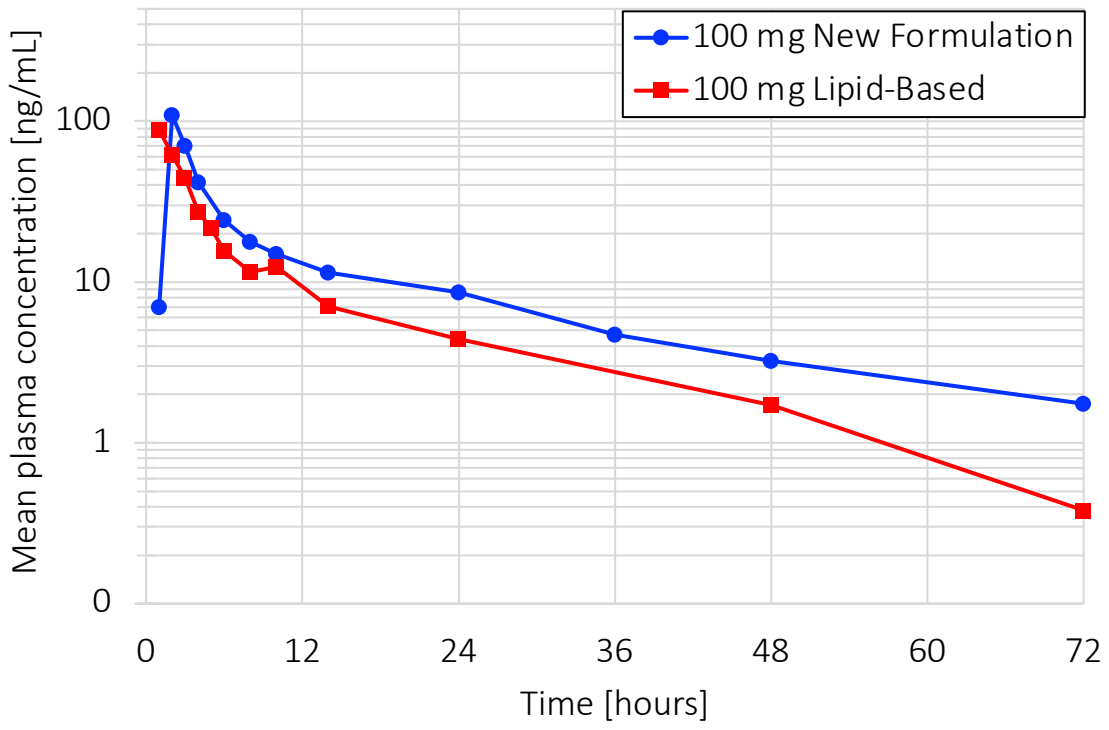
Parameter	Visit	Result	Units	Lower Limit	Upper Limit	Out of Range Flag	Change from Baseline
Creatine Kinase	Screening	298	U/L		251	High	
	Day -1	149	U/L		251	Normal	
	Day 1	92	U/L		251	Normal	-57
	Day 2	70	U/L		251	Normal	-79
	Day 4	65	U/L		251	Normal	-84
	End of Study, Day 14	5365	U/L		251	High	5216
	End of Study, Unscheduled	550	U/L		251	High	401

TEAE: Treatment-Emergent Adverse Event

Pharmacokinetic Results

Part A: Comparison of Lipid-Based and Powder-in-Capsule Formulation

IMU-935 concentration time profiles (log-linear scale)



Comparable PK for the Two Different Oral Formulations of IMU-935

Pharmacokinetic parameters (mean)	100 mg lipid-based formulation	100 mg new formulation
C_{max} (ng/mL)	95.7	119
T_{max} (hr)	1.3	2.2
$t_{1/2}$ (hr)	16.9	26.1
$AUC_{0\text{-}inf}$ (hr*ng/mL)	515	755

Non-compartmental analysis

New powder-in-capsule formulation provides improved PK profile, allowing easy switch from lipid-based pilot formulation to new powder-in-capsule formulation.

Interim data, PK analysis ongoing

C_{max}: maximum plasma drug concentration; T_{max}: time to reach maximum plasma concentration; hr: hours; $t_{1/2}$: half-life; $AUC_{0\text{-}inf}$: area under the concentration-time curve from zero to infinity; PK: pharmacokinetic

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Conclusions

Part A: Lipid-Based Formulation

- The semi-solid lipid-based formulation was adequate to enable initial non-clinical and clinical evaluations of IMU-935.
- However, an ongoing effort to improve the formulation led to its replacement with a new and improved powder-in-capsule formulation during execution of Part A of this clinical trial.
- Since then, the powder-in-capsule formulation has been used for further clinical investigations.

Powder-in-Capsule Formulation

Part A-N: Evaluation of Single Ascending Doses

Demographics
Part A-N

	Treatment						
	100 mg (N=5)	200 mg (N=6)	300 mg (N=6)	300 mg food effect (N=6)	400 mg (N=6)	Active (N=29)	Placebo (N=10)
Age (years), mean	26.8	35.3	23.3	21.3	33.5	28.1	33.4
Gender							
Male, n (%)	4 (80%)	4 (67%)	5 (83%)	2 (33%)	1 (17%)	16 (55%)	6 (60%)
Female, n (%)	1 (20%)	2 (33%)	1 (17%)	4 (67%)	5 (83%)	13 (45%)	4 (40%)
Race							
Asian, n (%)	2 (40%)	1 (17%)	-	-	-	3 (10%)	2 (20%)
Black or African American, n (%)	-	-	-	-	-	-	-
White, n (%)	2 (40%)	5 (83%)	6 (100%)	5 (83%)	6 (100%)	24 (83%)	8 (80%)
More than one race, n (%)	1 (20%)	-	-	1 (17%)	-	2 (7%)	-
Height (cm), mean	171.4	177.0	177.8	170.3	168.2	173.0	172.3
Weight (kg), mean	73.10	87.43	70.93	71.80	69.62	74.63	73.40
BMI (kg/m^2), mean	24.67	27.87	22.40	24.87	24.53	24.87	24.52

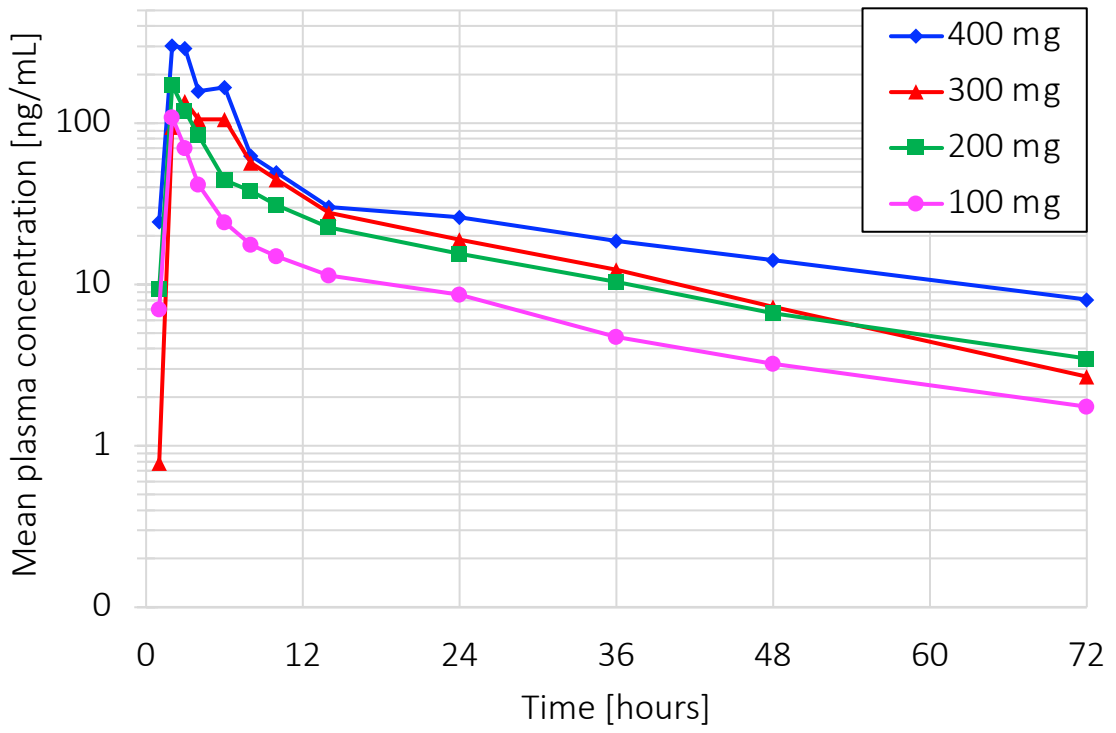
In total, 39 healthy male and female subjects entered part A single dose escalation with the new formulation.

Demographics were similar across cohorts.

Immunic THERAPEUTICS

Pharmacokinetic Results
Part A-N

IMU-935 concentration time profiles (log-linear scale)



Dose-Proportional PK of New Powder-in-Capsule Formulation of IMU-935

Pharmacokinetic parameters (mean)	100 mg	200 mg	300 mg	400 mg
C_{max} (ng/mL)	119	195	182	479
T_{max} (hr)	2.2	2.8	3.8	2.8
$t_{1/2}$ (hr)	26.1	24.4	16.5	31.0
$AUC_{0\text{-}inf}$ (hr*ng/mL)	755	1440	1710	2940

Non-compartmental analysis

New formulation showed T_{max} between 2 to 4 hours post-dose, half-life ranging from 16.5 to 31.0 hours and dose proportional increases of C_{max} and AUC across the investigated dose range.

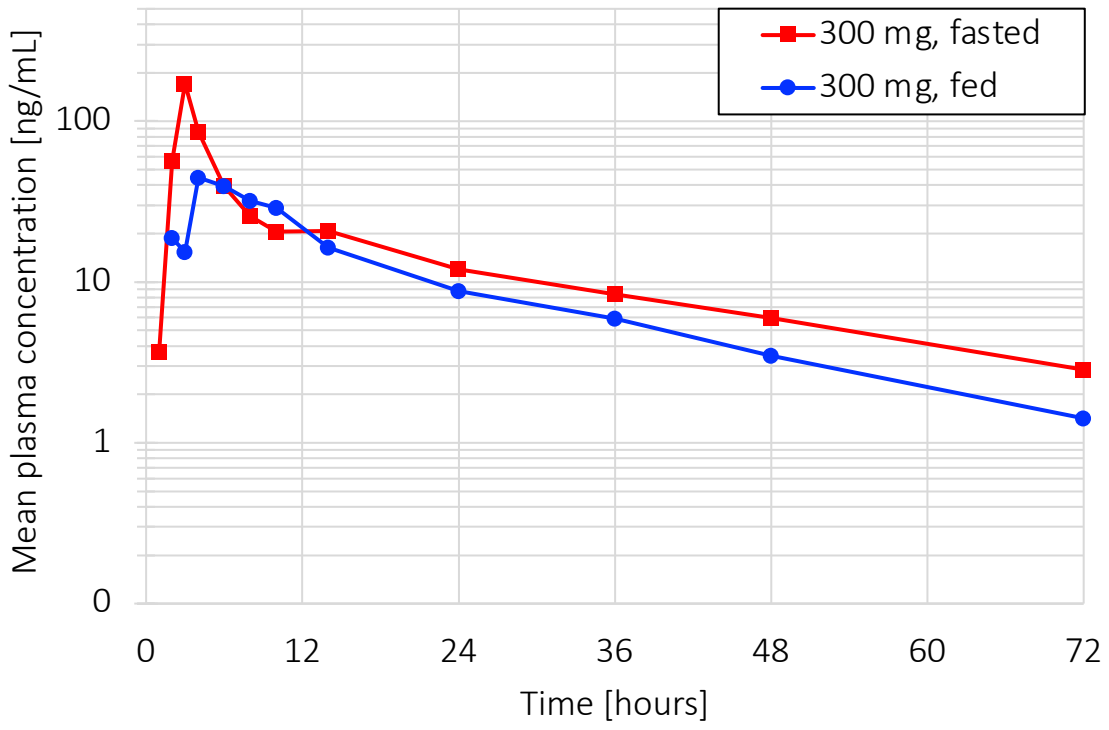
Interim data, PK analysis ongoing

C_{max}: maximum plasma drug concentration; T_{max}: time to reach maximum plasma concentration; hr: hours; $t_{1/2}$: half-life; $AUC_{0\text{-}inf}$: area under the concentration-time curve from zero to infinity; PK: pharmacokinetic

Immunic THERAPEUTICS

Pharmacokinetic Results
Part A-N

IMU-935 concentration time profiles (log-linear scale)



Minimal Food Effect of New Powder-in-Capsule Formulation of IMU-935

Pharmacokinetic parameters (mean)	300 mg fasted	300 mg fed
C_{max} (ng/mL)	304	123
T_{max} (hr)	2.8	5.6
$t_{1/2}$ (hr)	22.0	22.7
$AUC_{0\text{-}inf}$ (hr*ng/mL)	2010	1330

Non-compartmental analysis

Food intake delayed T_{max} and decreased C_{max} and AUC. These results favor the fasted use of IMU-935 in future clinical trials.

Interim data, PK analysis ongoing

C_{max}: maximum plasma drug concentration; T_{max}: time to reach maximum plasma concentration; hr: hours; $t_{1/2}$: half-life; $AUC_{0\text{-}inf}$: area under the concentration-time curve from zero to infinity; PK: pharmacokinetic

Immunic THERAPEUTICS

Overall Summary of TEAEs
Part A-N

Category	Treatment							
	100 mg (N=5)	200 mg (N=6)	300 mg (N=6)	300 mg fasted (N=6)	300 mg fed (N=6)	400 mg (N=6)	Active (N=29)	Placebo (N=10)
Subjects with TEAEs, n (%)	4 (80%)	4 (67%)	3 (50%)	5 (83%)	3 (50%)	4 (67%)	21 (72%)	8 (80%)
Subjects with mild TEAEs, n (%)	4 (80%)	4 (67%)	3 (50%)	5 (83%)	1 (17%)	4 (67%)	20 (69%)	8 (80%)
Subjects with moderate TEAEs, n (%)	-	1 (17%)	-	2 (33%)	2 (33%)	-	4 (14%)	1 (10%)
Subjects with severe TEAEs, n (%)	-	-	-	-	1 (17%)	-	1 (3%)	-
Subjects with SAEs, n (%)	-	-	-	-	-	-	-	-
Subjects with TEAEs leading to withdrawal, n (%)	-	-	-	-	-	-	-	-
Number of TEAEs	8	13	6	11	4	6	48	14
Number of mild TEAEs	8	12	6	9	1	6	42	12
Number of moderate TEAEs	-	1	-	2	2	-	5	2
Number of severe TEAEs	-	-	-	-	1	-	1	-
Number of SAEs	-	-	-	-	-	-	-	-
Number of TEAEs leading to withdrawal	-	-	-	-	-	-	-	-

TEAE: Treatment-Emergent Adverse Event; SAE: Serious Adverse Event
The treatments 300 mg fasted and fed were given (in two periods) to the same subjects of cohort 5NF.

Analysis of Laboratory Parameters
Part A-N

- 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
  - Almost all abnormalities in laboratory parameters were considered not clinically significant by the investigators
  - The following TEAEs associated with laboratory parameters were reported:
    - Blood creatine kinase increased, neutropenia, aspartate aminotransferase increased, lipase increased, transaminases increased (see following slide for details)

TEAE: Treatment-Emergent Adverse Event

Laboratory Parameters
Part A-N

- Narratives of TEAEs associated with laboratory parameters

Active Treatment Subject R015NF-707	Blood creatine kinase increased, Aspartate aminotransferase increased	After a single dose of 300 mg IMU-935 in the fed state, the subject had elevated CK (severe, unrelated) and elevated AST (moderate, unrelated) at the end-of-study visit (day 28) only. All other post-dose values of creatine kinase or AST prior to the end-of-study visit were in the normal range.
		The subject reported increased alcohol consumption and going rock climbing in the few days prior to the end-of-study visit (day 28). This event was assessed by the investigator as unrelated to study drug.
Active Treatment Subject R013N-204	Neutropenia	After a single dose of 100 mg IMU-935, subject had a neutropenia (mild, unrelated) on day 1. The subject was seen to have neutropenia already at screening (but not at baseline), hence this had to be reported as TEAE. The neutrophil values for this subject fluctuated throughout the entire study with pre-dose and post-dose values between 1.8 to 3.3 x 10e9/L (normal range: 2-8 x 10e9/L).
Active Treatment Subject R015N-208	Transaminases increased	After a single dose of 300 mg IMU-935, subject had elevated AST and ALT (mild, unrelated) at the end-of-study visit. The subject had an infected pilonidal cyst and was treated with antibiotics (flucloxacillin) and pain relief (paracetamol, ibuprofen) in the few days prior to the end-of-study visit (day 14). All other post-dose values of AST and ALT prior to the end-of-study visit were in the normal range.
Placebo Subject R016N-202	Lipase increased	After a single dose of placebo, subject had elevated lipase (mild, related) on day 2. All other post-dose values of lipase were in the normal range. The lipase increase was asymptomatic and without any clinically significant increase of amylase or other laboratory parameters.

- All changes of laboratory parameters in the active treatment group have plausible explanations or can be clearly related to life events in these subjects. All such changes were therefore assessed as unrelated to study medication.
- The were 3 patients in the active treatment group and 1 subject in the placebo group. This is exactly the ratio of randomization to IMU-935 and Placebo. There is no probability excess in laboratory changes in the active treatment group.

Laboratory Parameters
Part A-N

- Narratives of TEAEs associated with laboratory parameters
  - Blood creatine kinase increased

    After a single dose of 300 mg IMU-935 in the fed state, subject R015NF-707 had elevated CK (severe, unrelated) at the end-of-study visit. The subject reported increased alcohol consumption and going rock climbing in the few days prior to the end-of-study visit (day 28). All other post-dose values of creatine kinase prior to the end-of-study visit were in the normal range.

Parameter	Visit	Result	Units	Lower Limit	Upper Limit	Out of Range Flag	Change from Baseline
Creatine Kinase	Screening	280	U/L	0	190	High	
	Screening, Unscheduled	120	U/L	0	190	Normal	
	Day -1	100	U/L	0	190	Normal	
	Day 1	83	U/L	0	190	Normal	-17
	Day 2	67	U/L	0	190	Normal	-33
	Day 4	78	U/L	0	190	Normal	-22
	Day 14	160	U/L	0	190	Normal	
	Day 15	100	U/L	0	190	Normal	-60
	Day 16	95	U/L	0	190	Normal	-65
	Day 18	100	U/L	0	190	Normal	-60
	End of Study, Day 28	8400	U/L	0	190	High	8240
	End of Study, Unscheduled	230	U/L	0	190	High	70

TEAE: Treatment-Emergent Adverse Event

Laboratory Parameters
Part A-N

- Narratives of TEAEs associated with laboratory parameters
  - Aspartate aminotransferase increased

    After a single dose of 300 mg IMU-935 in the fed state, subject R015NF-707 had elevated AST (moderate, unrelated) at the end-of-study visit. The subject reported increased alcohol consumption and going rock climbing in the few days prior to the end-of-study visit (day 28). All other post-dose values of AST prior to the end-of-study visit were in the normal range

Parameter	Visit	Result	Units	Lower Limit	Upper Limit	Out of Range Flag	Change from Baseline
Aspartate Aminotransferase	Screening	44	U/L	0	41	High	
	Screening, Unscheduled	26	U/L	0	41	Normal	
	Day -1	20	U/L	0	41	Normal	
	Day 1	18	U/L	0	41	Normal	-2
	Day 2	18	U/L	0	41	Normal	-2
	Day 4	25	U/L	0	41	Normal	5
	Day 14	28	U/L	0	41	Normal	
	Day 15	22	U/L	0	41	Normal	-6
	Day 16	27	U/L	0	41	Normal	-1
	Day 18	37	U/L	0	41	Normal	9
	End of Study, Day 28	232	U/L	0	41	High	204
	End of Study, Unscheduled	53	U/L	0	41	High	25

TEAE: Treatment-Emergent Adverse Event; AST: Aspartate Aminotransferase

Laboratory Parameters
Part A-N

- Narratives of TEAEs associated with laboratory parameters
  - Neutropenia

    After a single dose of 100 mg IMU-935, subject R013N-204 had a neutropenia (mild, unrelated) on day 1. The subject was seen to have neutropenia already at screening (but not at baseline), hence this had to be reported as TEAE. The neutrophil values for this subject fluctuated throughout the entire study with pre-dose and post-dose values between 1.8 to 3.3 x 10e9/L (normal range: 2-8 x 10e9/L)

Parameter	Visit	Result	Units	Lower Limit	Upper Limit	Out of Range Flag	Change from Baseline
Neutrophils	Screening	1.8	10^9/L	2.0	8.0	Low	
	Day -1	3.3	10^9/L	2.0	8.0	Normal	
	Day 1, Unscheduled	1.5	10^9/L	2.0	8.0	Low	
	Day 1	1.5	10^9/L	2.0	8.0	Low	0.0
	Day 2	1.4	10^9/L	2.0	8.0	Low	-0.1
	Day 4	1.7	10^9/L	2.0	8.0	Low	0.2
	End of Study, Day 14	1.4	10^9/L	2.0	8.0	Low	-0.1
	End of Study, Unscheduled	1.4	10^9/L	2.0	8.0	Low	-0.1

TEAE: Treatment-Emergent Adverse Event

Laboratory Parameters
Part A-N

- Narratives of TEAEs associated with laboratory parameters
  - Lipase increased

    After a single dose of placebo, subject R016N-202 had elevated lipase (mild, related) on day 2. All other post-dose values of lipase were in the normal range. The lipase increase was asymptomatic and without any clinically significant increase of amylase or other laboratory parameters

Parameter	Visit	Result	Units	Lower Limit	Upper Limit	Out of Range Flag	Change from Baseline
Lipase	Screening	48	U/L	0	70	Normal	
	Day -1	43	U/L	0	70	Normal	
	Day 1	62	U/L	0	70	Normal	19
	Day 2	87	U/L	0	70	High	44
	Day 3, Unscheduled	59	U/L	0	70	Normal	16
	Day 4	43	U/L	0	70	Normal	0
	End of Study, Day 14	52	U/L	0	70	Normal	9

TEAE: Treatment-Emergent Adverse Event

Laboratory Parameters
Part A-N

- Narratives of TEAEs associated with laboratory parameters
  - Transaminases increased

    After a single dose of 300 mg IMU-935, subject R015N-208 had elevated AST and ALT (mild, unrelated) at the end-of-study visit. The subject had an infected pilonidal cyst and was treated with antibiotics (flucloxacillin) and pain relief (paracetamol, ibuprofen) in the few days prior to the end-of-study visit (day 14). All other post-dose values of AST and ALT prior to the end-of-study visit were in the normal range.

Parameter	Visit	Result	Units	Lower Limit	Upper Limit	Out of Range Flag	Change from Baseline
Alanine Aminotransferase	Screening	9	U/L	n/a	51	Normal	
	Day -1	19	U/L	n/a	51	Normal	
	Day 1	9	U/L	n/a	51	Normal	-10
	Day 2	8	U/L	n/a	51	Normal	-11
	Day 4	7	U/L	n/a	51	Normal	-12
	End of Study, Day 14	84	U/L	n/a	51	High	65
	End of Study, Unscheduled	77	U/L	n/a	51	High	58
	End of Study, Unscheduled	35	U/L	n/a	51	Normal	16

TEAE: Treatment-Emergent Adverse Event; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase

Laboratory Parameters
Part A-N

- Narratives of TEAEs associated with laboratory parameters
  - Transaminases increased (cont.)

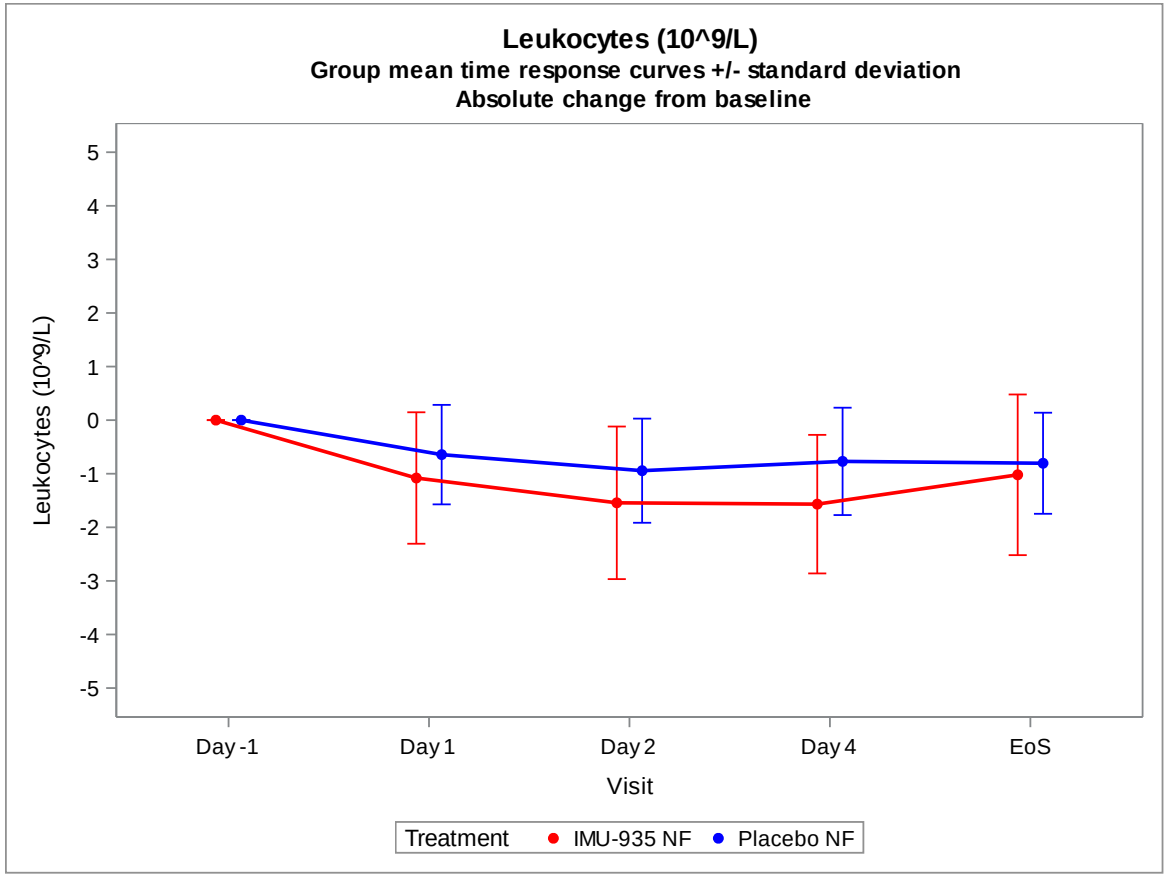
    After a single dose of 300 mg IMU-935, subject R015N-208 had elevated AST and ALT (mild, unrelated) at the end-of-study visit. The subject had an infected pilonidal cyst and was treated with antibiotics (flucloxacillin) and pain relief (paracetamol, ibuprofen) in the few days prior to the end-of-study visit (day 14). All other post-dose values of AST and ALT prior to the end-of-study visit were in the normal range.

Parameter	Visit	Result	Units	Lower Limit	Upper Limit	Out of Range Flag	Change from Baseline
Aspartate Aminotransferase	Screening	19	U/L	n/a	41	Normal	
	Day -1	18	U/L	n/a	41	Normal	
	Day 1	18	U/L	n/a	41	Normal	0
	Day 2	17	U/L	n/a	41	Normal	-1
	Day 4	16	U/L	n/a	41	Normal	-2
	End of Study, Day 14	56	U/L	n/a	41	High	38
	End of Study, Unscheduled	52	U/L	n/a	41	High	34
	End of Study, Unscheduled	28	U/L	n/a	41	Normal	10

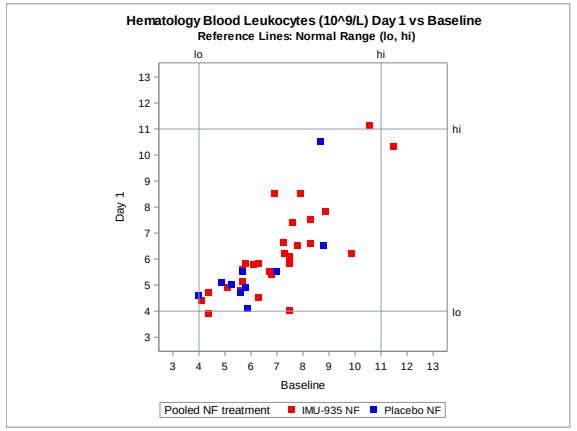
TEAE: Treatment-Emergent Adverse Event; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase

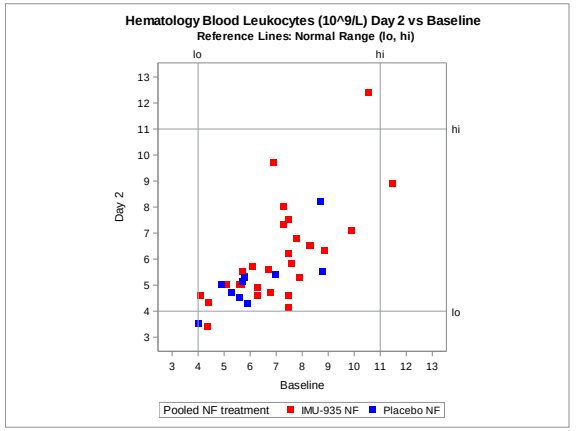
Laboratory Parameters: Leukocytes
Part A-N

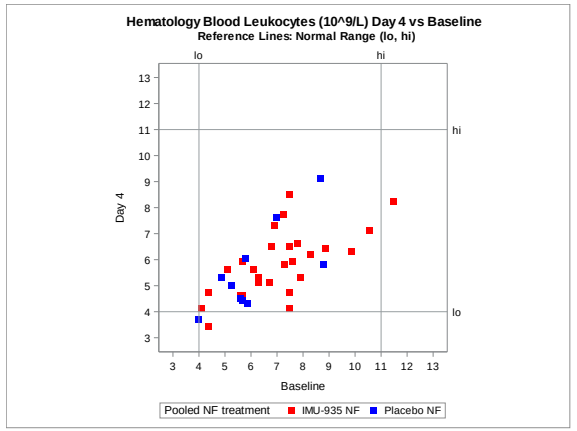
Laboratory Values Over Time
Hematology - Leukocytes

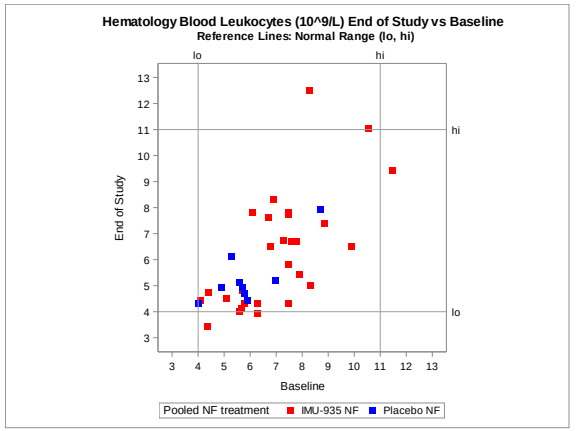


Individual Laboratory Values
Hematology - Leukocytes



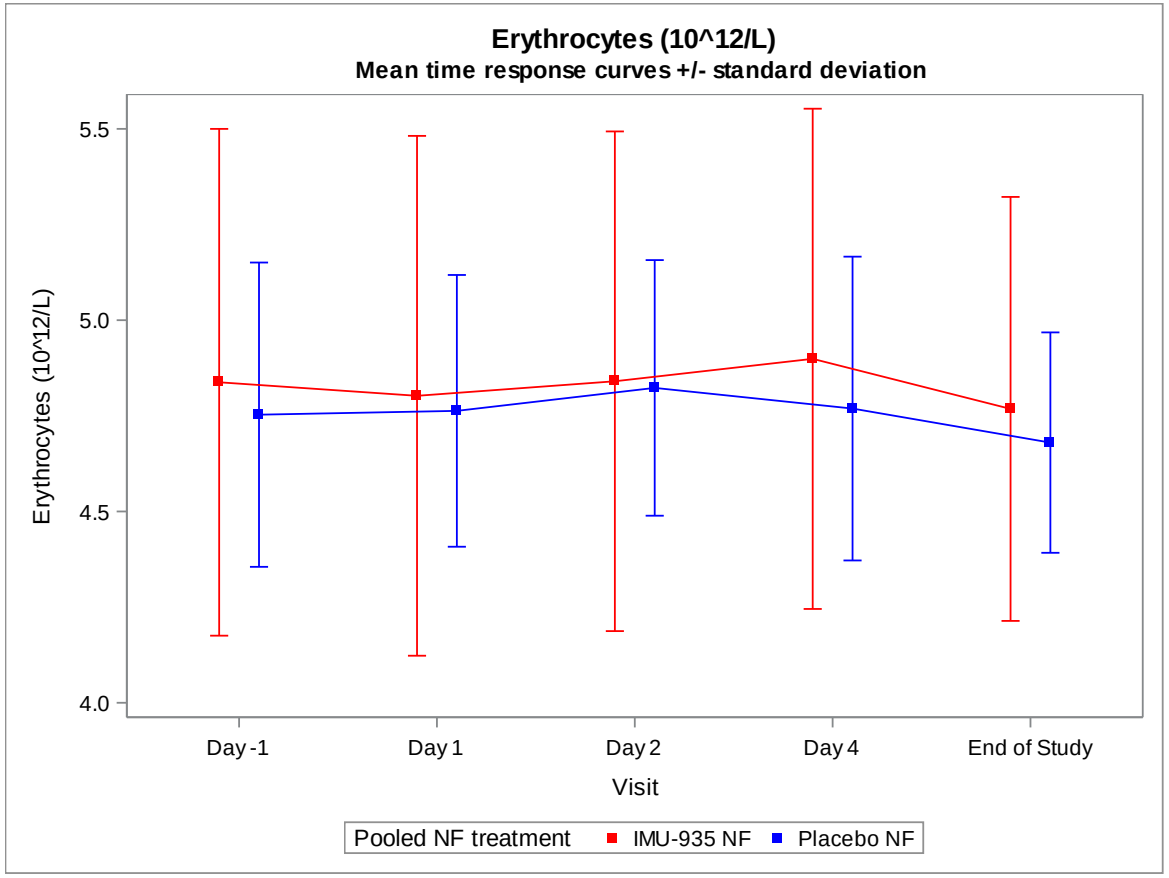




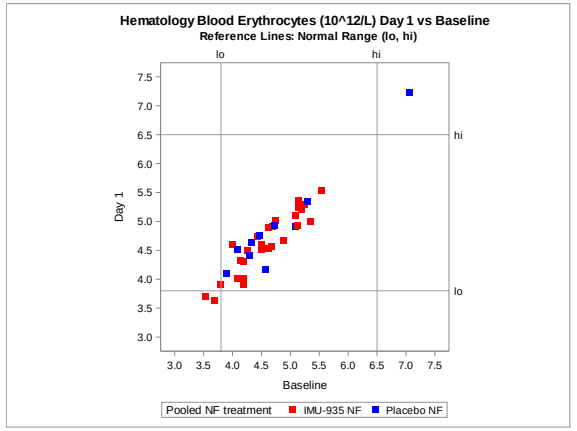


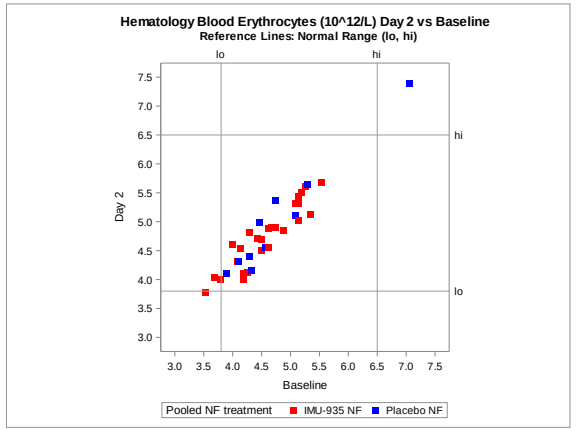
Laboratory Parameters: Erythrocytes
Part A-N

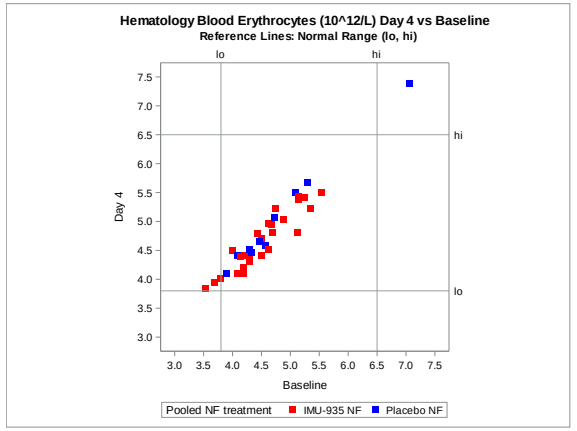
Laboratory Values Over Time
Hematology - Erythrocytes

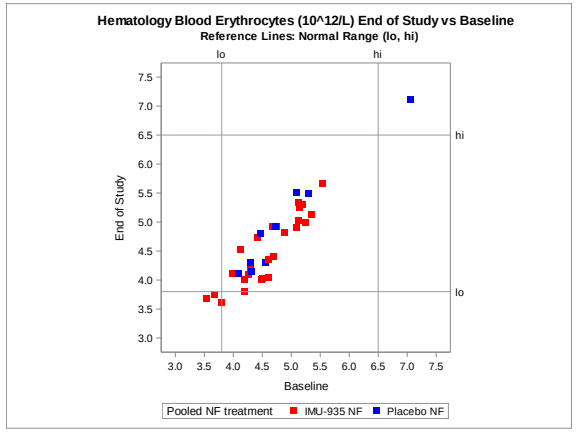


Individual Laboratory Values
Hematology - Erythrocytes



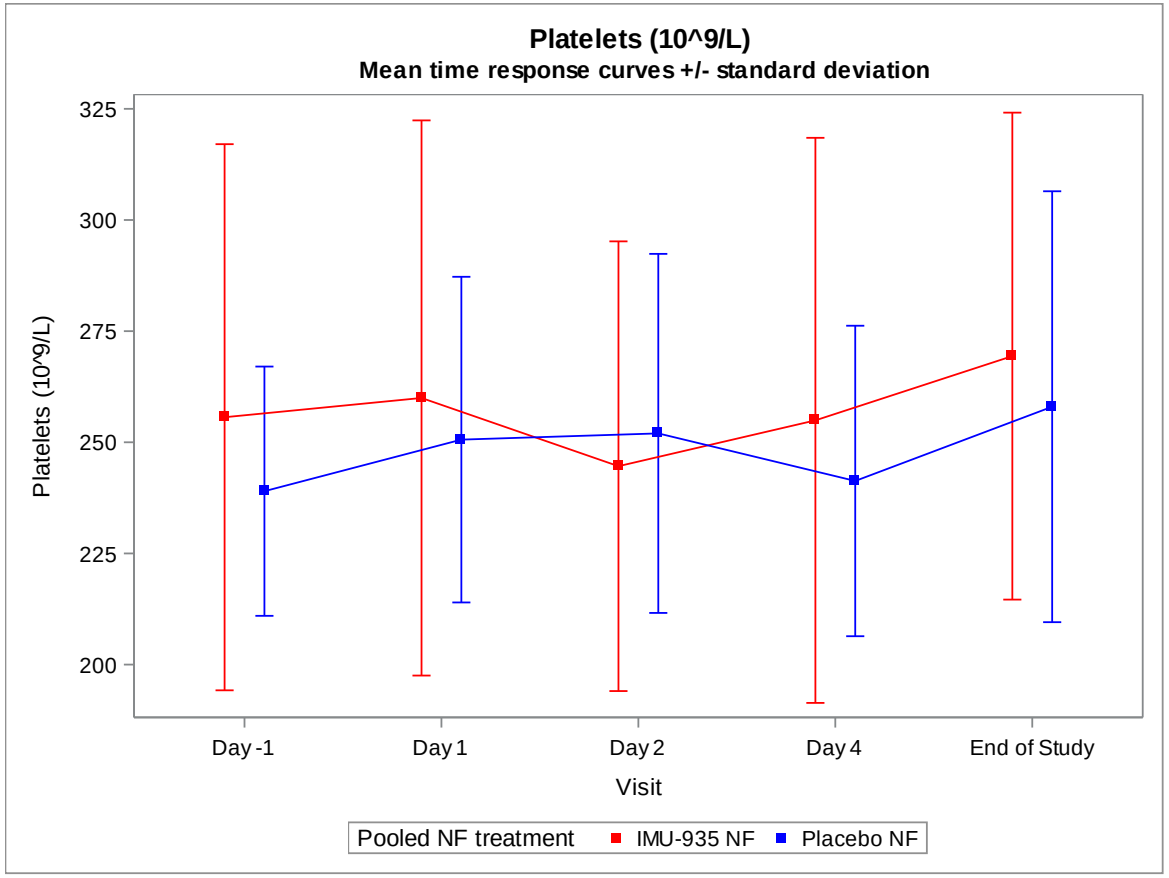




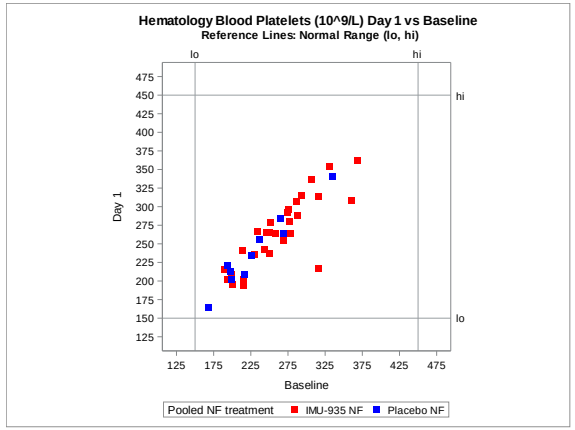


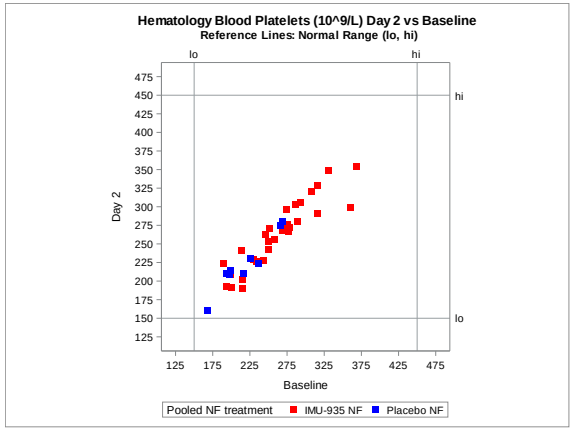
Laboratory Parameters: Platelets
Part A-N

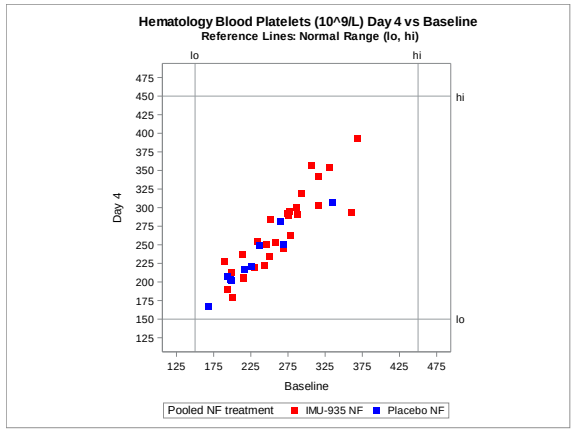
Laboratory Values Over Time
Hematology - Platelets

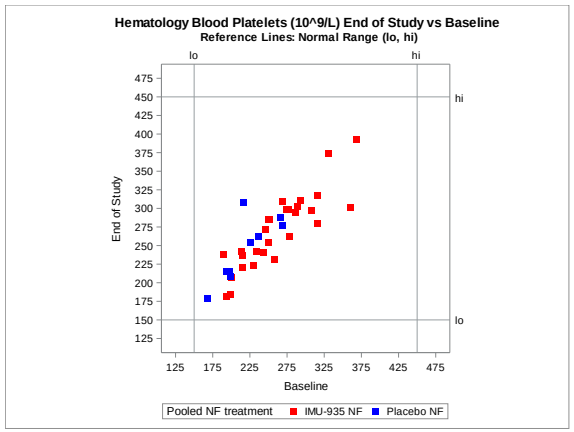


Individual Laboratory Values
Hematology - Platelets



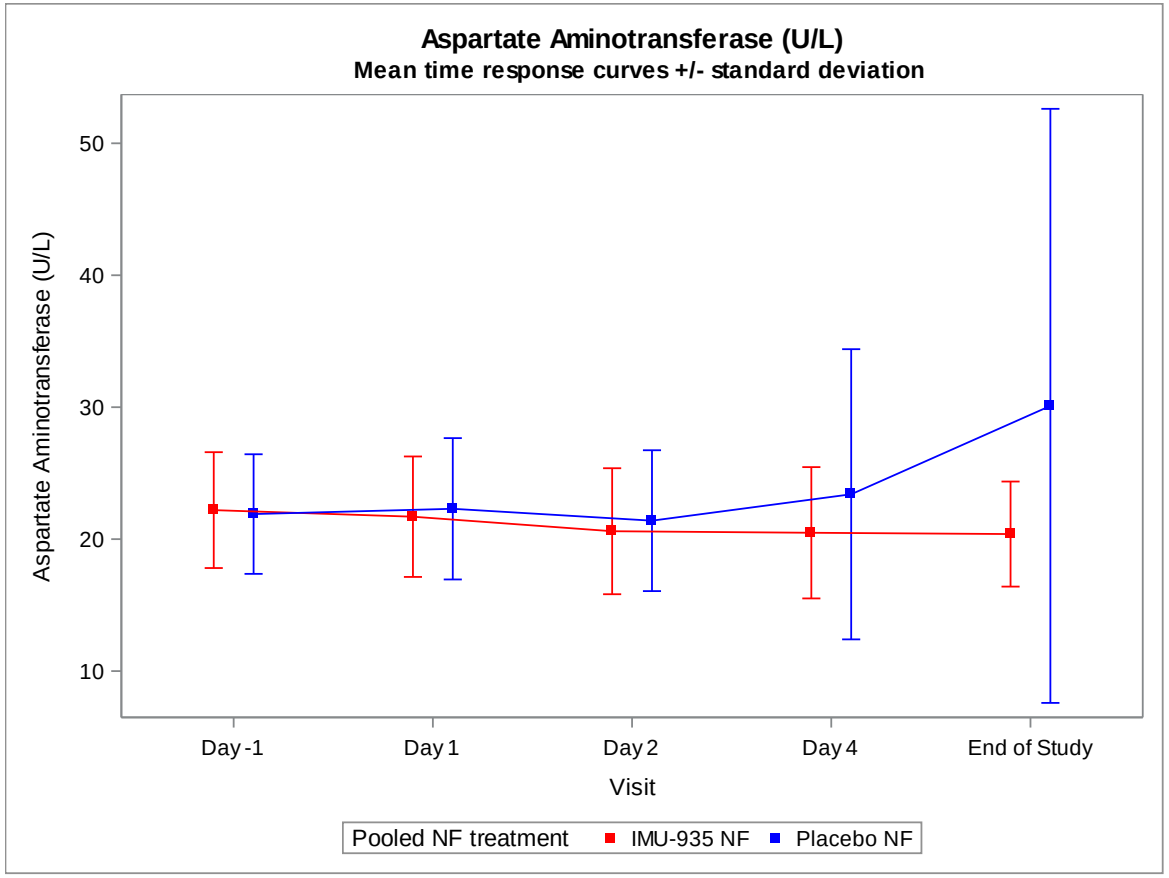




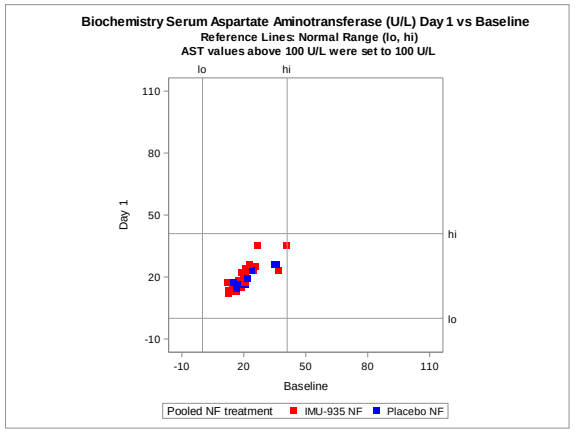


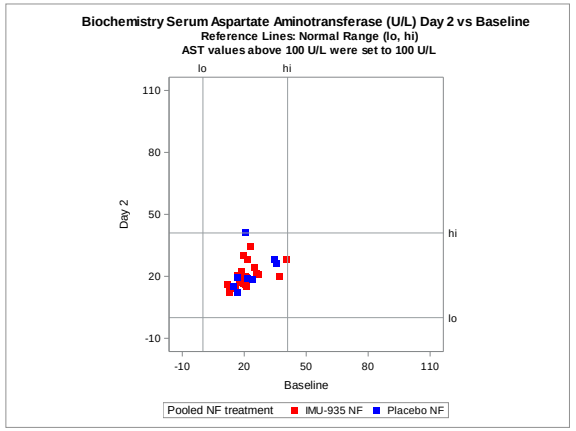
Laboratory Parameters: AST
Part A-N

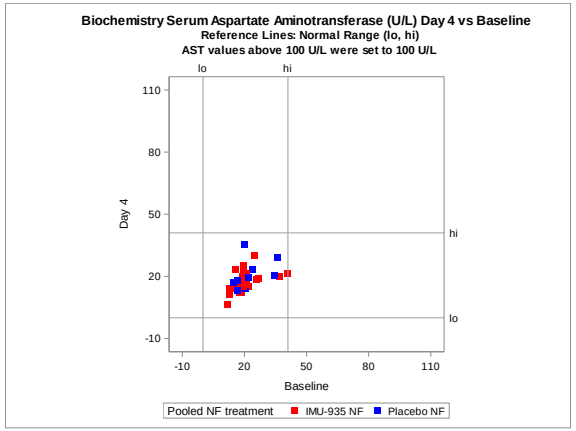
Laboratory Values Over Time
Biochemistry - AST

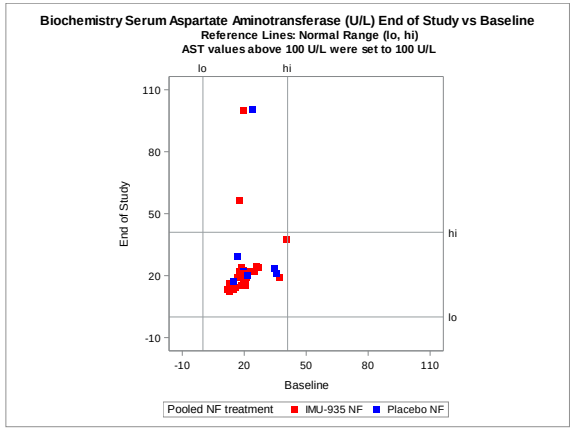


Individual Laboratory Values
Biochemistry - AST







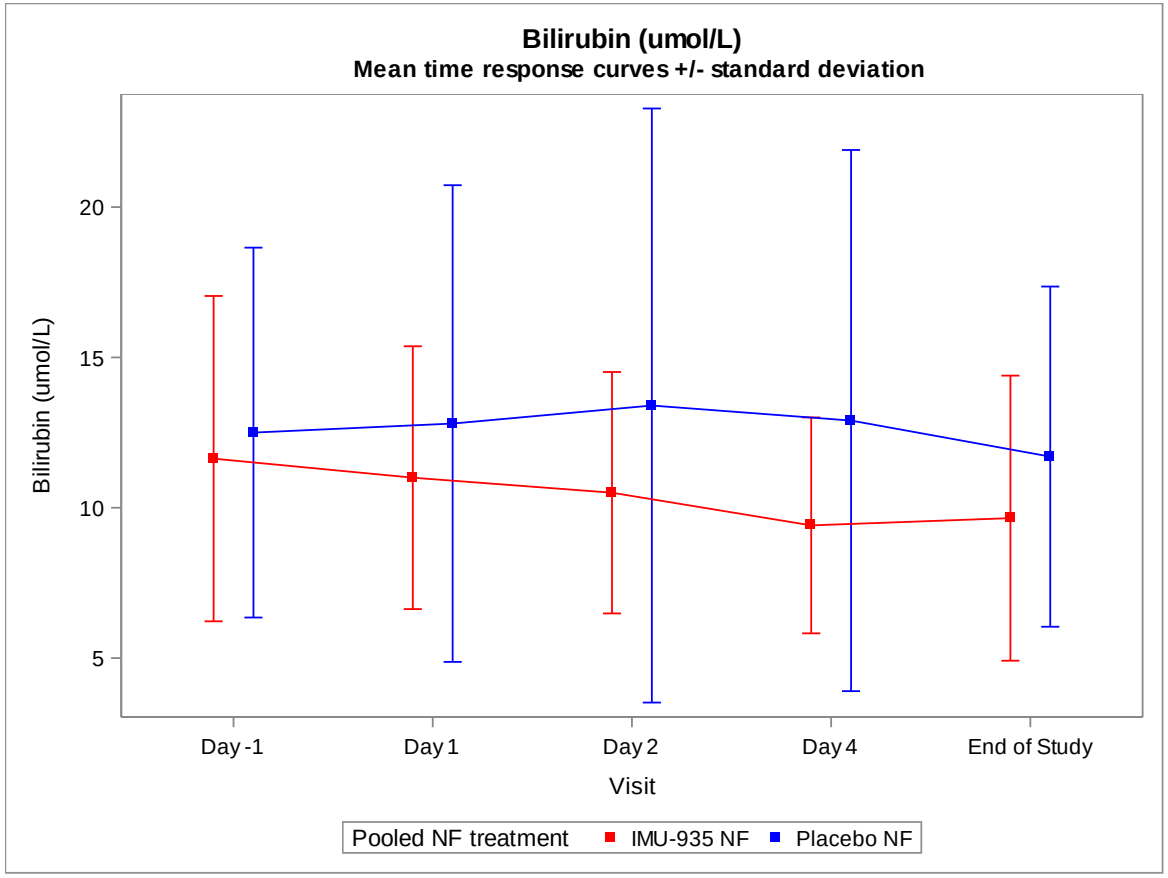


AST: Aspartate Aminotransferase

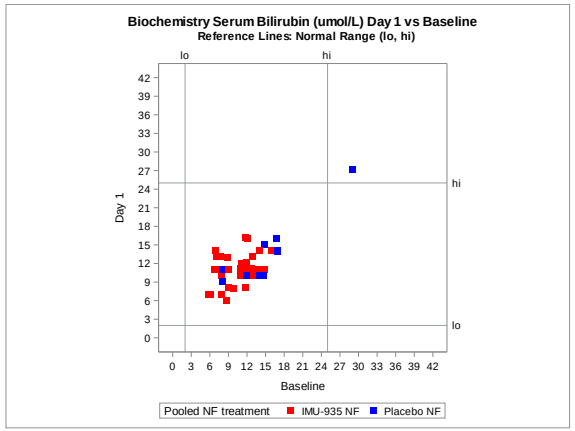
Immunic THERAPEUTICS

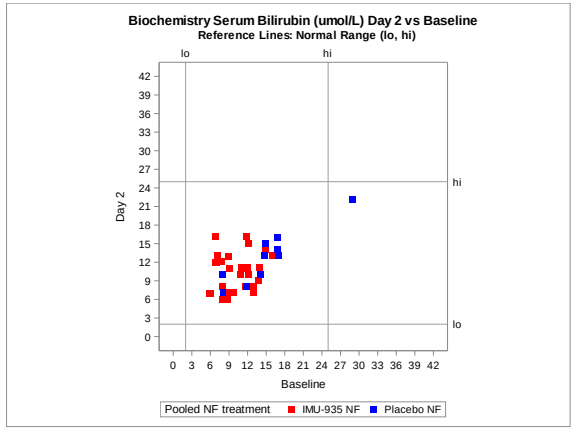
Laboratory Parameters: Bilirubin
Part A-N

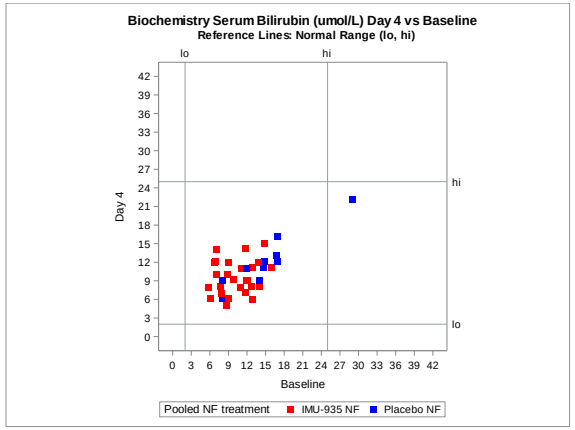
Laboratory Values Over Time
Biochemistry - Bilirubin

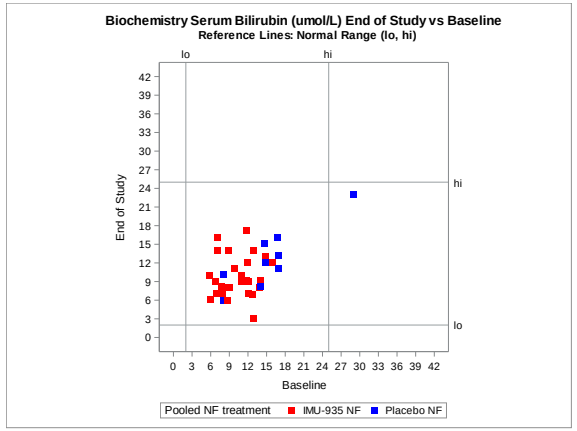


Individual Laboratory Values
Biochemistry - Bilirubin









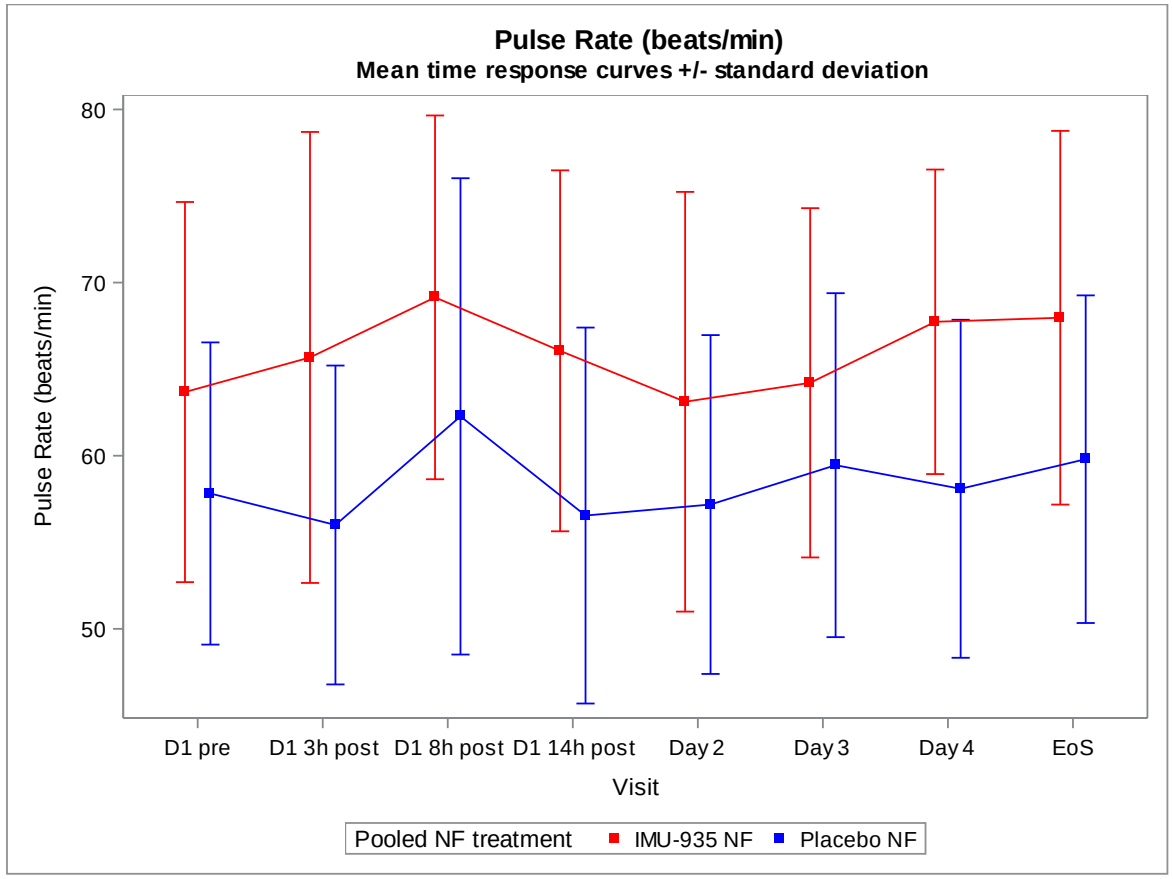
Analysis of Vital Signs
Part A-N

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

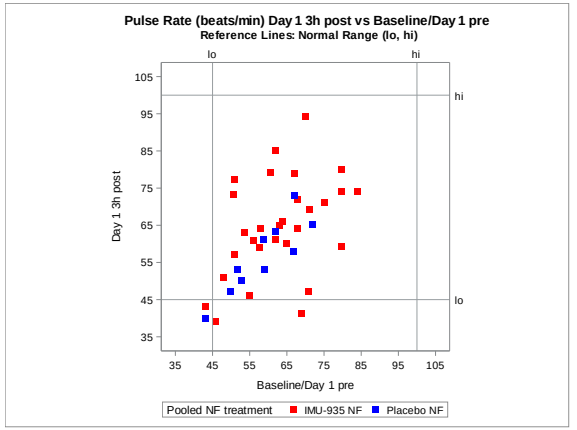
TEAE: Treatment-Emergent Adverse Event

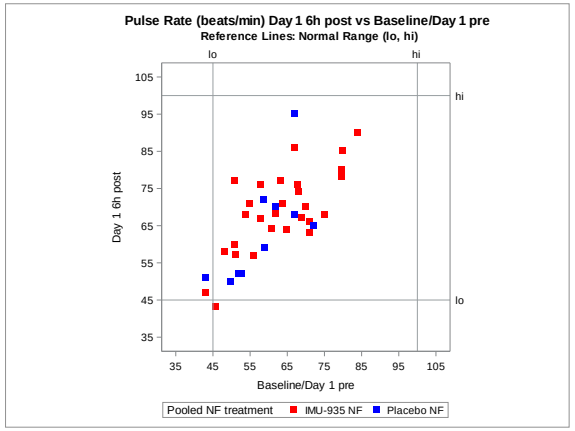
Vital Signs: Pulse Rate
Part A-N

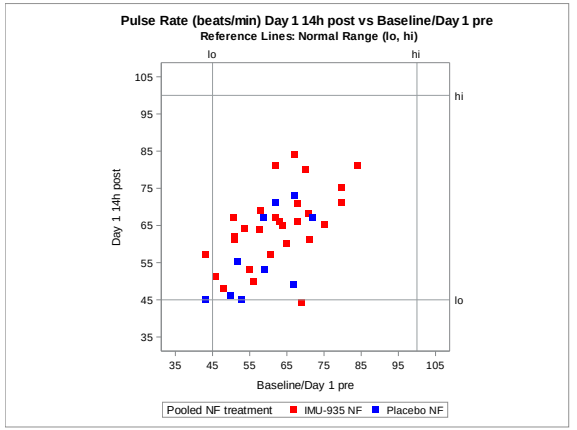
Vital Signs Over Time
Pulse Rate

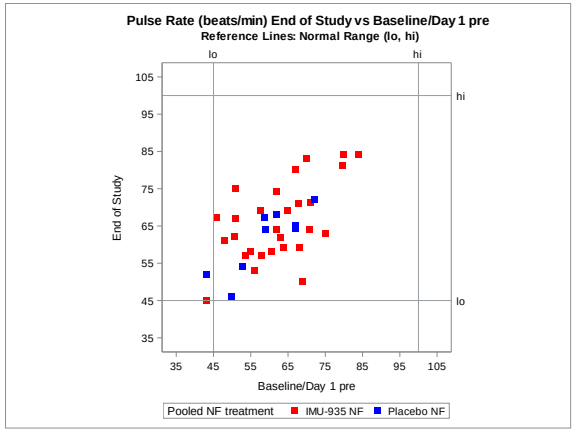


Individual Vital Signs
Pulse Rate



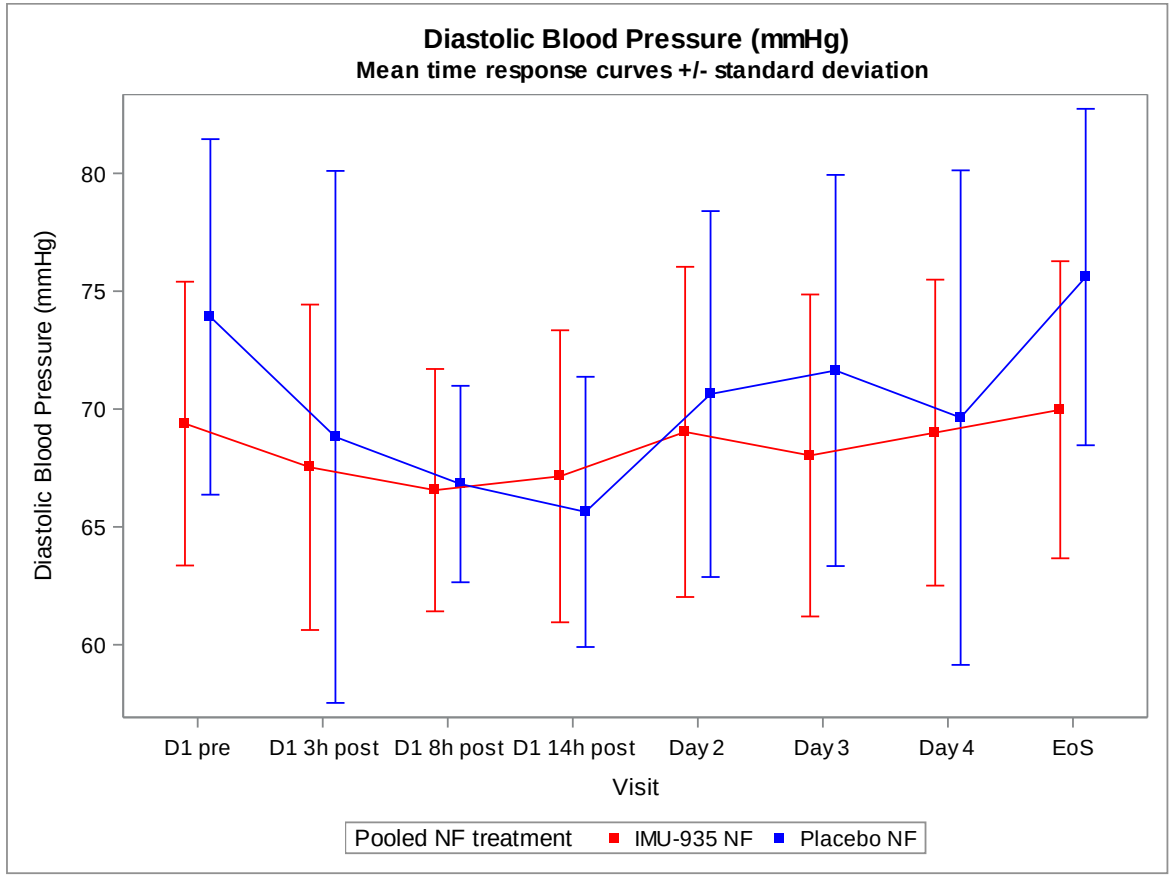




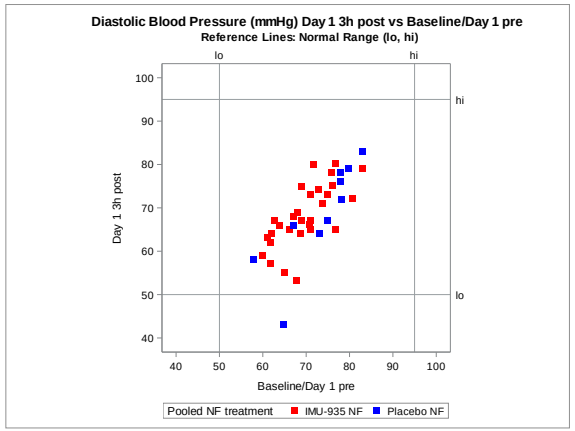


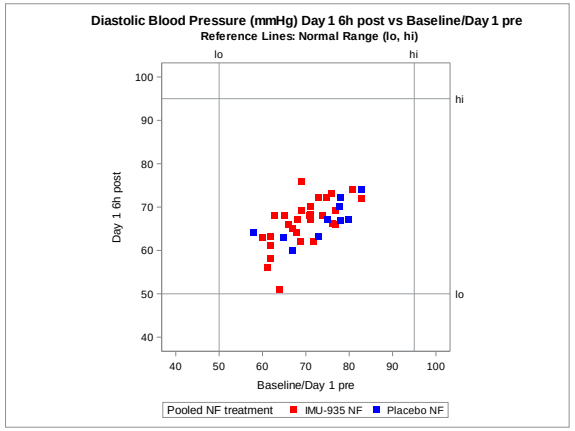
Vital Signs: Diastolic Blood Pressure
Part A-N

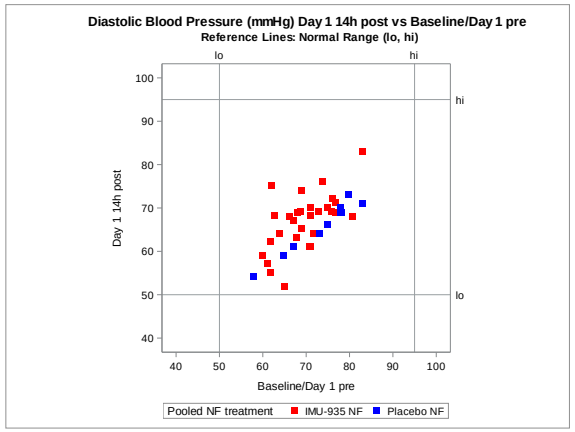
Vital Signs Over Time
Diastolic Blood Pressure

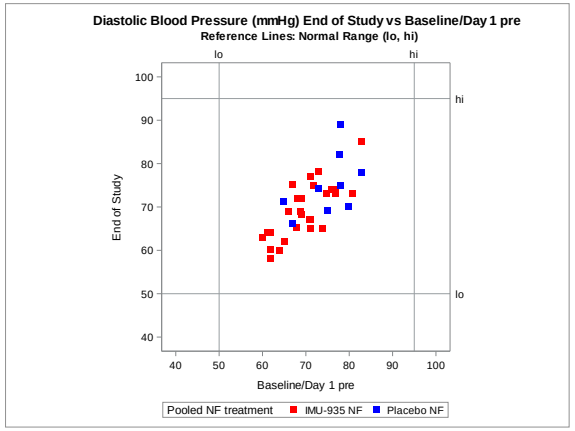


Individual Vital Signs
Diastolic Blood Pressure



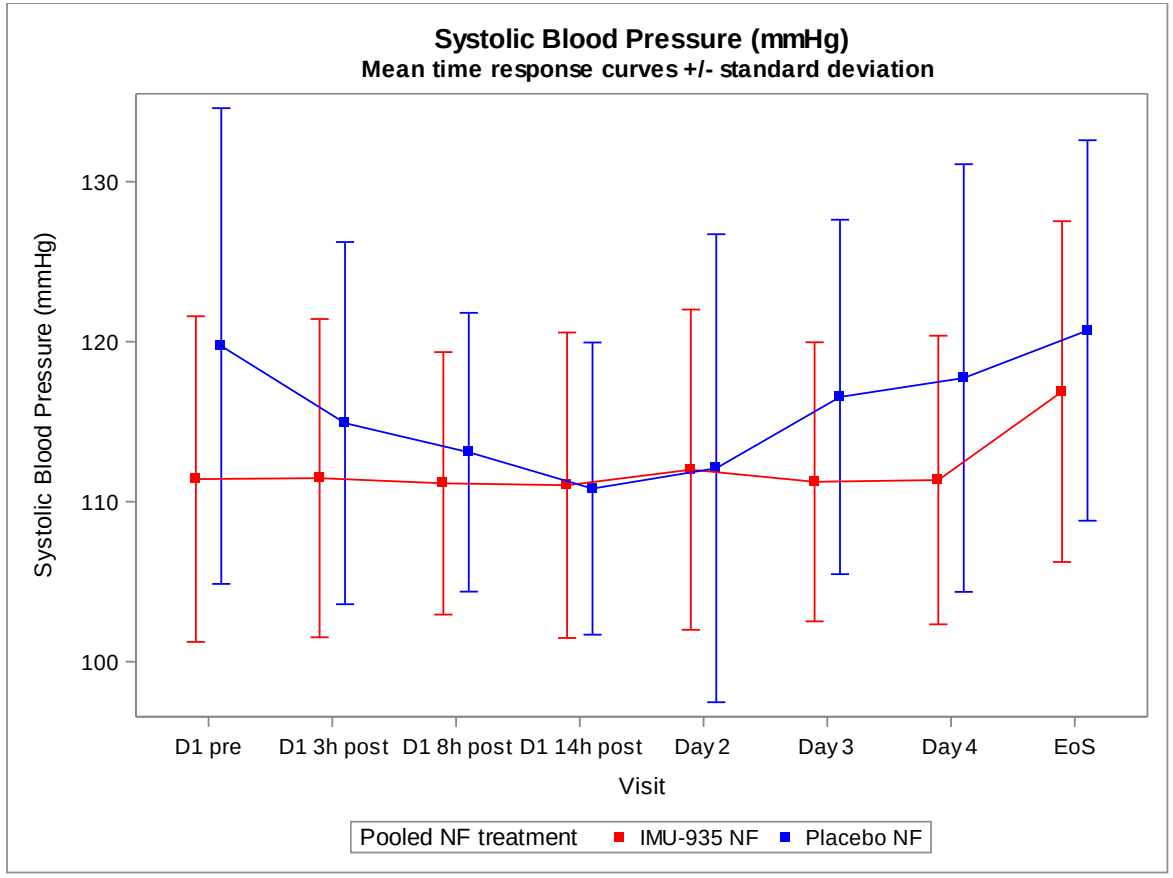




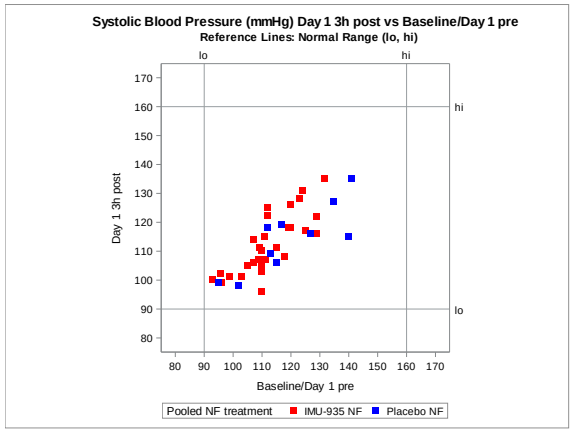


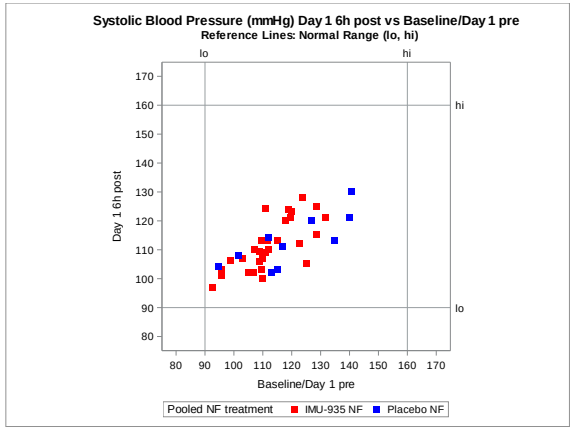
Vital Signs: Systolic Blood Pressure
Part A-N

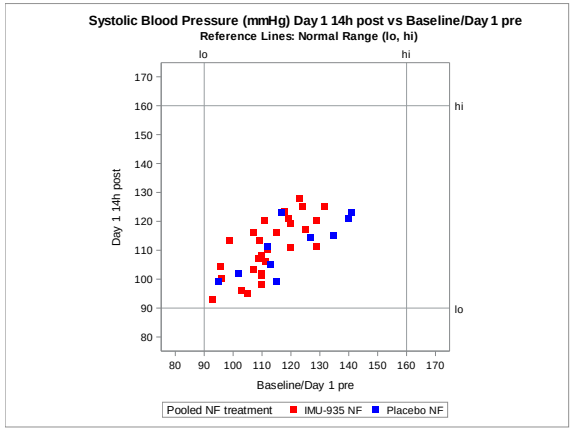
Vital Signs Over Time
Systolic Blood Pressure

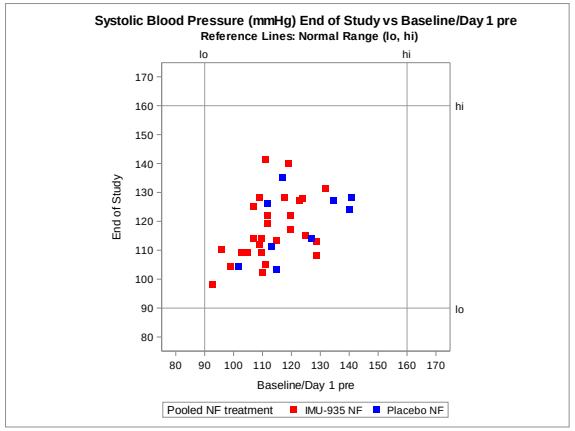


Individual Vital Signs
Systolic Blood Pressure









Analysis of 12-Lead Electrocardiograms
Part A-N

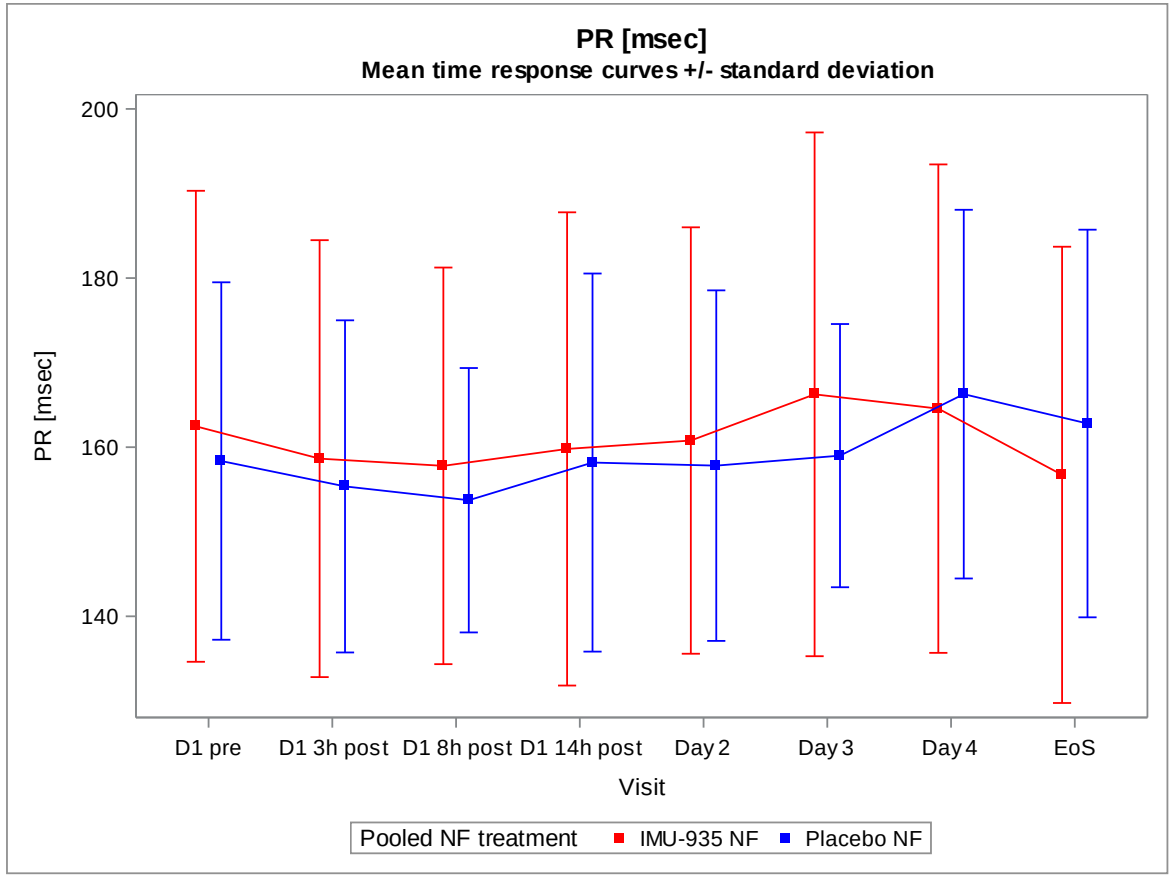
- 12-lead ECG parameters over time
  - Descriptive statistics showed no trend of values over time for any parameter
- Individual changes
  - Shift tables showed no trend of individual changes beyond the normal range for any parameter
  - In subjects with normal QTcF at baseline, no post-dose changes above 440ms were seen
- 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

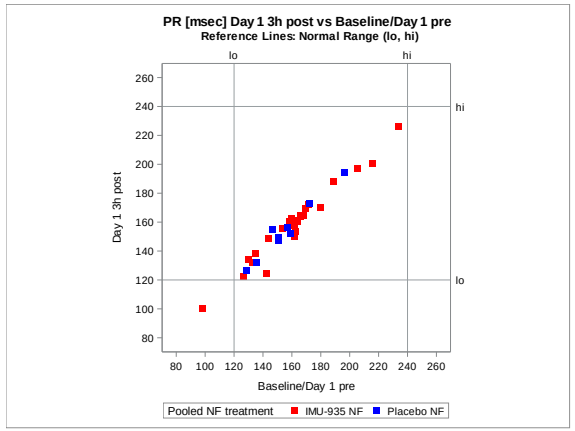
12-Lead Electrocardiograms: PR Interval

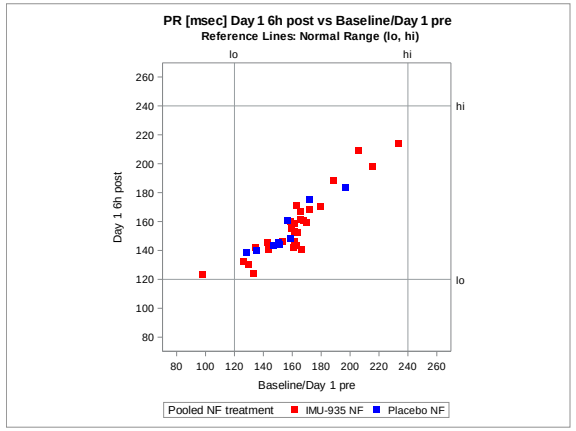
Part A-N

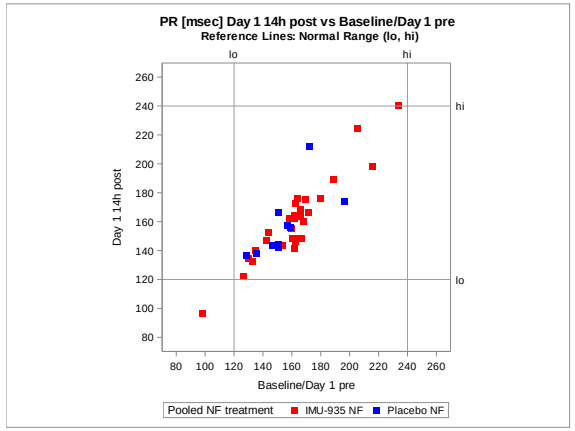
12-Lead ECGs Over Time
PR Interval

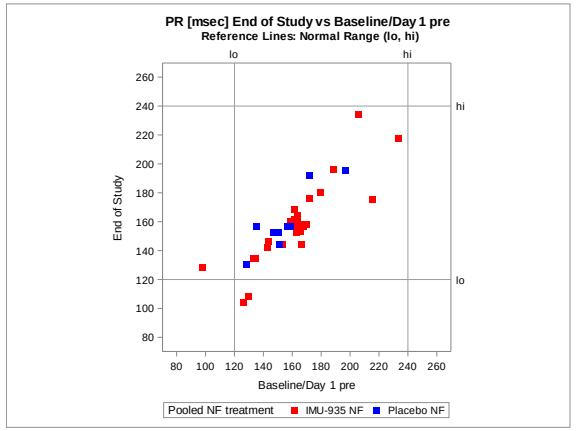


Individual 12-Lead ECGs
PR Interval







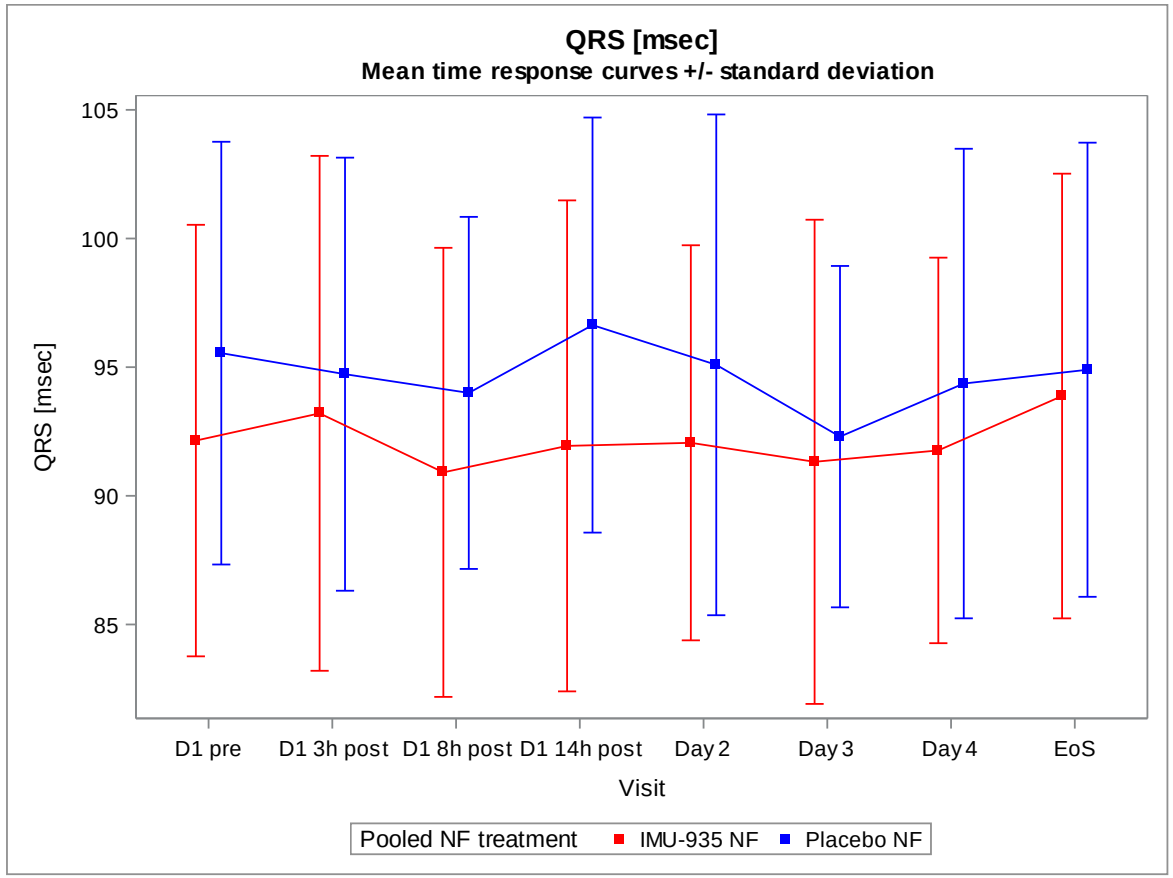


ECG: electrocardiogram

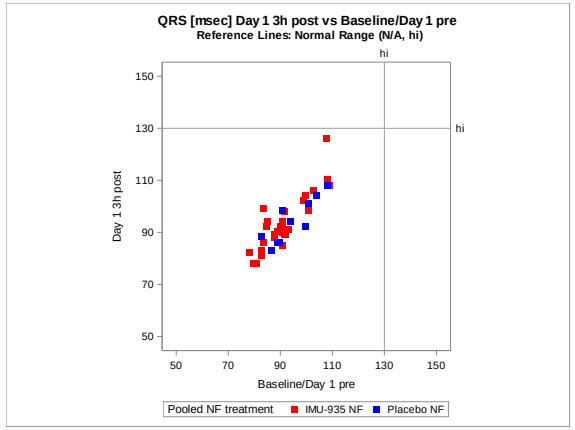
12-Lead Electrocardiograms: QRS Duration

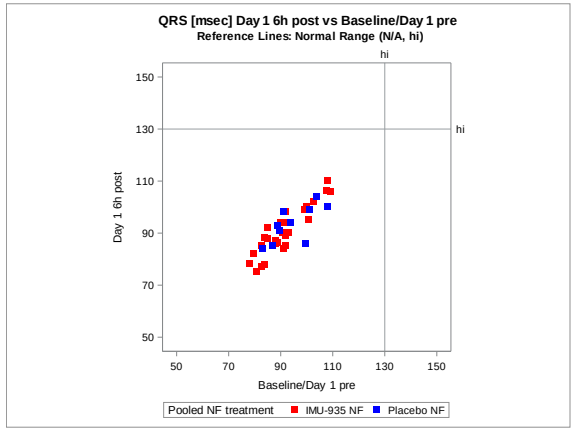
Part A-N

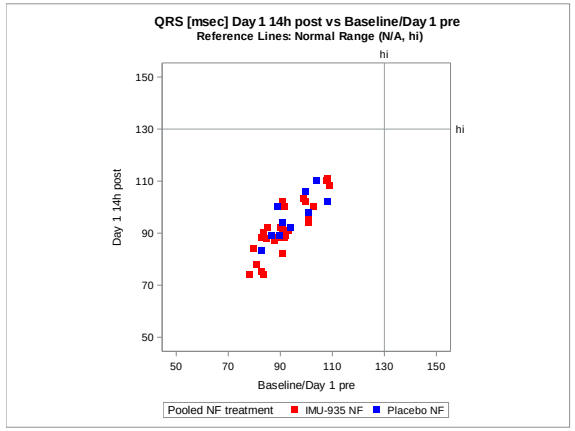
12-Lead ECGs Over Time
QRS Duration

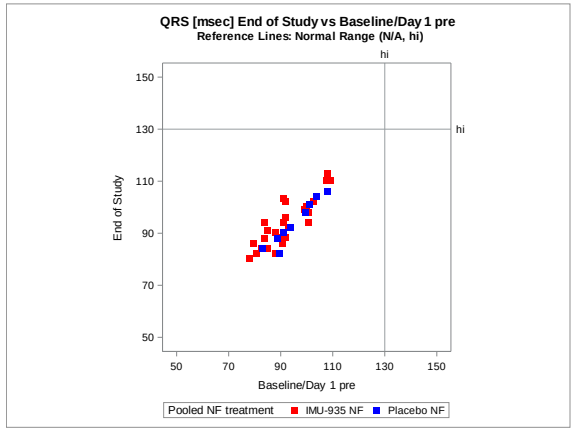


Individual 12-Lead ECGs
QRS Duration







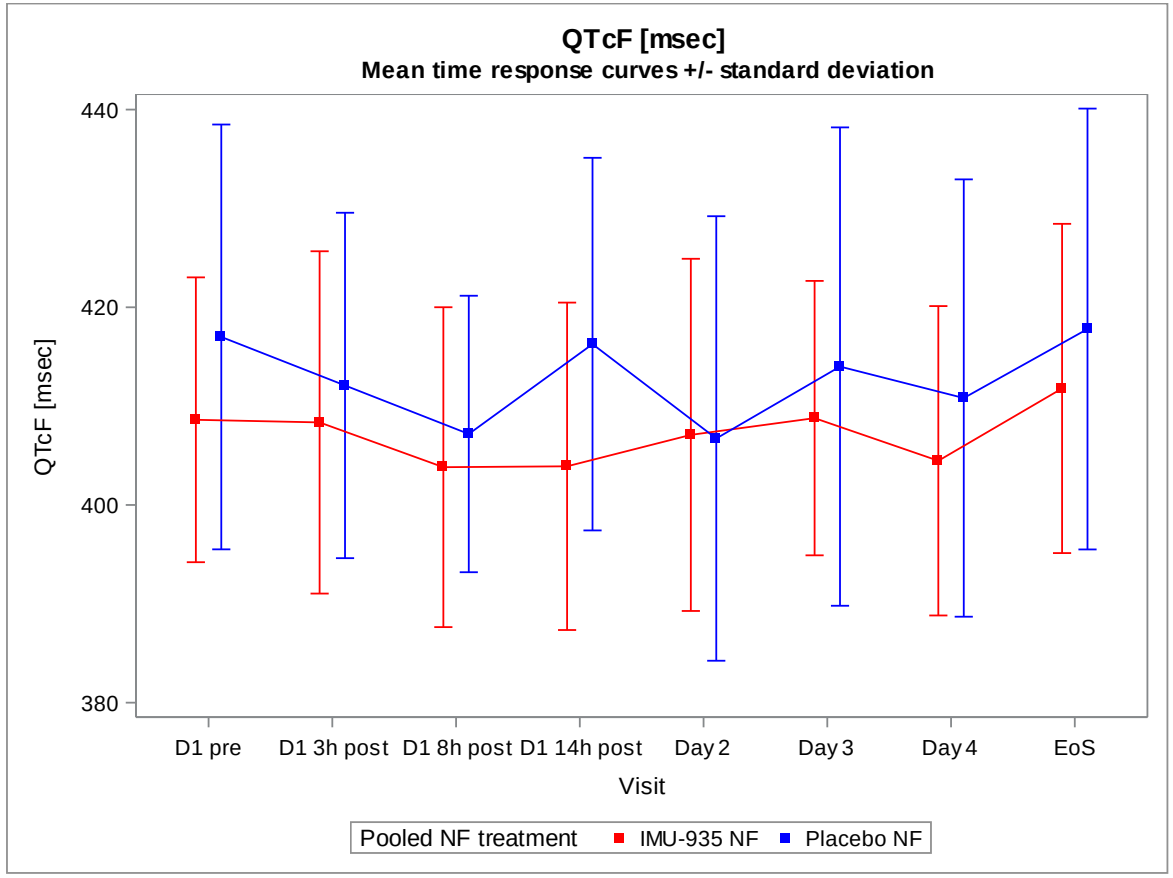


ECG: electrocardiogram

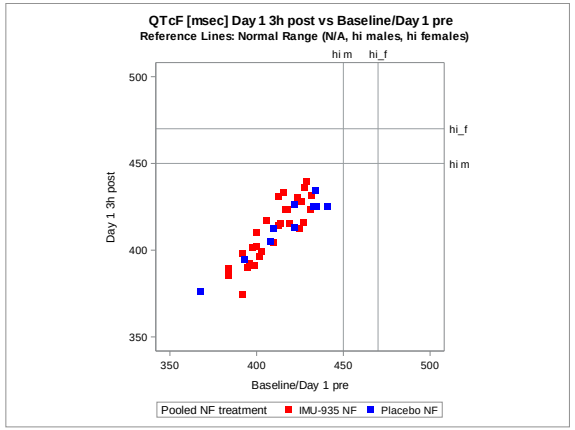
12-Lead Electrocardiograms: QTcF Interval

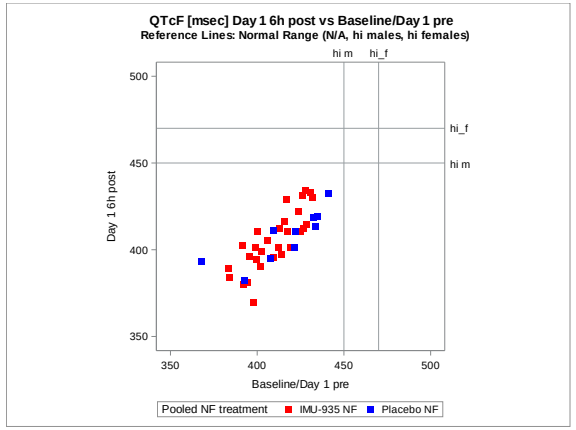
Part A-N

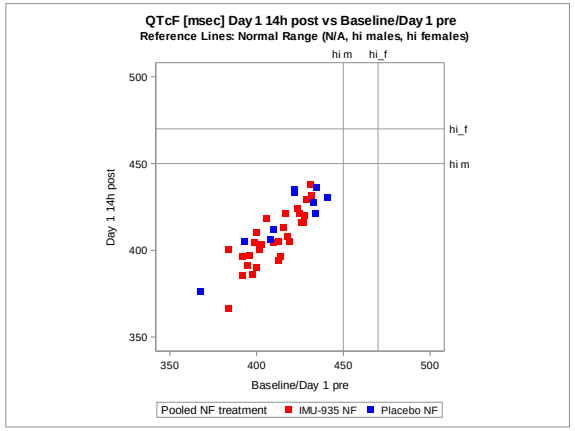
12-Lead ECGs Over Time
QTcF Interval

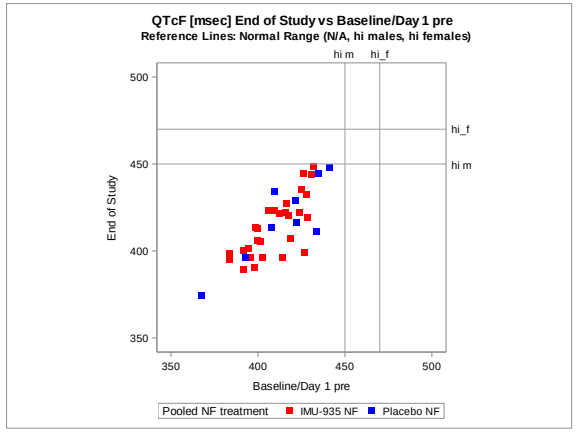


Individual 12-Lead ECGs
QTcF Interval









ECG: electrocardiogram

Powder-in-Capsule Formulation

Part B: Evaluation of Multiple Ascending Doses

Demographics
Part B

	Treatment			
	150 mg QD (N=6)	150 mg BID (N=5)	Active (N=11)	Placebo (N=4)
Age (years), mean	34.8	36.4	35.5	31.0
Gender				
Male, n (%)	4 (67%)	2 (40%)	6 (55%)	1 (25%)
Female, n (%)	2 (33%)	3 (60%)	5 (45%)	3 (75%)
Race				
Asian, n (%)	1 (17%)	-	1 (9%)	-
Black or African American, n (%)	1 (17%)	-	1 (9%)	-
White, n (%)	4 (67%)	5 (100%)	9 (82%)	4 (100%)
More than one race, n (%)	-	-	-	-
Height (cm), mean	168.7	168.8	168.7	170.5
Weight (kg), mean	77.32	81.54	79.24	81.90
BMI (kg/m^2), mean	27.00	28.54	27.70	28.29

In total, 15 healthy male and female subjects entered part B multiple dose escalation with the new formulation.

Demographics were similar across cohorts.

QD: quaque die = once-daily; BID: bis in die = two times daily

Immunic THERAPEUTICS

Related TEAEs by Incidence and Treatment
Part B

MedDRA Preferred Term	Number (%) of subjects with related TEAEs [Number of related TEAEs reported]			
	150 mg QD (N=6)	150 mg BID (N=5)	Active (N=11)	Placebo (N=4)
Headache	1 (17%) [1]	3 (60%) [3]	4 (36%) [4]	1 (25%) [4]
Electrocardiogram PR prolongation	1 (17%) [1]	-	1 (9%) [1]	-
Epistaxis	1 (17%) [2]	-	1 (9%) [2]	-
Somnolence	1 (17%) [1]	-	1 (9%) [1]	-
Constipation	-	-	-	1 (25%) [1]

TEAE: Treatment-Emergent Adverse Event

Analysis of TEAEs
Part B

- SAEs
  - None
- Severe TEAEs
  - None
- Moderate related TEAEs
  - Constipation

    After multiple doses of placebo BID, subject R0108-002 reported constipation (moderate, related). The TEAE occurred on day 16 (i.e., 2 days after completion of dosing), required no treatment and resolved within 7 days.
- TEAEs associated with liver function tests or urinalysis
  - None
- TEAEs associated with vital signs or 12-lead ECGs
  - PR prolongation

    After a multiple dose of 150 mg IMU-935 QD, subject R0107-001 had a prolonged PR interval (mild, related) on day 13. The PR interval returned to normal values in the few days thereafter and was found normal at the end-of-study visit (14 days after the last dose). The participant disclosed at the end-of-study visit that he had used large amounts of topical diclofenac gel, multiple times per day throughout the study for treatment of low back pain. The investigator believed that, given the temporal association, the PR prolongation was more likely to be related to the diclofenac than IMU-935. Prolonged PR interval is known to be a benign electrocardiographic finding in healthy individuals and it is not associated with an increased risk of all-cause or cardiovascular mortality [1].

TEAE: Treatment-Emergent Adverse Event; SAE: Serious Adverse Event; ECG: electrocardiogram

[1] Aro AL, et al. Prognostic significance of prolonged PR interval in the general population. Eur Heart J. 2014 Jan;35(2):123-9

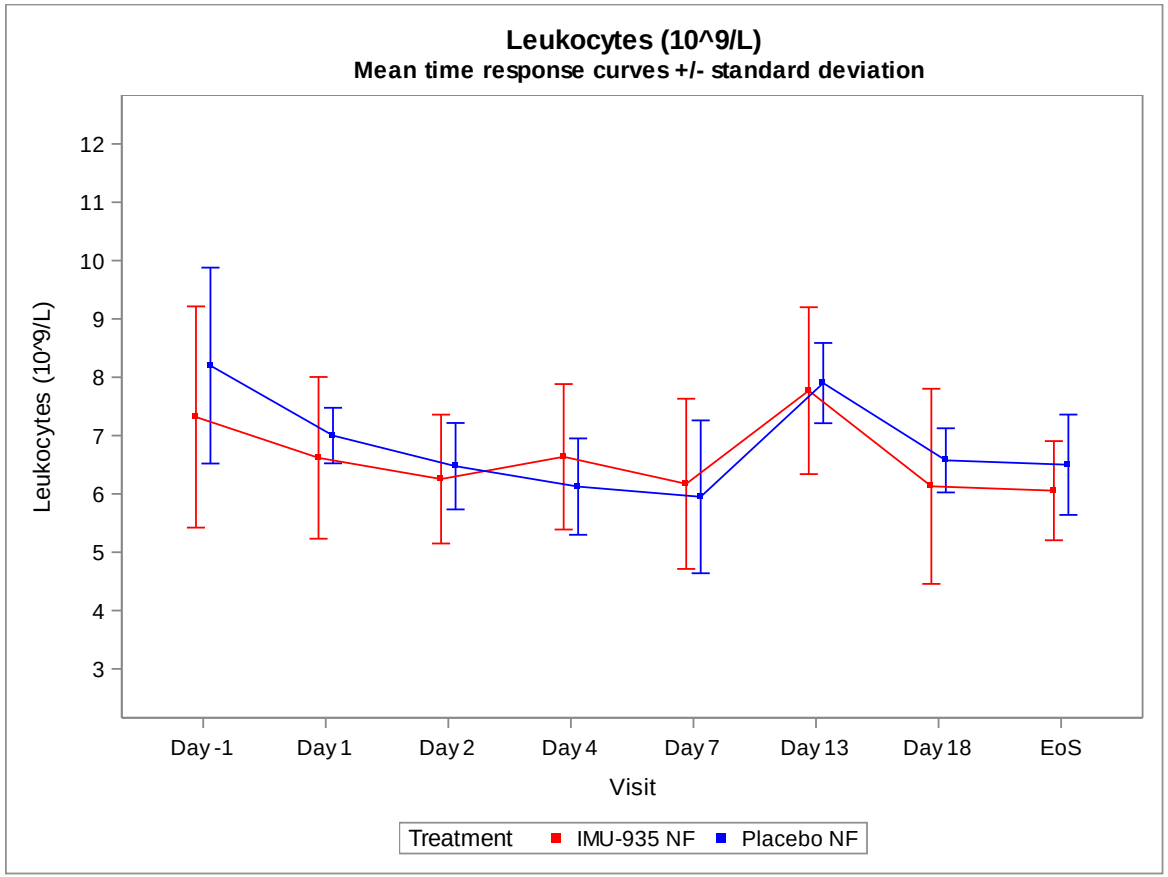
Analysis of Laboratory Parameters
Part B

- 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
  - Abnormalities in laboratory parameters were considered not clinically significant by the investigators
  - Thus, no TEAEs associated with laboratory parameters have been reported

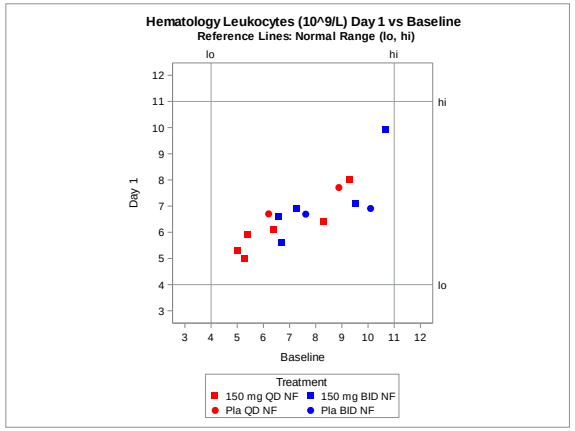
TEAE: Treatment-Emergent Adverse Event

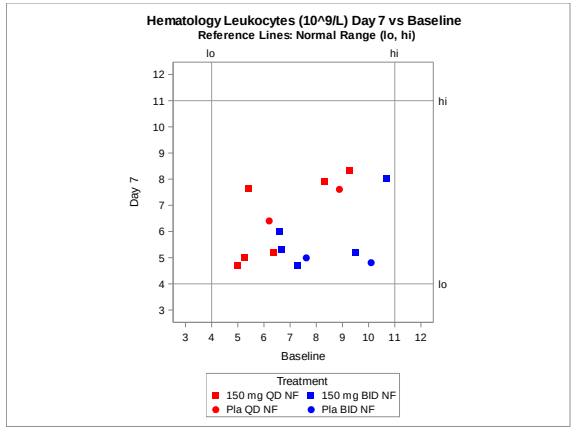
Laboratory Parameters: Leukocytes
Part B

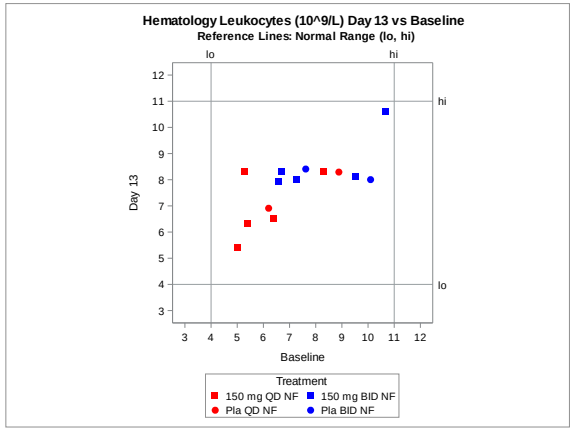
Laboratory Values Over Time
Hematology - Leukocytes

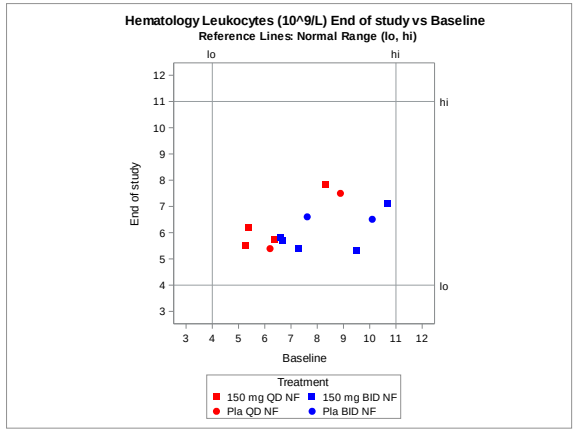


Individual Laboratory Values
Hematology - Leukocytes



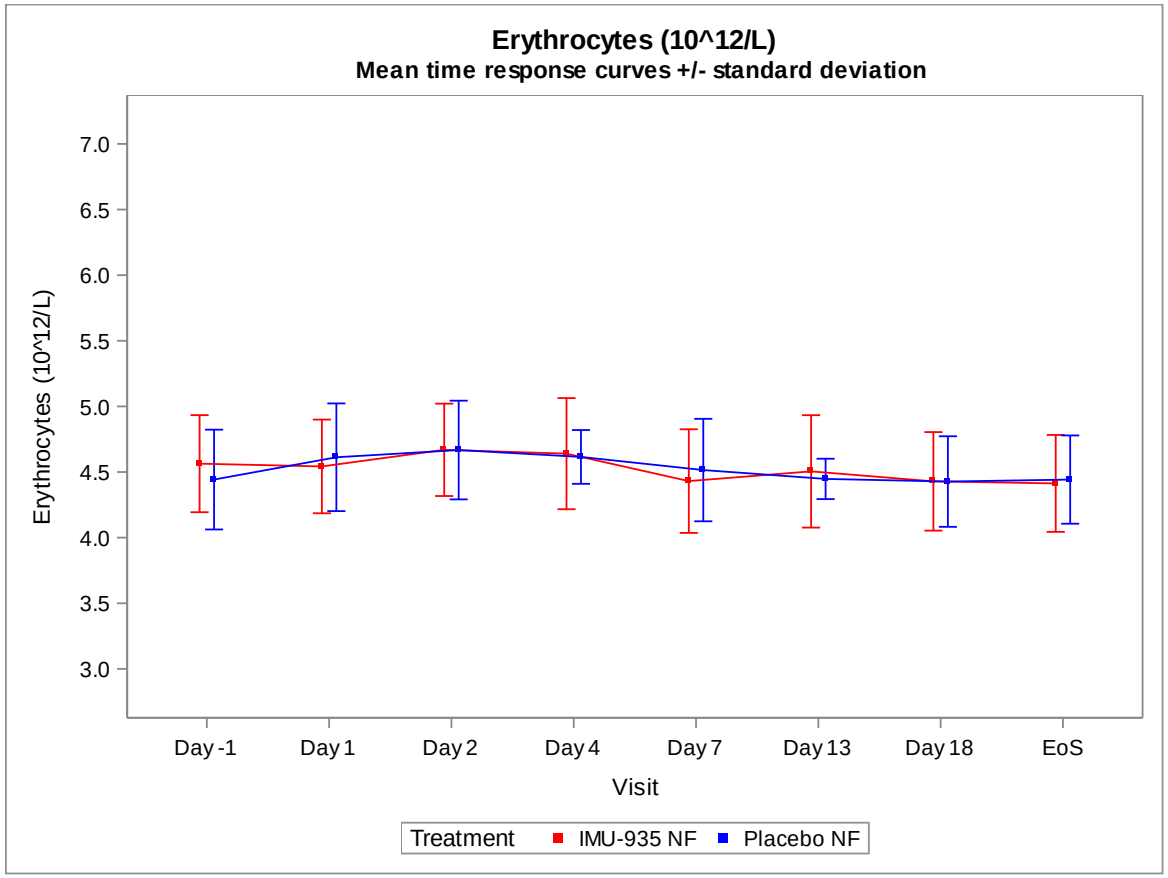




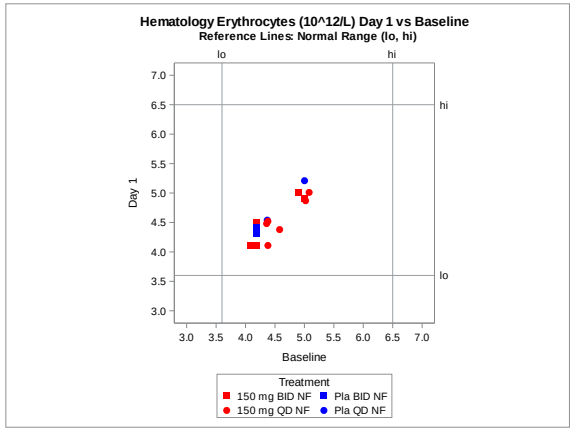


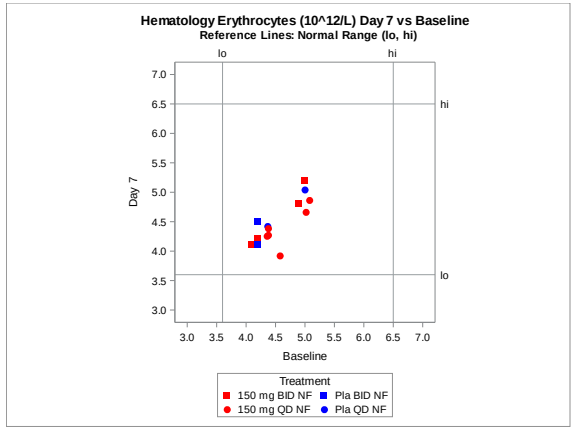
Laboratory Parameters: Erythrocytes
Part B

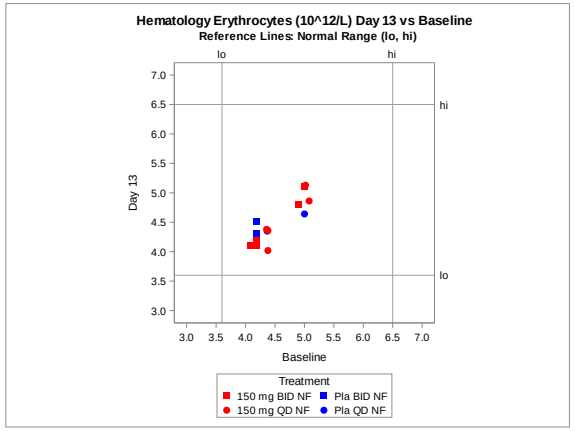
Laboratory Values Over Time
Hematology - Erythrocytes

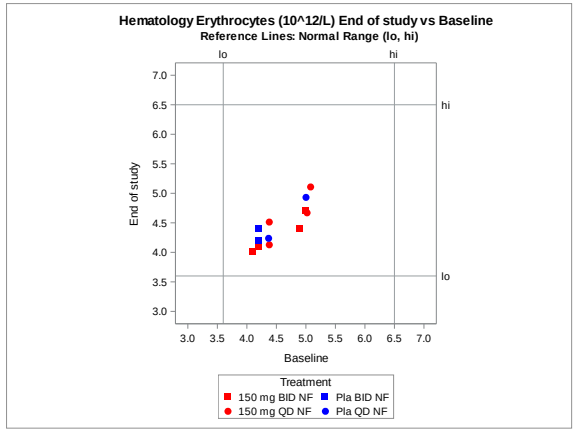


Individual Laboratory Values
Hematology - Erythrocytes



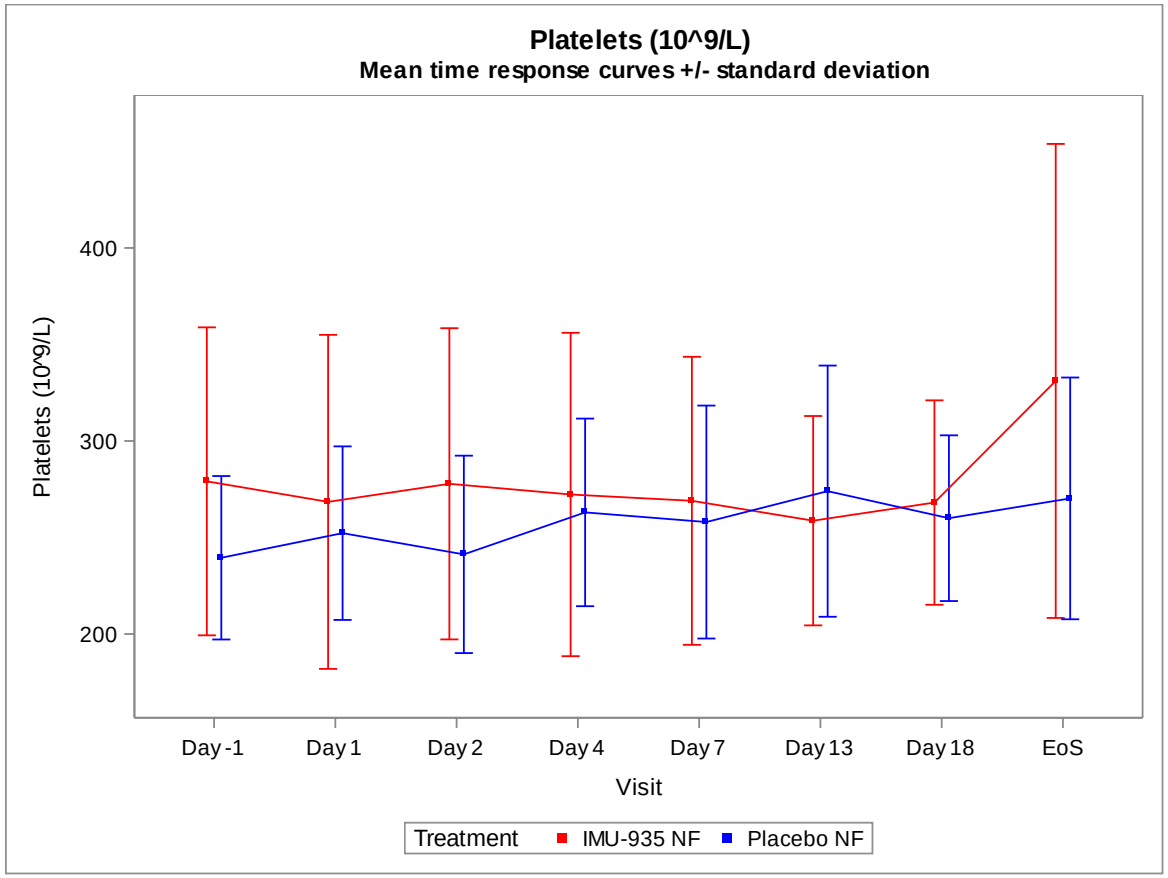




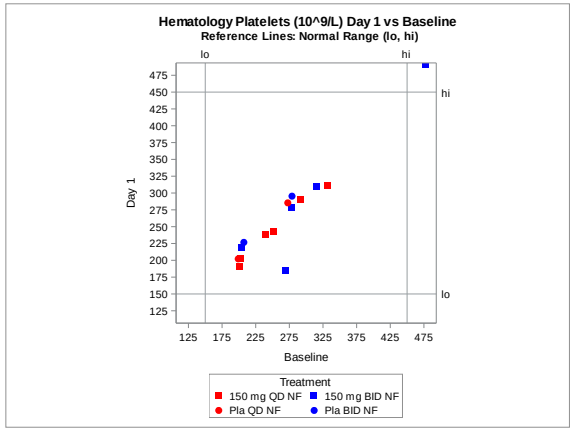


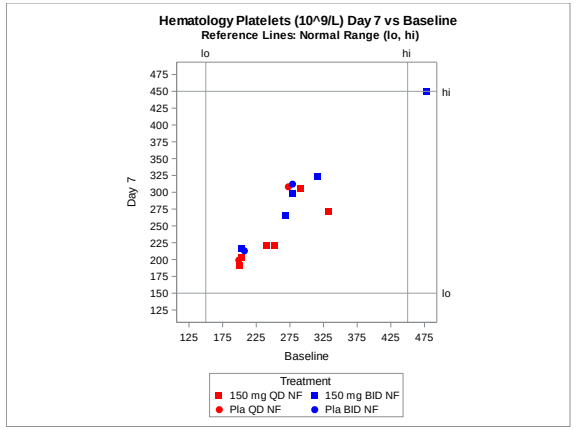
Laboratory Parameters: Platelets
Part B

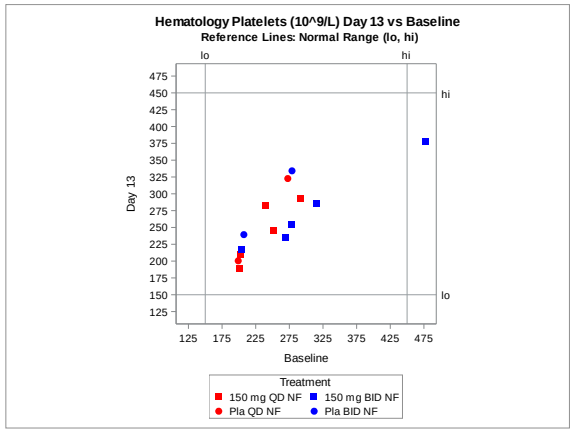
Laboratory Values Over Time
Hematology - Platelets

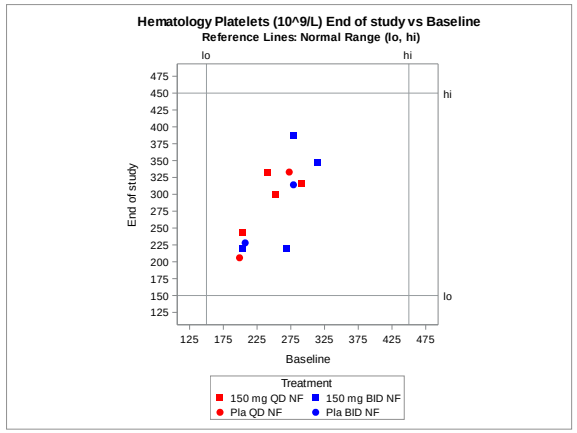


Individual Laboratory Values
Hematology - Platelets



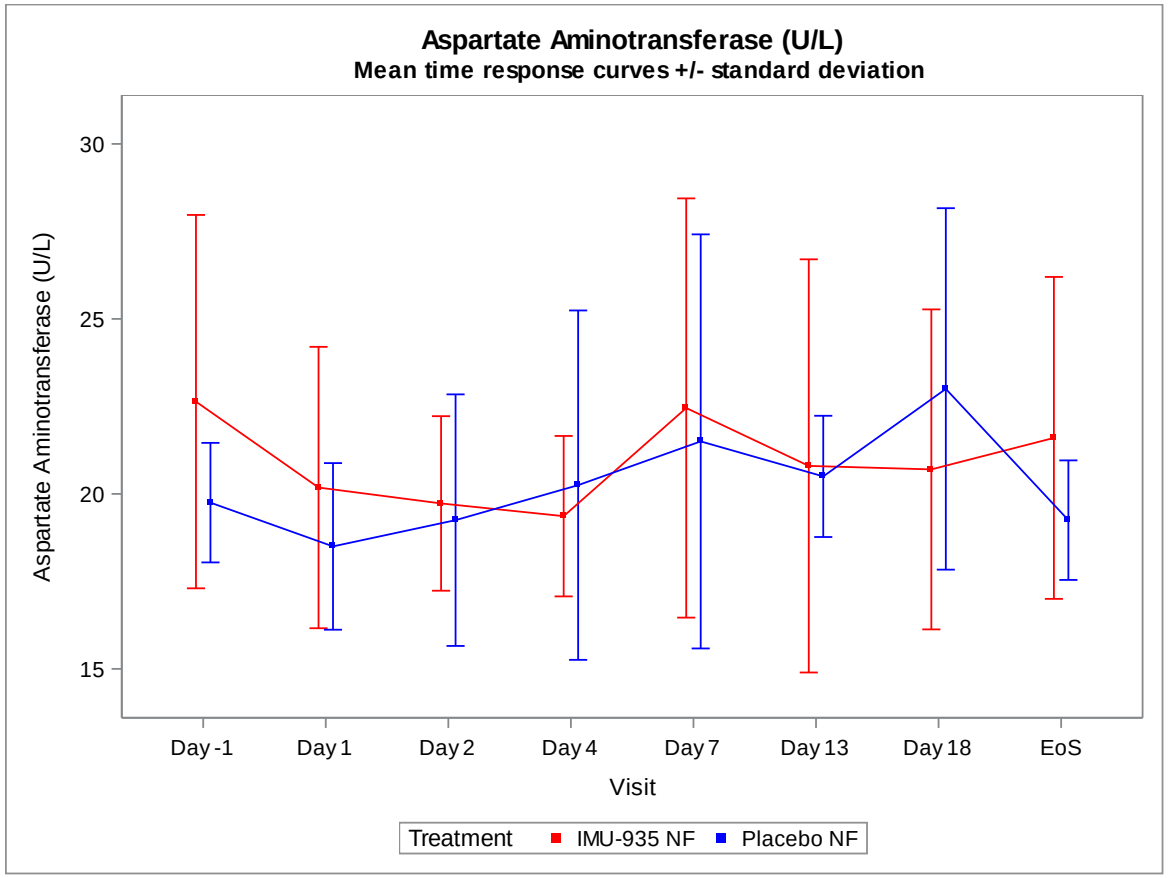




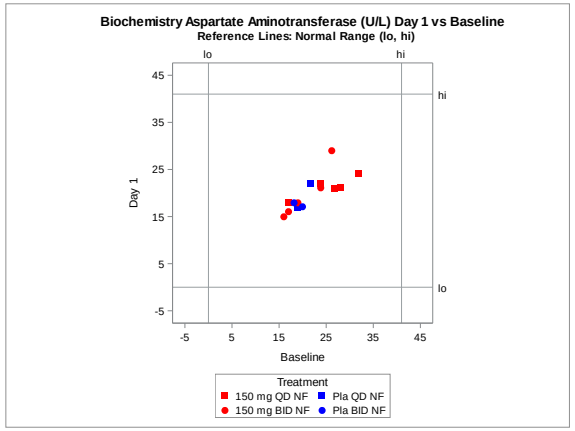


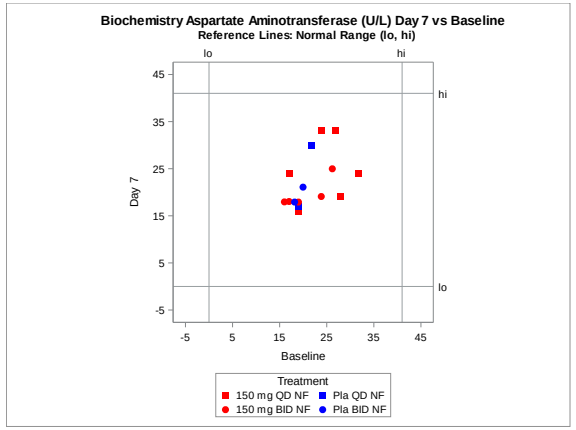
Laboratory Parameters: AST
Part B

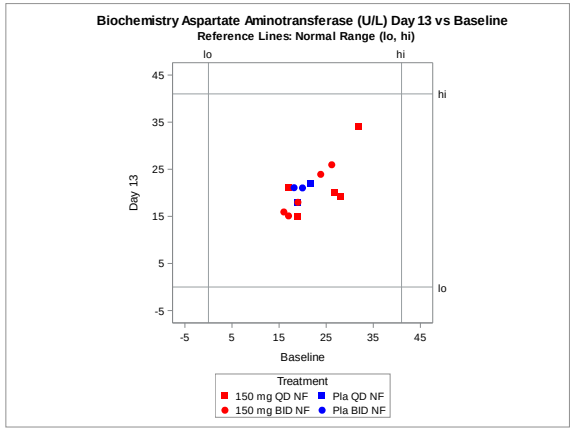
Laboratory Values Over Time
Biochemistry - AST

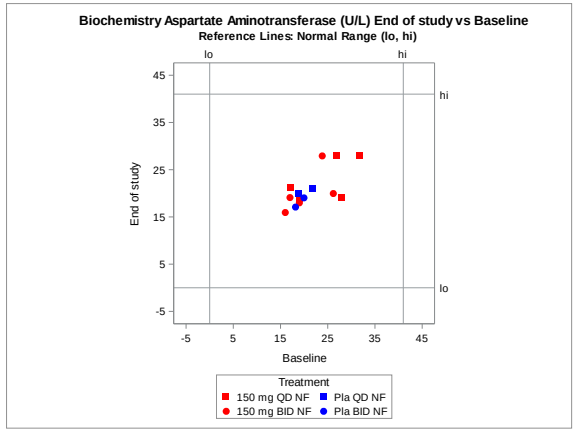


Individual Laboratory Values
Biochemistry - AST





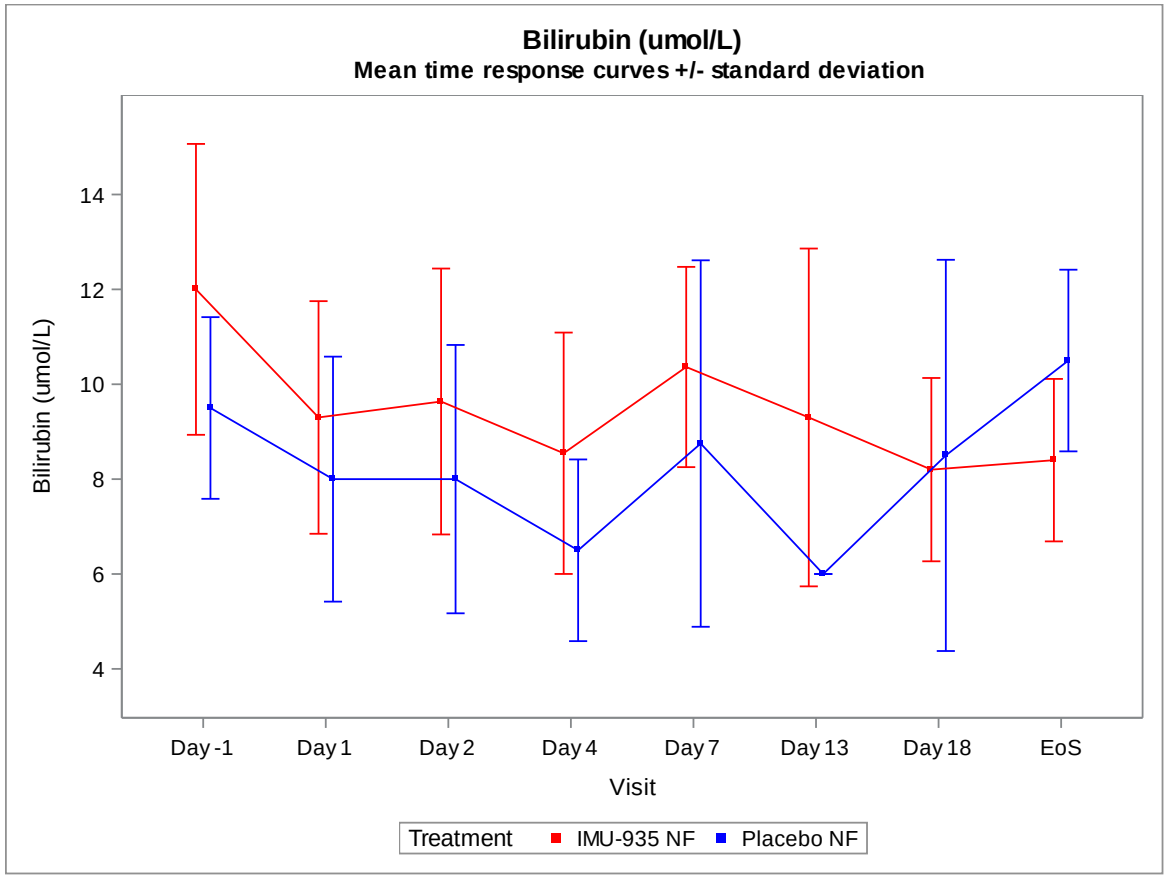




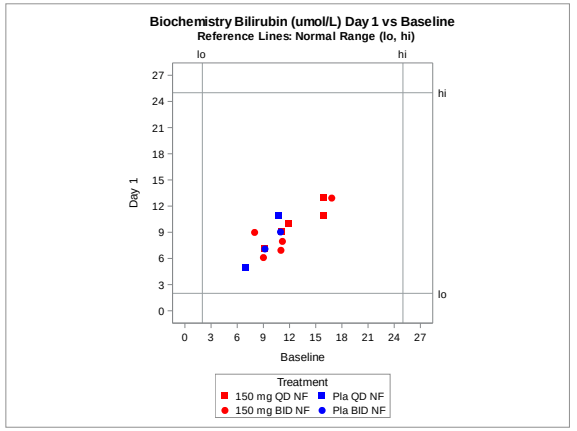
AST: Aspartate Aminotransferase

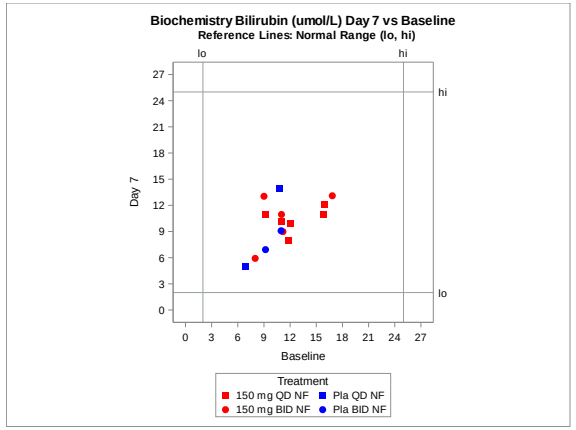
Laboratory Parameters: Bilirubin
Part B

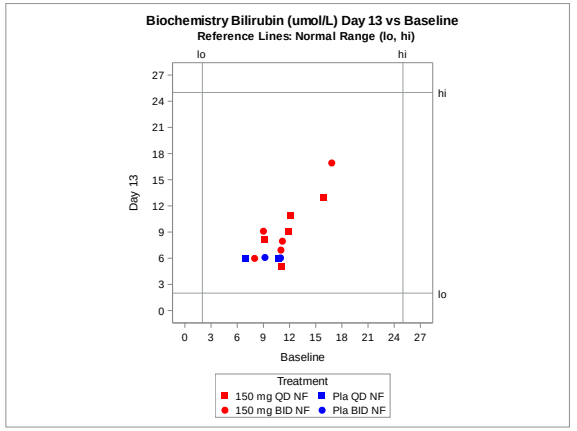
Laboratory Values Over Time
Biochemistry - Bilirubin

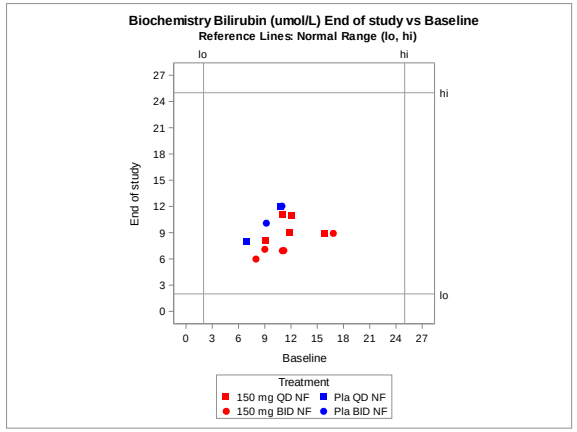


Individual Laboratory Values
Biochemistry - Bilirubin









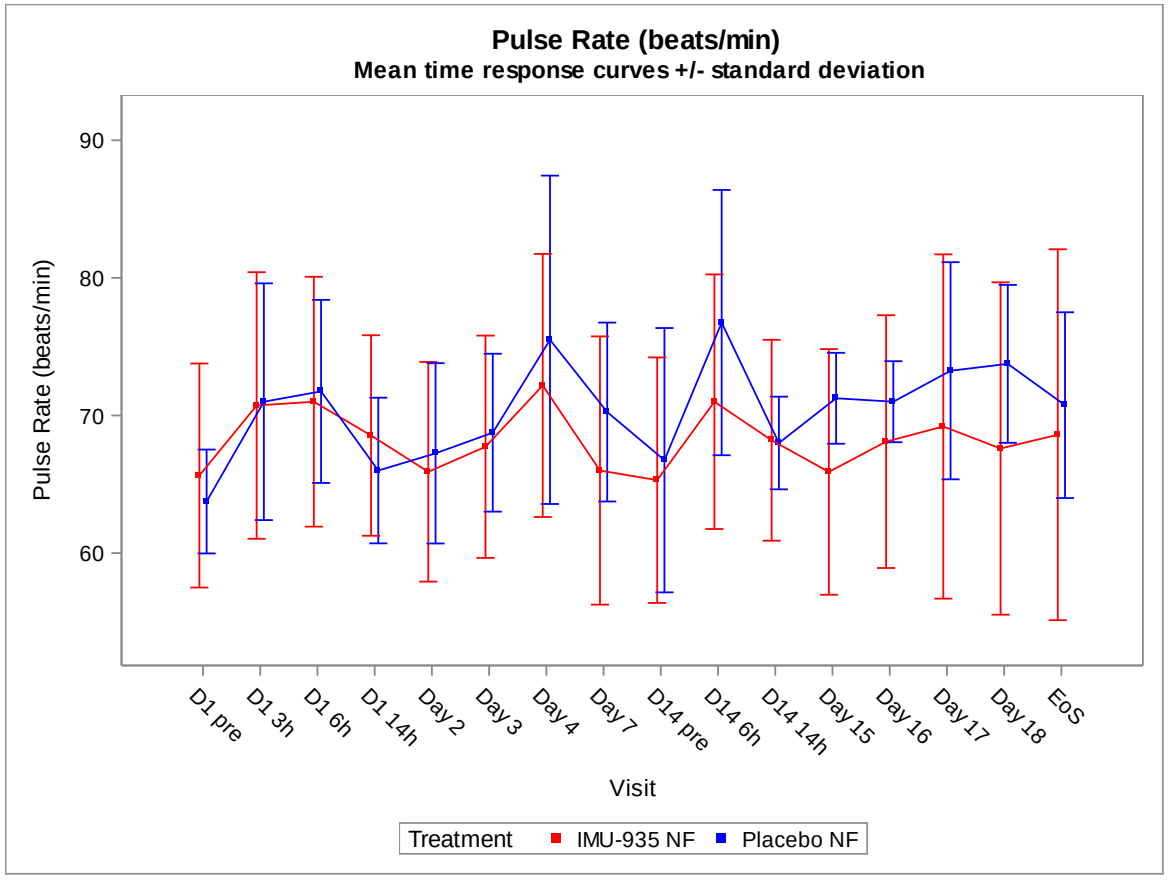
Analysis of Vital Signs
Part B

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

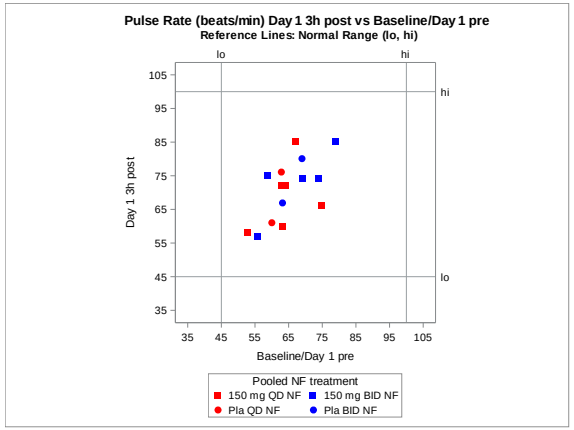
TEAE: Treatment-Emergent Adverse Event

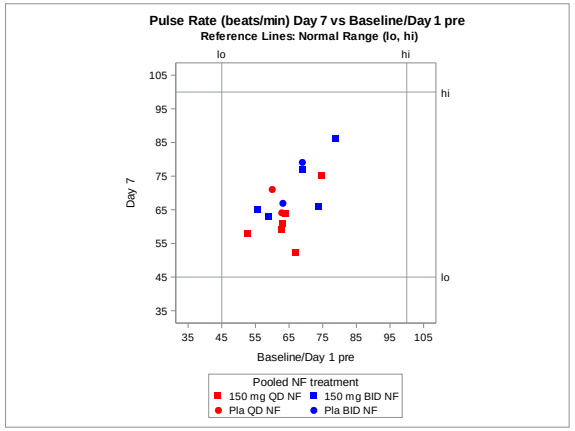
Vital Signs: Pulse Rate
Part B

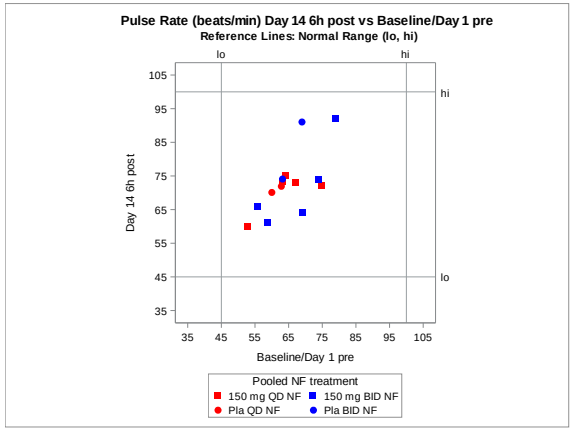
Vital Signs Over Time
Pulse Rate

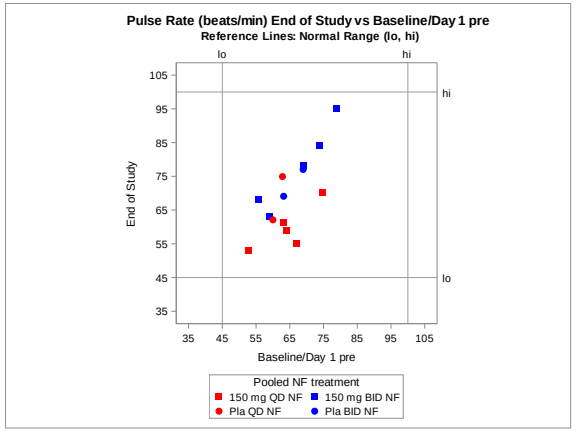


Individual Vital Signs
Pulse Rate



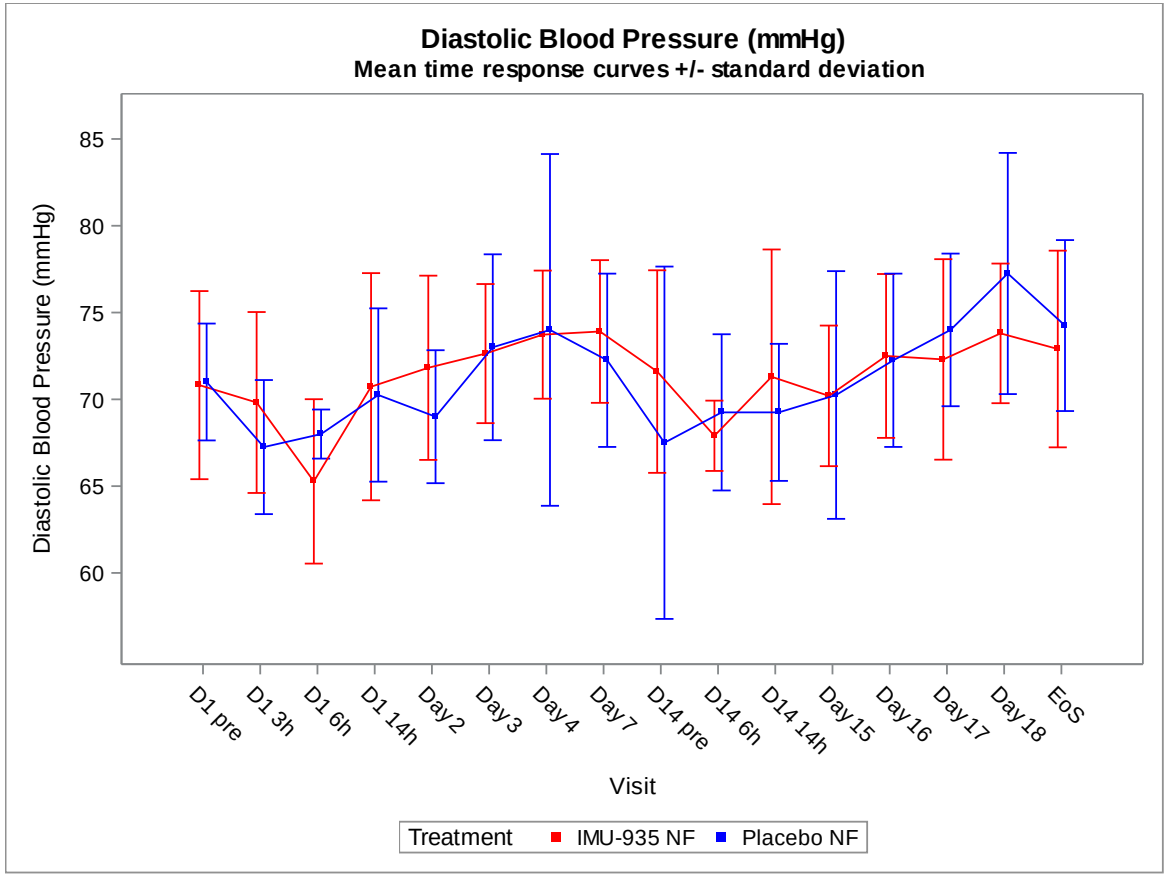




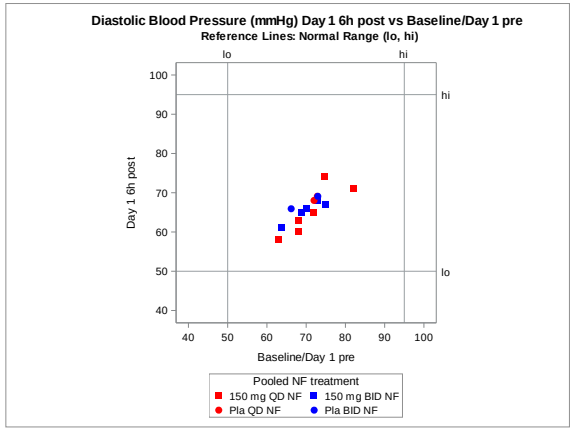


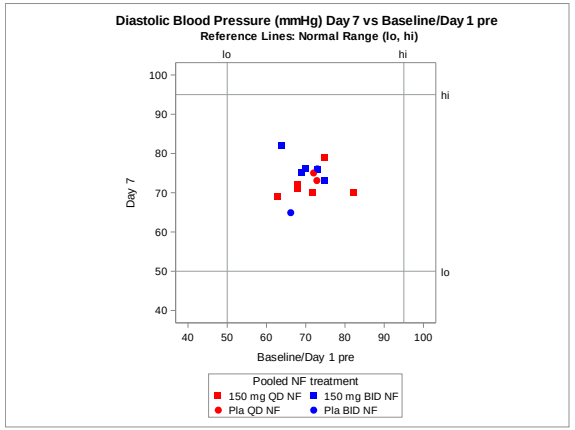
Vital Signs: Diastolic Blood Pressure
Part B

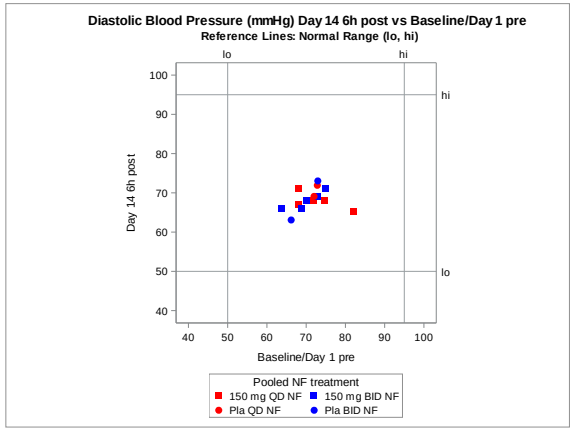
Vital Signs Over Time
Diastolic Blood Pressure

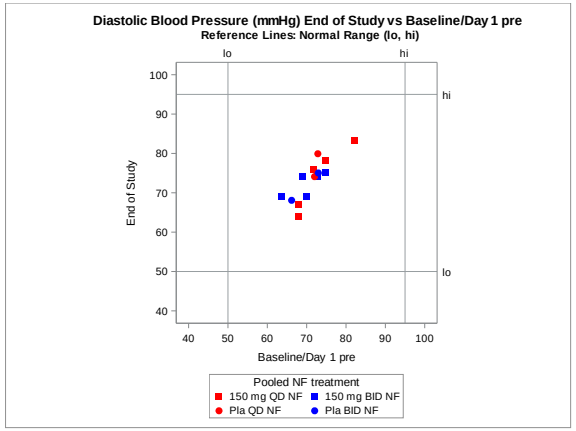


Individual Vital Signs
Diastolic Blood Pressure



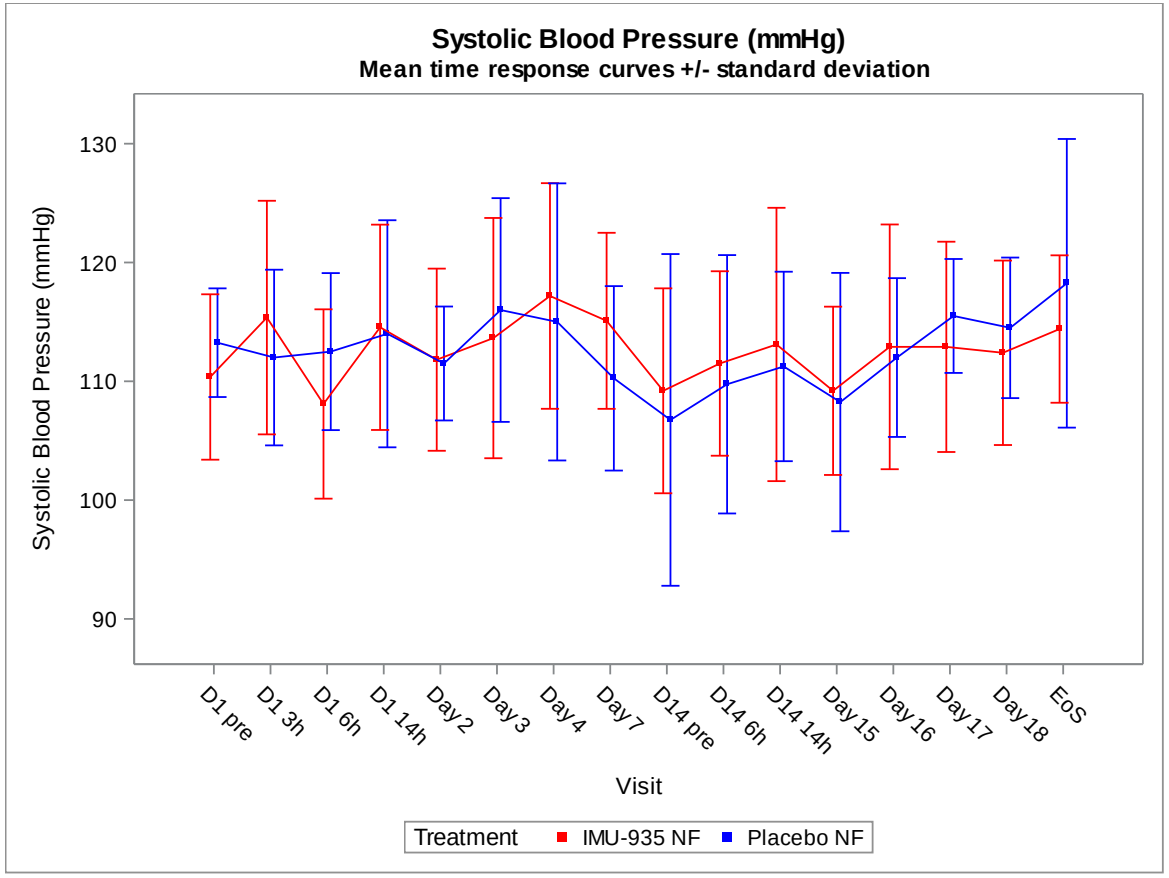




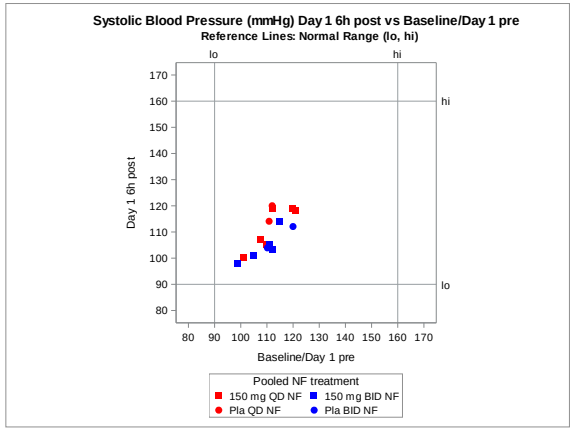


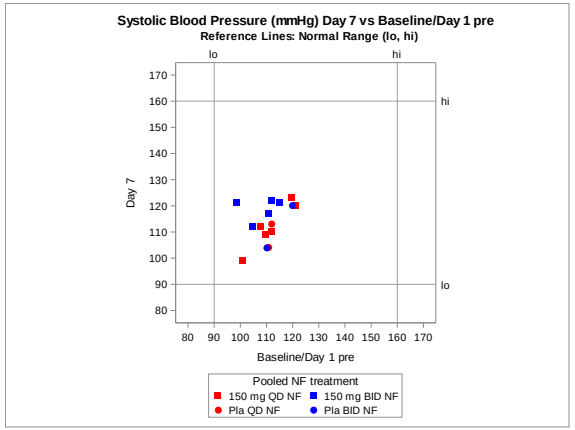
Vital Signs: Systolic Blood Pressure
Part B

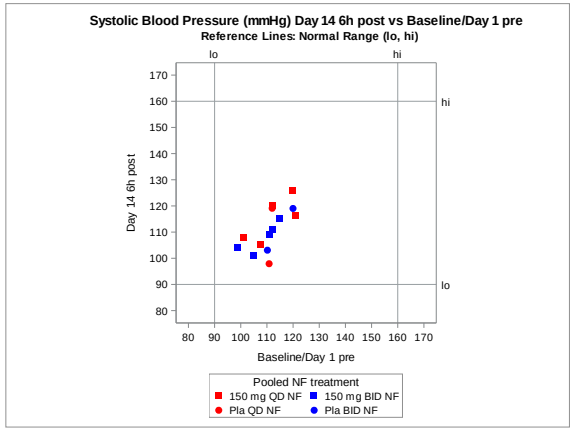
Vital Signs Over Time
Systolic Blood Pressure

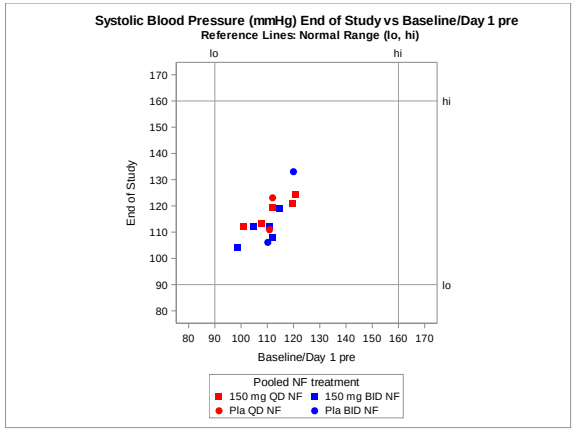


Individual Vital Signs
Systolic Blood Pressure









Analysis of 12-Lead Electrocardiograms
Part B: Powder-in-Capsule Formulation

- 12-lead ECG parameters 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
  - In subjects with normal QTcF at baseline, no post-dose changes above 440ms were seen
- Individual clinically significant abnormalities
  - Almost all abnormalities in 12-lead ECG parameters were considered not clinically significant by the investigators
  - A single TEAE associated with 12-lead ECG parameters was reported:
    - PR prolongation (see following slide for details)

ECG: electrocardiogram; TEAE: Treatment-Emergent Adverse Event

12-Lead Electrocardiograms
Part B

- Narrative of TEAE associated with 12-lead ECG parameters
  - PR prolongation

    After a multiple dose of 150 mg IMU-935 QD, subject R0107-001 had a prolonged PR interval (mild, related) on day 13. The PR interval returned to normal values in the few days thereafter and was found normal at the end-of-study visit (14 days after the last dose). The participant disclosed at the end-of-study visit that he had used large amounts of topical diclofenac gel, multiple times per day throughout the study for treatment of low back pain. The investigator believed that, given the temporal association, the PR prolongation was more likely to be related to the diclofenac than IMU-935. Prolonged PR interval is known to be a benign electrocardiographic finding in healthy individuals and it is not associated with an increased risk of all-cause or cardiovascular mortality [1].

Parameter	Visit	Timepoint	Result
PR interval	Screening	-	182
	Day -1	-	202
	Day 1	Pre-dose	197
		3 Hour Post Dose	182
		6 Hour Post Dose	196
		14 Hour Post Dose	230
	Day 2	-	195
	Day 3	-	200
	Day 4	-	180
	Day 7	-	209

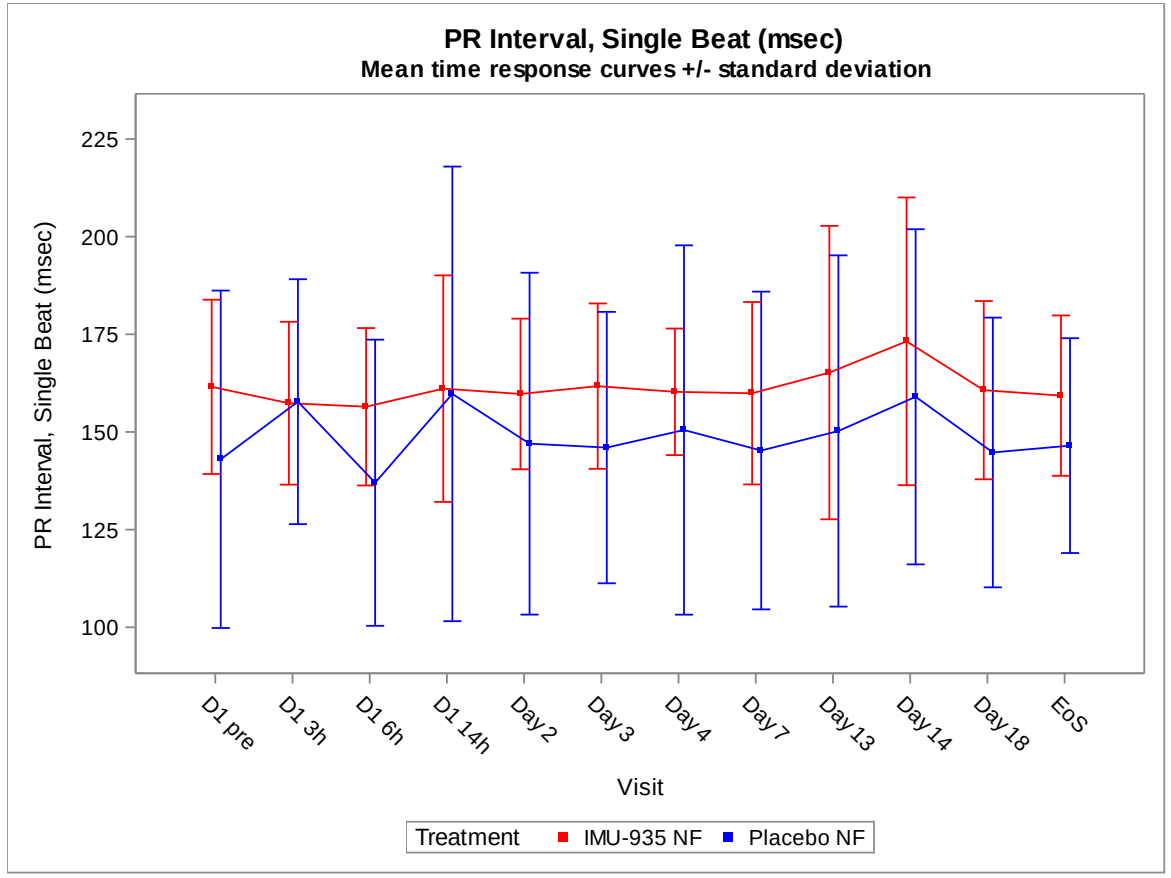
Parameter	Visit	Timepoint	Result
PR interval	Day 13	-	261
	Day 14	-	264
	Day 15, Unscheduled	-	173
	Day 16, Unscheduled	-	238
	Day 17, Unscheduled	-	245
	Day 18	-	203
	End of Study	-	196

TEAE: Treatment-Emergent Adverse Event

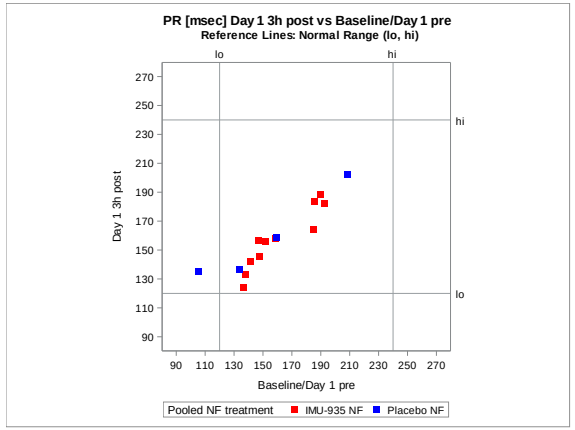
[1] Aro AL, et al. Prognostic significance of prolonged PR interval in the general population. Eur Heart J. 2014 Jan;35(2):123-9

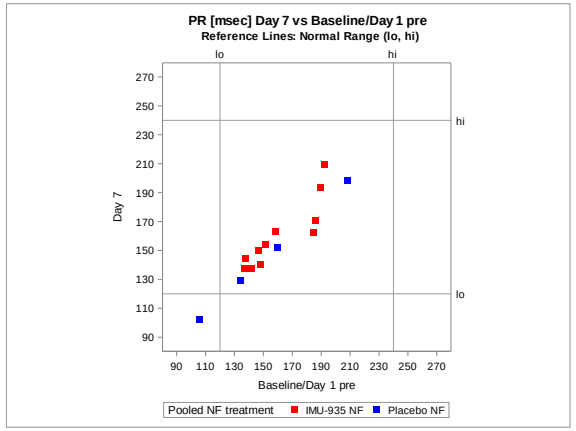
12-Lead Electrocardiograms: PR Interval
Part B

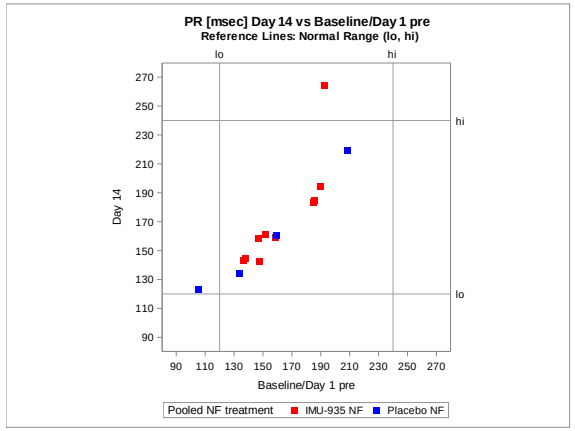
12-Lead ECGs Over Time
PR Interval

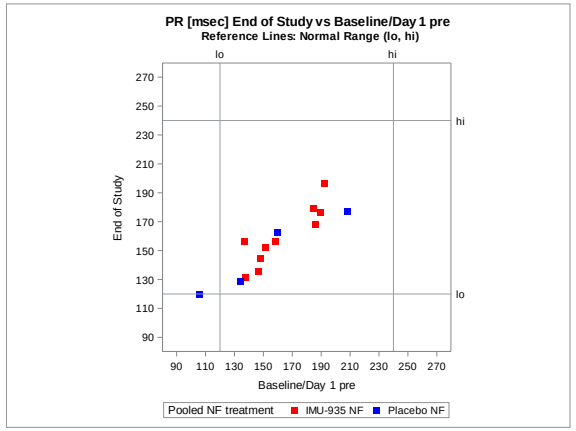


Individual 12-Lead ECGs
PR Interval





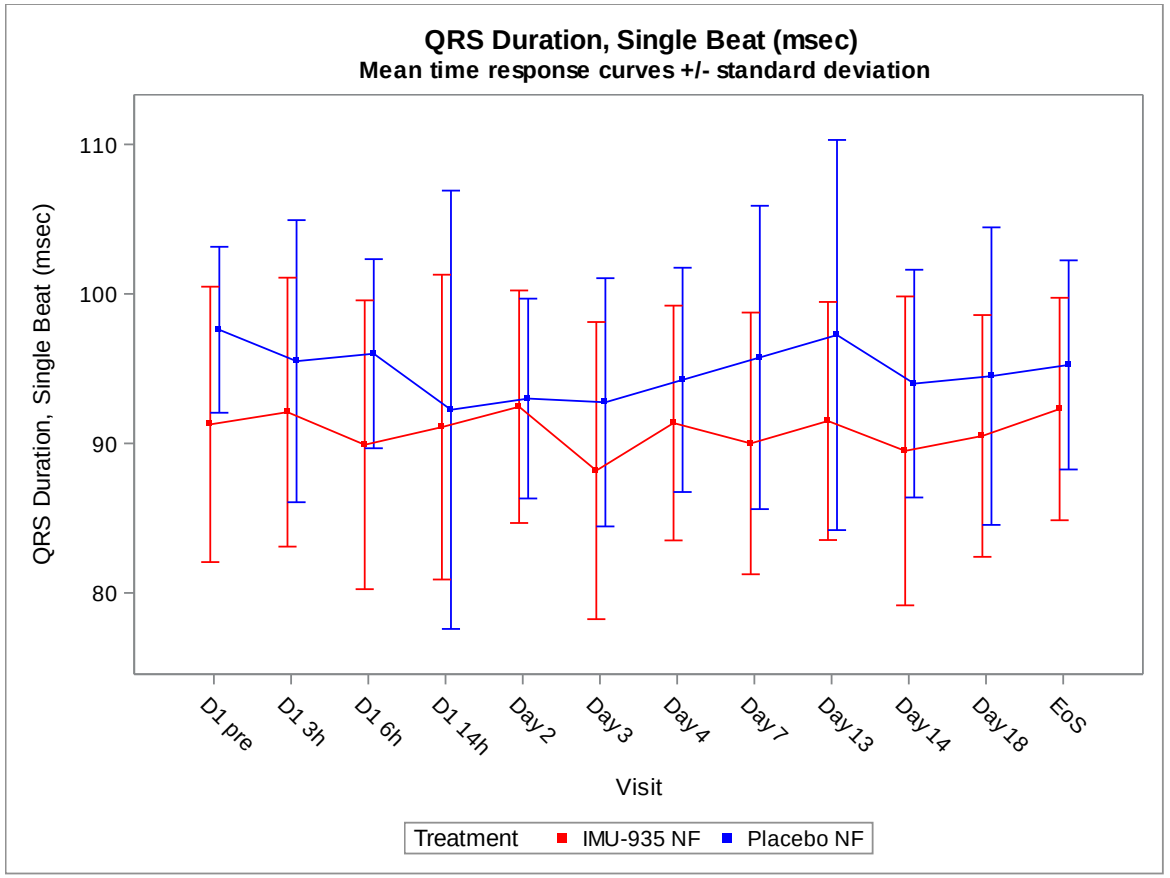




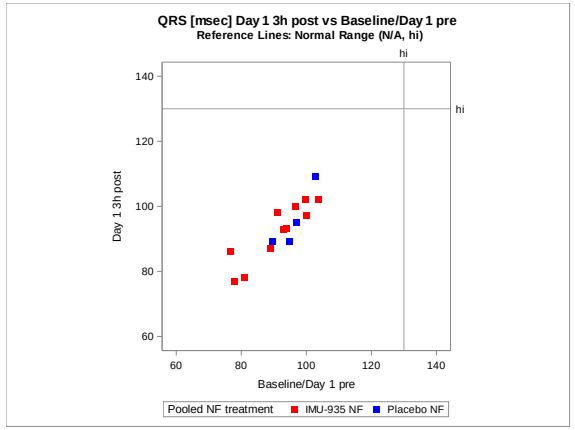
ECG: electrocardiogram

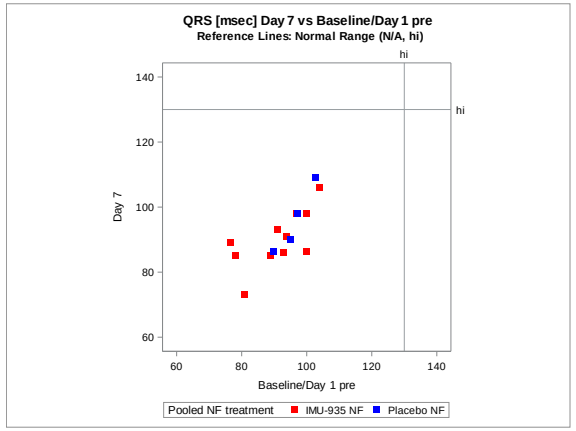
12-Lead Electrocardiograms: QRS Duration
Part B

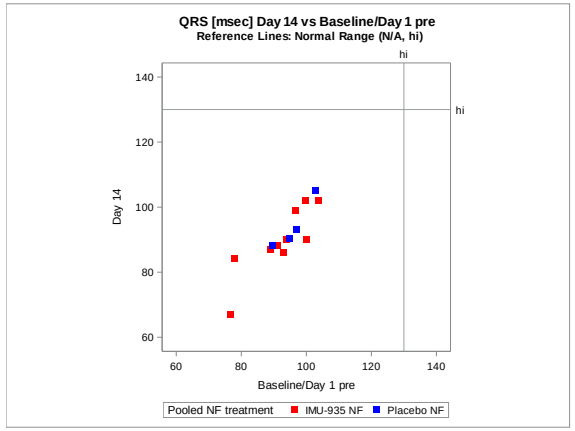
12-Lead ECGs Over Time
QRS Duration

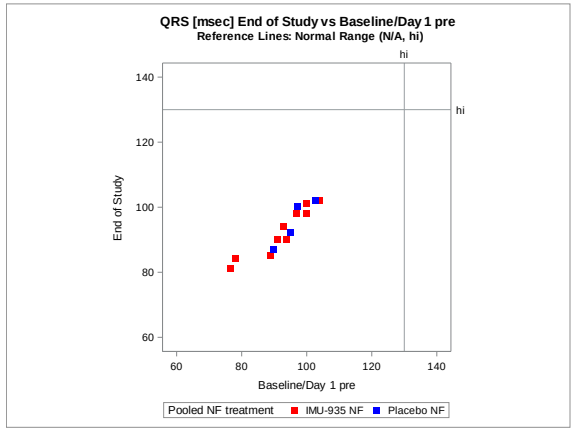


Individual 12-Lead ECGs
QRS Duration





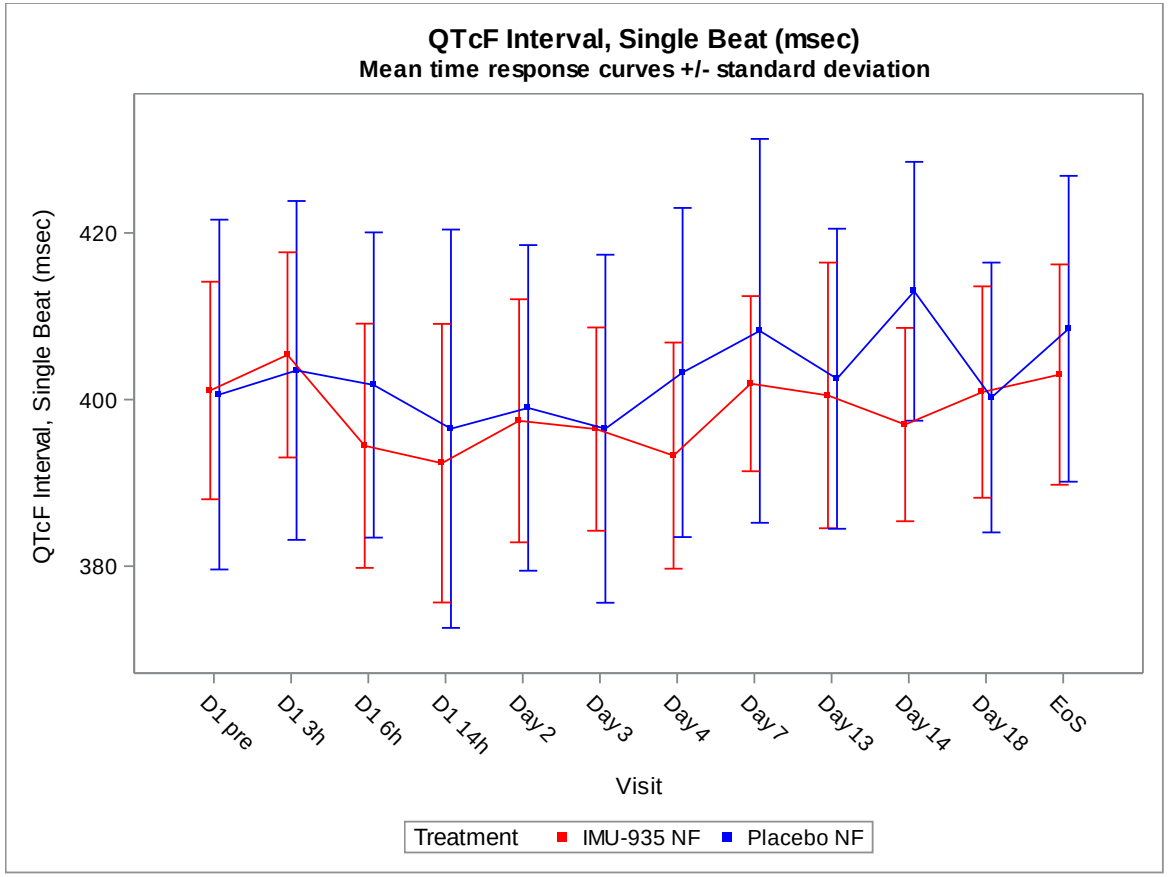




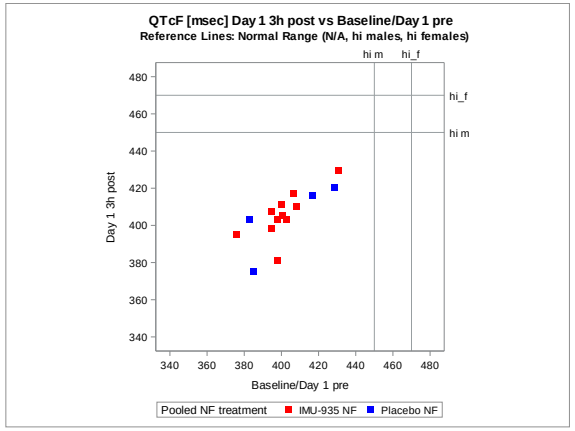
ECG: electrocardiogram

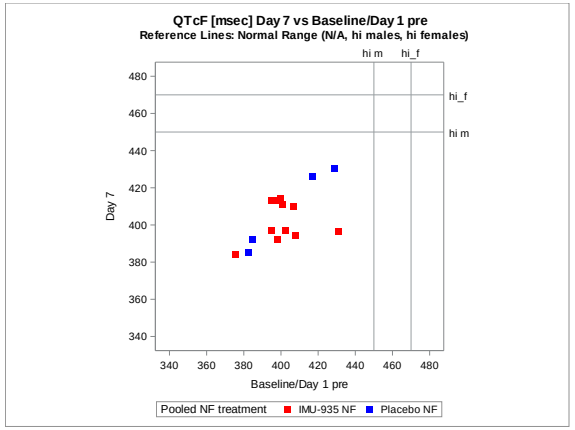
12-Lead Electrocardiograms: QTcF Interval
Part B

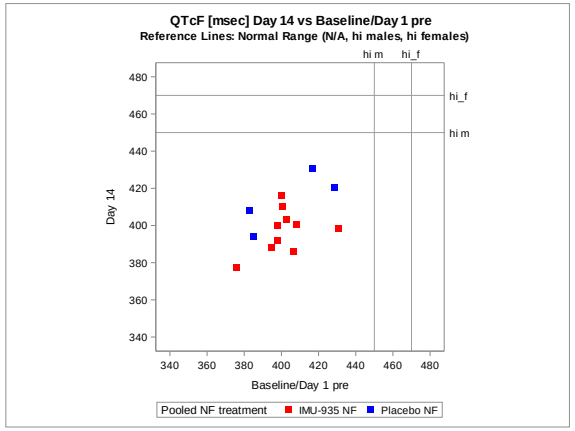
12-Lead ECGs Over Time
QTcF Interval

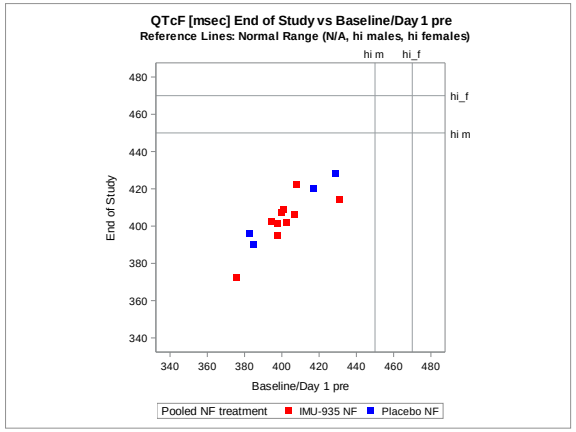


Individual 12-Lead ECGs
QTcF Interval









ECG: electrocardiogram

Immunic THERAPEUTICS

Phase 1 Clinical Trial of IMU-935

Part C: Evaluation of 28-Day Multiple Ascending Doses in Psoriasis Patients

Ongoing First-in-Human Study
Part C: IMU-935 in Psoriasis Patients

Eligibility Criteria

- Age 18 to 65 years (inclusive)
- Diagnosis of chronic plaque-type psoriasis for at least 6 months:
  - PASI score ≥ 10, or PASI score < 10 and DLQI score >10, plus
  - Psoriasis BSA involvement ≥ 10%, plus
  - PGA score ≥ 3
- Failed to fully respond to or is intolerant and/or has a contraindication to at least one topical therapy for psoriasis

Key Objectives/Endpoints

Primary:

- Safety and tolerability

Secondary:

- Trough plasma concentrations of IMU-935
- Effects on skin symptoms (PASI, DLQI, BSA, PGA, itch rating scale, target lesion assessments)

Exploratory:

- Pharmacodynamic markers (skin biopsies, cytokines)

PASI: Psoriasis Area and Severity Index; DLQI: Dermatology Quality of Life Index; BSA: body surface area; PGA: Physician Global Assessment