Immunic Therapeutics

Conference Call and Webcast

NASDAQ: IMUX | February 18, 2021

Cautionary Note Regarding Forward-Looking Statements

This presentation contains “forward-looking statements” that involve substantial risks and uncertainties for purposes of the safe harbor within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These include statements regarding management’s intentions, plans, beliefs, expectations or forecasts for the future, and, therefore, you are cautioned not to place undue reliance on them. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Immunic undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise, except to the extent required by law. We use words such as “anticipates,” “believes,” “plans,” “expects,” “projects,” “future,” “intends,” “may,” “will,” “should,” “could,” “estimates,” “predicts,” “potential,” “continue,” “guidance,” and similar expressions to identify these forward-looking statements that are intended to be covered by the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995.

Such forward-looking statements are based on our expectations and involve risks and uncertainties; consequently, actual results may differ materially from those expressed or implied in the statements due to a number of factors, including, but not limited to, risks relating to strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives of management. Risks and uncertainties that may cause actual results to differ materially from those expressed or implied in any forward-looking statement include, but are not limited to: Immunic’s plans to develop and commercialize its product candidates, including IMU-838, IMU-935 and IMU-856; the timing of initiation of Immunic’s planned clinical trials; the potential for IMU-838 to safely and effectively target and treat infections associated with coronavirus disease 2019 (COVID-19) or primary sclerosing cholangitis (PSC); the impact of future preclinical and clinical data on IMU-838 and the Company’s other product candidates; the availability or efficacy of Immunic’s potential treatment options for patients with COVID-19 or PSC that may be supported by the Company’s phase 2 CALVID-1 trial data or the investigator-sponsored phase 2 proof-of-concept trial data discussed herein; expectations regarding potential market size; the timing of the availability of data from Immunic’s clinical trials; the timing of any planned investigational new drug application or new drug application; Immunic’s plans to research, develop and commercialize its current and future product candidates; Immunic’s ability to successfully collaborate with existing collaborators or enter into new collaboration agreements, and to fulfill its obligations under any such collaboration agreements; the clinical utility, potential benefits and market acceptance of Immunic’s product candidates; Immunic’s commercialization, marketing and manufacturing capabilities and strategy; Immunic’s ability to identify additional products or product candidates with significant commercial potential; developments and projections relating to Immunic’s competitors and industry; the impact of government laws and regulations; Immunic’s ability to protect its intellectual property position; Immunic’s listing on The Nasdaq Global Select Market; expectations regarding the capitalization, resources and ownership structure of the company; the executive and board structure of the company; Immunic’s estimates regarding future revenue, expenses, capital requirements and need for additional financing; the nature, strategy and focus of the company; and the other risks set forth in the company’s Annual Report on Form 10-K for the year ended December 31, 2019 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed with the Securities and Exchange Commission (“SEC”).

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	Indication	Target	Preclinical	Phase 1	Phase 2	Phase 3
IMU-838	Multiple Sclerosis	DHODH	■	■	■	□
	Ulcerative Colitis	DHODH	■	■	■	
	Crohn's Disease	DHODH	■	■		
	Primary Sclerosing Cholangitis	DHODH	■	■	■	Investigator-Sponsored Trial performed at Mayo Clinic / NIH
	COVID-19*	DHODH	■	■	■	□
IMU-935	Psoriasis	RORγt	■	■		
	Guillain-Barré Syndrome	RORγt	■	□		
IMU-856	Gastrointestinal Diseases	Intestinal Barrier Function	■	■		

■ Completed or ongoing □ In preparation or planned

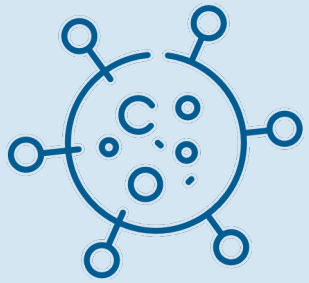
* Additional investigator-sponsored phase 2 clinical trial of IMU-838 in combination with oseltamivir in patients with moderate-to-severe COVID-19 ongoing in collaboration with the University Hospitals Coventry and Warwickshire NHS Trust, UK

Immunic THERAPEUTICS

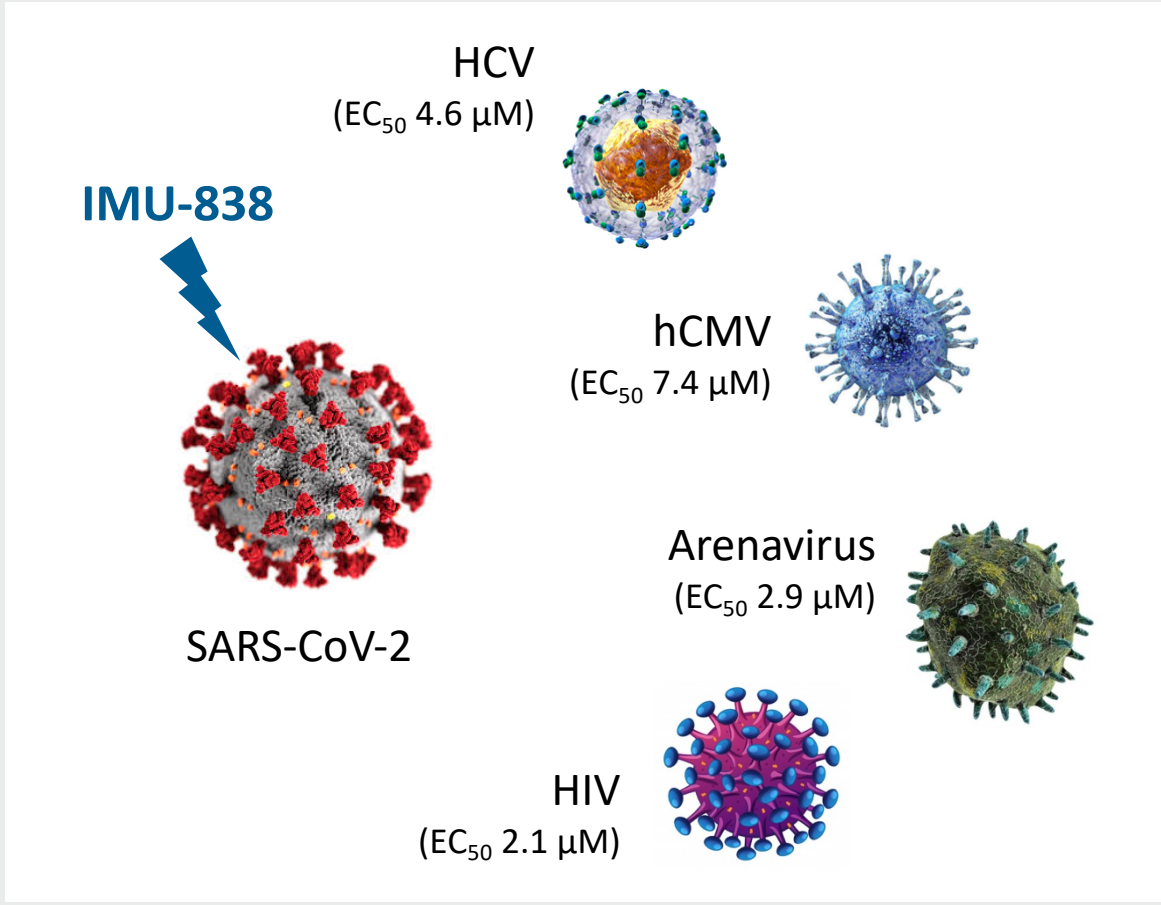
IMU-838 Fighting COVID-19

Leveraging DHODH's Broad-Spectrum Antiviral Activity

IMU-838 Antiviral Activity Against SARS-CoV-2 and Other Viruses



- IMU-838 is active against SARS-CoV-2
- IMU-838 has shown broad-spectrum antiviral activity against different pathogenic viruses with EC_{50} values in single digit µM range



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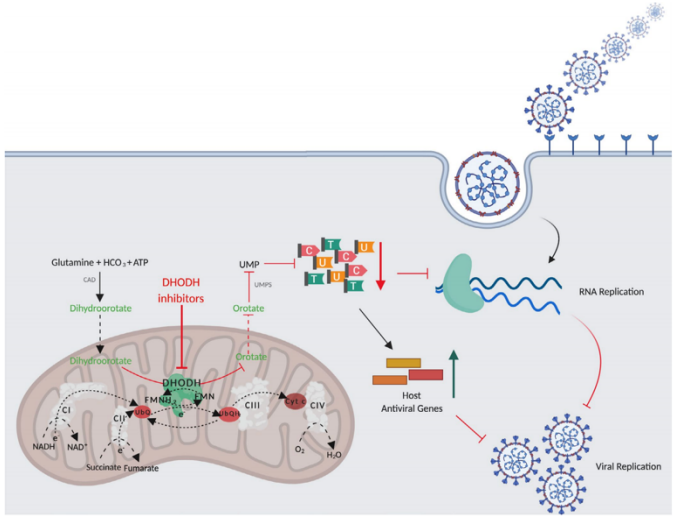
IMU-838: Host Cell Based Approach Active Against Different Virus Variants



IMU-838 was not yet tested against different mutant forms of SARS-CoV-2, but due to its host-based mechanism, mutations are not expected to have any impact on IMU-838‘s activity.

- Viruses in general rely on the host cell‘s infrastructure for nucleotide supply
- Inhibition of the host cell‘s enzyme DHODH by IMU-838 leads to a depletion of pyrimidine nucleotides that are needed for the
  - Production of viral RNA (virus genome replication) and
  - Production of viral proteins (via mRNA)
- This mechanism is host cell based and therefore independent of any mutations in virus proteins
  - As all variants require intracellular replication in human host cells
- By targeting the host cell metabolism, IMU-838 is active against different RNA and DNA viruses
  - Such as SARS-CoV-2, HIV, CMV, HCV, Arena virus, etc.
  - Demonstrating that even significant differences in the genome (different virus types vs mutations of SARS-CoV-2) rely on the same mechanism for nucleotide supply

Eur J Clin Invest. 2020;50:e13366

CALVID-1 Trial of IMU-838 in Moderate COVID-19

Study Background

CALVID-1: Study Flow Chart

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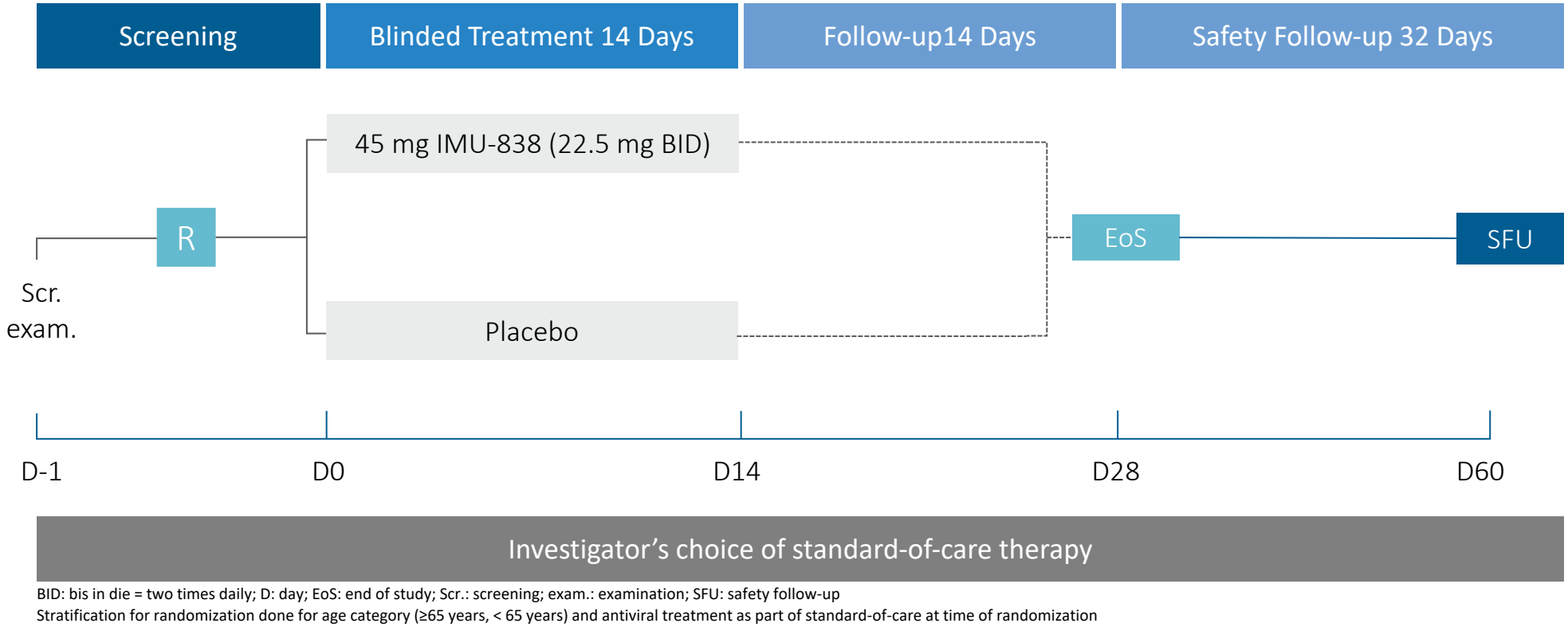
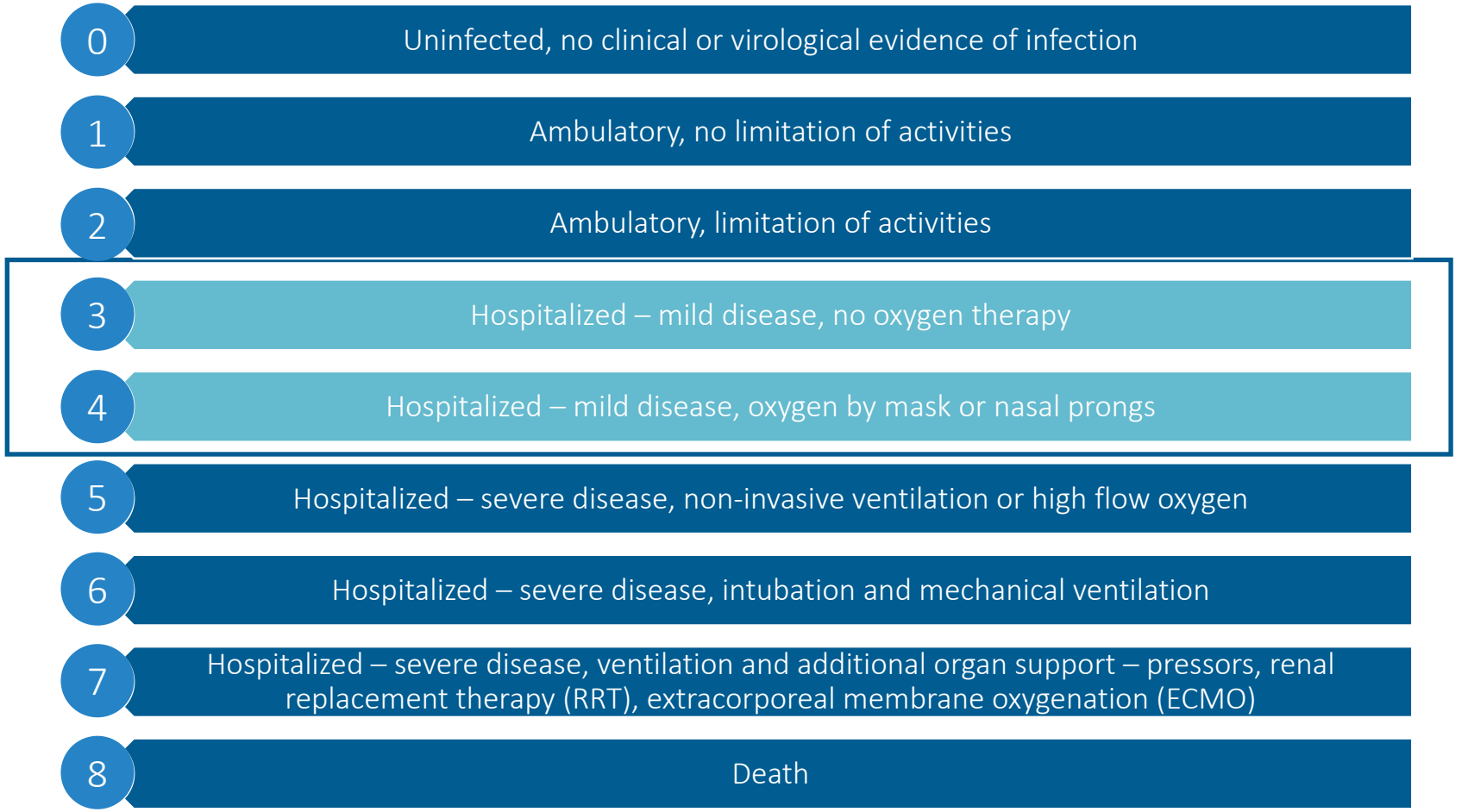


BID: bis in die = two times daily; D: day; EoS: end of study; Scr.: screening; exam.: examination; SFU: safety follow-up
Stratification for randomization done for age category (≥65 years, < 65 years) and antiviral treatment as part of standard-of-care at time of randomization

- n=204 patients
- 20 clinical sites in the United States and Europe

- USD 29 million EIB venture loan accessible for further phase 2/3 development

WHO Nine-Category Ordinal Scale

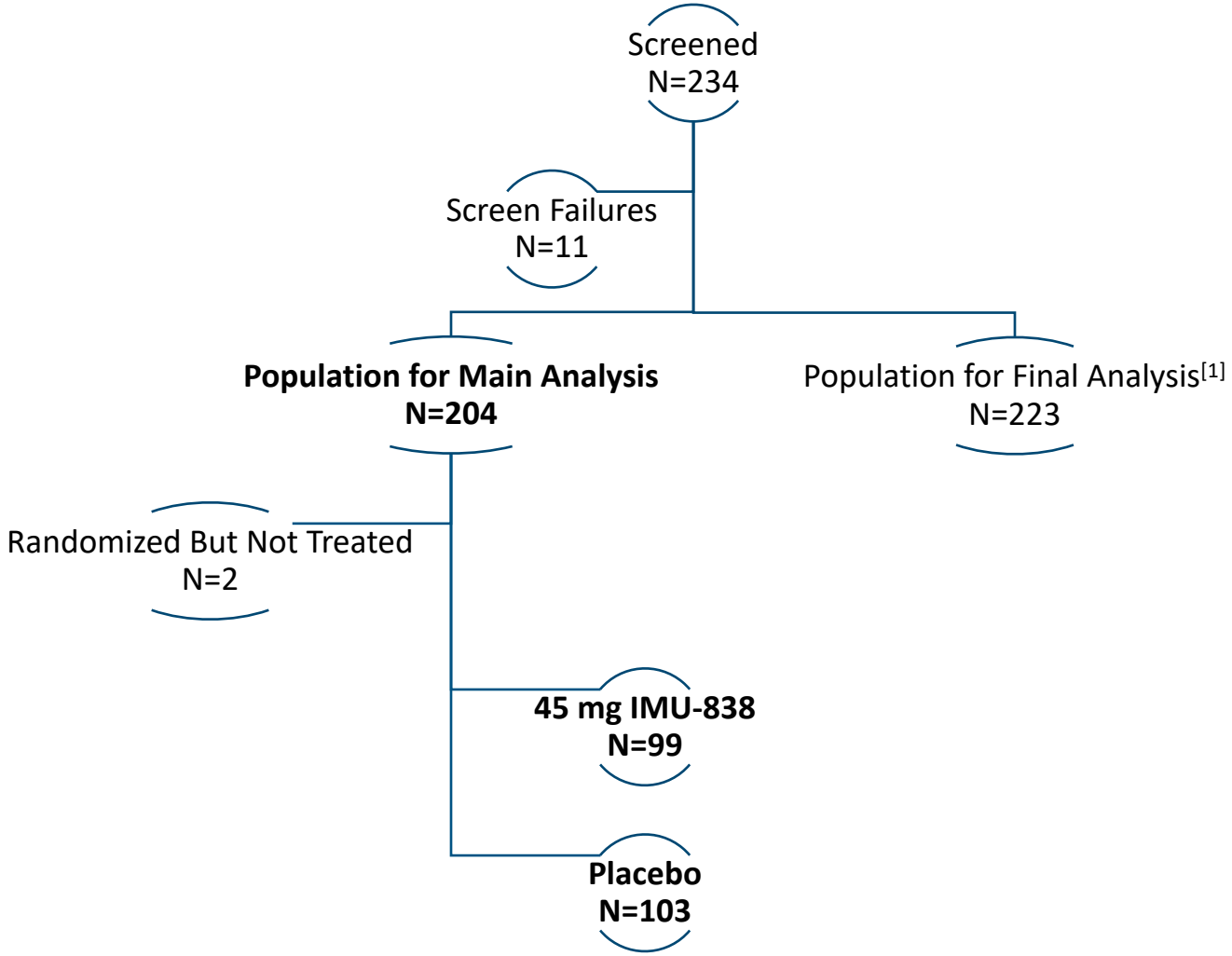


WHO R&D: Blueprint Novel Coronavirus COVID-19 Therapeutic Trial Synopsis [Internet] 2020. Available from: https://www.who.int/blueprint/priority-diseases/key-action/COVID-19_Treatment_Trial_Design_Master_Protocol_synopsis_Final_18022020.pdf

CALVID-1 Trial of IMU-838 in Moderate COVID-19

Baseline Characteristics

Study Recruitment



- Regulatory approvals were received in:
  USA, Germany, Bulgaria, North Macedonia, Greece, Hungary, Russia, Romania, Moldova, Bosnia and Herzegovina, and Ukraine
- A total of 20 active study sites enrolled at least 1 patient
- Of the 204 patients randomized:
  - 2 patients did not receive any study drug
  - 26 patients prematurely discontinued before Day 28
    - Of which 3 patients discontinued due to adverse events (n=2 IMU-838, n=1 Placebo)
  - 176 patients completed the trial (Day 28)
- Full Analysis Set (FAS): n=202
- Modified Full Analysis Set (mFAS): excludes either patients with required and fixed 14-day hospitalization duration (Bulgaria) or patients missing positive centralized virology confirmations, depending on endpoint*

[1] The final analysis will contain data from all randomized patients in this trial. The additional 19 patients (as compared to the Main Analysis) were enrolled after the randomization deadline for the Main Analysis (31-Oct-2020).
* This will be specified in the footnotes of each slide in the data presentation.

Presence of COVID-19 Risk Factors and Disease Markers

Baseline Characteristics

Risk Factor		IMU-838	Placebo
Age >= 65 Years	%	24.2	23.3
Body Mass Index [kg/m²]	Mean (SD)	29.08 (5.34)	28.40 (4.55)
Pre-Existing Cardiovascular Disease	%	52.5	39.8
C-Reactive Protein [nmol/L]	Mean (SD)	3.95 (3.84)	2.99 (3.21)
Interleukin-6 [ng/L]	Mean (SD)	6.2 (8.32)	5.1 (6.5)
D-Dimer [ng/L]	Mean (SD)	970.7 (2072.1)	653.5 (787.3)
Current or Recent Immunosuppressive Treatment	%	3.0	1.0

There is a trend that patients in the IMU-838 treatment arm have a higher presence of risk factors and higher levels of disease markers which may imply a potentially more severe disease course of COVID-19 disease for patients in the IMU-838 arm.

SD: Standard Deviation

Selected Concomitant Medications
Used as Standard of Care

	IMU-838		Placebo	
	N	%	N	%
Systemic Corticosteroids (Including Dexamethasone)	65	65.7	66	64.1
Remdesivir	6	6.1	6	5.8
Lopinavir/Ritonavir	2	2.0	7	6.8
Favirapivir	1	1.0	0	0
Darunavir	9	9.1	9	8.7
Lopinavir	0	0	1	1.0
Ritonavir	9	9.1	9	8.7
Rimantidine	1	1.0	0	0
Tocilizumab	0	0	1	1.0

Total n=202, IMU-838 n=99, Placebo n=103

CALVID-1 Trial of IMU-838 in Moderate COVID-19

Efficacy

Primary Endpoint

Proportion of Patients Without Any Need for Invasive Ventilation Through Day 28

- The sample size of the trial was determined based on early reports indicating a high need for invasive ventilation in hospitalized COVID-19 patients:
  - Shortage of ventilator units and other medical resources was a prominent feature during the first COVID-19 wave in early 2020
  - Trial was powered to investigate whether IMU-838 can reduce the need for invasive ventilation (mechanical ventilation of the patient through an artificial airway)
  - Early reports in the first wave of COVID-19 indicated a comparatively high rate of invasive ventilation between 6.1%[1] and 12.2%[2] of hospitalized COVID-19 patients (including data from all disease severities)
- The trial found an actual rate of <1% of invasive ventilation for hospitalized moderate COVID-19 patients[3].
  - This low event rate, consistent with the findings of many recent third-party trials in COVID-19, prevented the primary endpoint from being evaluable.

[1] Guan WJ, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30;382(18):1708-1720
[2] Richardson S, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020 May 26;323(20):2052-2059
[3] Only 2 patients in this trial received invasive ventilation (n=1 for IMU-838, n=1 for Placebo)
Note: For the evaluation of the primary endpoint, regulatory agencies also count patients as positive for the primary endpoint (treatment failures) based on premature treatment discontinuation. Patients who are lost to follow-up or discontinue the trial on or before the last treatment day in this trial due to any reason other than death and discontinue with a last observed WHO clinical status no lower than that at screening, and patients who die without a need for invasive ventilation assessed by a treating physician will be considered treatment failures for the primary endpoint. However, the number given here only lists the actual patients that had received invasive ventilation during this trial.

Key Secondary Endpoints

28-Day Mortality, Survival Without Respiratory Failure, and ICU Admission

- The trial was also designed to investigate IMU-838's ability to reduce the probability of major complications for COVID-19 patients, such as 28-day mortality, survival without respiratory failure, as well as probability of requirement of intensive care unit (ICU) treatment.
- The following data were available when planning the trial in early 2020:
  - Mortality rates were between 2.2%[1] and 21.0%[2] of hospitalized COVID-19 patients (including data from all disease severities)
  - Need for ICU admission was between 5.0%[1] and 14.2%[2] of hospitalized COVID-19 patients (including data from all disease severities)
- The trial found a rate of <2% for 28-day mortality[3], balanced between the two arms, and <4.5% of patients required an ICU stay[4].
  - Based on the low complication rates in this trial and due to the known variability of the disease course, Immunic believes that the evaluation of these key secondary endpoints is also not feasible.

[1] Guan WJ, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30;382(18):1708-1720

[2] Richardson S, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020 May 26;323(20):2052-2059

[3] There were 4 on-study deaths (n=2 for IMU-838, n=2 for Placebo)

[4] Only 9 patients were admitted to the ICU (n=4 for IMU-838, n=5 for Placebo)

Note: For the evaluation of these key secondary endpoints, based on the consultation with regulatory agencies, the study established certain rules for patients who were lost to follow-up, discontinued the trial or died during the trial and how such patients will be considered for these endpoints. However, the number given here only lists the actual patients that had died during this trial.

ARDS: acute respiratory distress syndrome; ICU: intensive care unit

Proportion of Patients with Clinical Recovery

IMU-838 Increases the Number of Patients Achieving Clinical Recovery

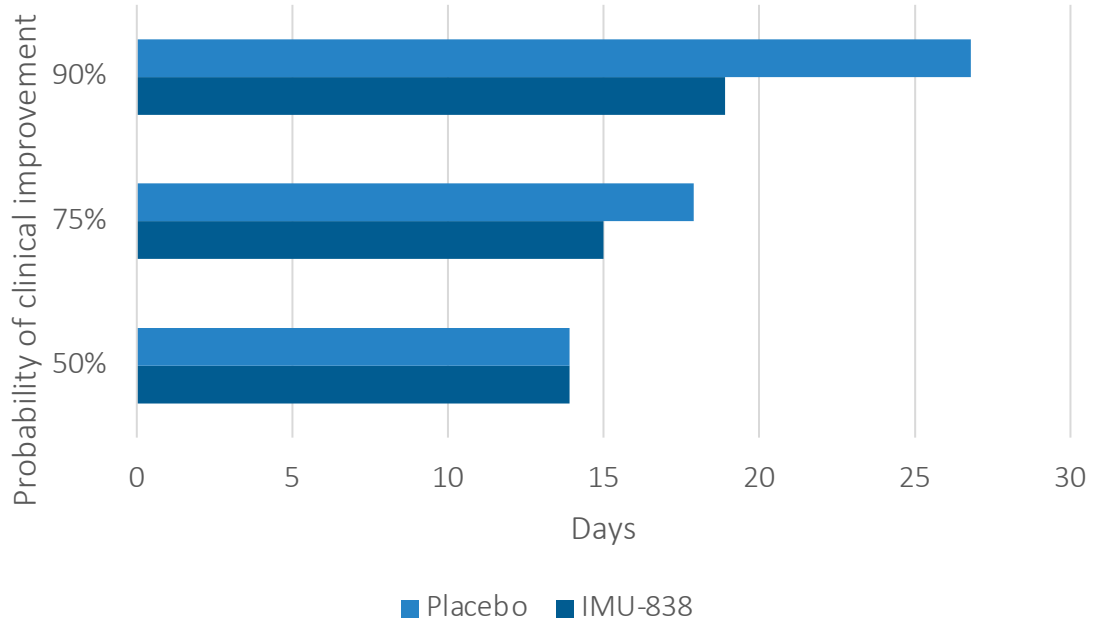
Proportion of Patients With Clinical Recovery (Based on Symptoms Body Temperature, Respiratory Frequency and Blood Oxygenation)	IMU-838		Placebo	
	N	%	N	%
Day 7	15	18.5	10	12.8
Day 28	57	71.3	58	66.7

Full analysis set (FAS, n=99 for IMU-838, n=103 for Placebo)
Clinical recovery is defined as as axillary temperature <= 36.6 °C, or oral temperature <= 37.2 °C, or rectal or tympanic temperature <= 37.8 °C, and respiratory frequency <= 24 times/min without oxygen inhalation and oxygen saturation >= 98%. Clinical recovery is only assumed if it is confirmed in the evening and at the next visit (if applicable).

Time to Clinical Improvement

IMU-838 Shows Acceleration of Time to Clinical Improvement

	mFAS Population[1]		
Probability of Clinical Improvement *(Centrally Calculated)*	IMU-838 (Days)	Placebo (Days)	**Difference in Favor of IMU-838 (Days)**
50%	13.9	13.9	**0.0**
75%	15.0	17.9	**2.9**
90%	18.9	26.8	**7.9**



Clinical improvement is defined as an improvement of at least two points on the derived WHO nine-category ordinal scale, or live discharge from hospital without oxygen supplementation, whichever comes first. The WHO nine-category ordinal scale is derived using SARS-CoV-2 test results provided by the central laboratory (only nasopharyngeal swabs).

[1] Modified full analysis (mFAS) set (n=61 for IMU-838, n=69 for Placebo): In centers in Bulgaria, as per request by the regulatory agency, patients must be hospitalized during the entire treatment period until Day 14. Thus, these patients are excluded from this analysis, as the derived WHO status includes the hospitalization status and the required 14-day hospitalization interferes with the assessment of the patient status. Additionally, patients that had positive local virus tests during screening period but no confirmation was possible by centralized virology laboratory (presumably due to sampling and storage issues) at later time points were also excluded as virus status was not assessable for the WHO score.

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Time to Clinical Improvement (High-Risk Patients)

IMU-838 Provides Patients with High-Risk Factors With Higher Improvements

Probability of Clinical Improvement *(Centrally calculated)*	All Patients			Patients With Presence of High-Risk Factors[1]			Elderly Patients Aged ≥ 65 Years		
	IMU-838 (Days)	Placebo (Days)	**Difference in Favor of IMU-838 (Days)**	IMU-838 (Days)	Placebo (Days)	**Difference in Favor of IMU-838 (Days)**	IMU-838 (Days)	Placebo (Days)	**Difference in Favor of IMU-838 (Days)**
50%	13.9	13.9	**0.0**	13.9	13.8	**-0.1**	14.8	14.0	**-0.8**
75%	15.0	17.9	**2.9**	15.0	18.8	**3.8**	15.0	19.8	**4.8**
90%	18.9	26.8	**7.9**	17.9	26.8	**8.9**	N.C.	N.C.	**N.C.**

Modified full analysis set (mFAS), all patients (n=61 for IMU-838, n=69 for Placebo), high-risk patients (n=41 for IMU-838, n=41 for Placebo), elderly patients (n=17 for IMU-838 , n=17 for Placebo), N.C.= not calculated because of too few patients in this category

[1] High-risk factors are age ≥65 years, cardiovascular disease (including hypertension), pre-existing pulmonary disease, diabetes, malignancy, medical conditions leading to immunodeficiency, current or recent (within three months) immunosuppressive treatment.

Clinical improvement is defined as an improvement of at least two points on the derived WHO nine-category ordinal scale, or live discharge from hospital without oxygen supplementation, whichever comes first. The WHO nine-category ordinal scale is derived using SARS-CoV-2 test results provided by the central laboratory (only nasopharyngeal swabs). The evaluations of high-risk and elderly populations are a post hoc analysis and were not pre-specified in the statistical analysis plan.

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Time to Clinical Improvement (Early Treatment Start)

IMU-838 Provides Better Improvements When Used Early

Probability of Clinical Improvement *(Centrally Calculated)*	Study Treatment Start ≤ 8 Days After First Symptoms			Study Treatment Start > 8 Days After First Symptoms		
	IMU-838 (Days)	Placebo (Days)	**Difference in Favor of IMU-838 (Days)**	IMU-838 (Days)	Placebo (Days)	**Difference in Favor of IMU-838 (Days)**
50%	14.8	14.9	**0.1**	13.8	12.0	**-1.8**
75%	15.9	20.9	**5.0**	14.8	14.9	**0.1**
90%	24.0	26.8	**2.8**	14.9	19.0	**4.1**

Modified full analysis set (mFAS): Excluding Bulgarian patients with fixed hospitalization period and patients with missing positive centralized virology assessments

Patients treated ≤ 8 days after first symptoms n=65 (n=33 for IMU-838, n=32 for Placebo), patients treated > 8 days after first symptoms n=63 (n=27 for IMU-838, n=37 for Placebo), onset of first symptoms unknown n=1

Clinical improvement is defined as an improvement of WHO nine-category ordinal scale when decreased by at least two points compared to baseline. The WHO nine-category ordinal scale is derived using SARS-CoV-2 test results provided by the central laboratory (only nasopharyngeal swabs).

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Proportion of Patients with Clinical Improvement (All Patients)

IMU-838 Increases the Number of Patients Achieving Clinical Improvement

Proportion of Patients With Improvement of WHO Nine-Category Ordinal Scale by at Least Two Points *(Based on Investigator Assessment)*	IMU-838		Placebo	
	N	%	N	%
Day 14	38	42.7	35	38.5
Day 28	90	90.9	90	87.4

The relative proportion of patients improving was greater in the IMU-838 treatment arm than in the placebo arm at 14 days and at 28 days.

Full analysis set (FAS, n=99 for IMU-838, n=103 for Placebo)
Clinical improvement is defined as an improvement of WHO nine-category ordinal scale (as assessed by the investigator, including based on local and central virus tests) when decreased by at least two points compared to baseline.

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Proportion of Patients with Clinical Improvement (Elderly Patients)

IMU-838 Increases the Number of Elderly Patients (≥65 Years) Achieving Clinical Improvement

Proportion of Patients With Improvement of WHO Nine-Category Ordinal Scale by at Least Two Points *(Based on Investigator Assessment)*	IMU-838		Placebo	
	N	%	N	%
Day 14	8	36.4	4	22.2
Day 28	19	95.0	17	94.4

IMU-838 contributed to a faster improvement in WHO scores by at least two points in elderly patients (≥65 years), as compared to placebo.

Elderly patients: modified full analysis set (mFAS, n=22 for IMU-838, n=18 for Placebo)
Clinical improvement is defined as an improvement of WHO nine-category ordinal scale (as assessed by the investigator, including based on local and central virus tests) when decreased by at least two points compared to baseline..

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Time to Clinical Improvement

Considering Antiviral Treatment

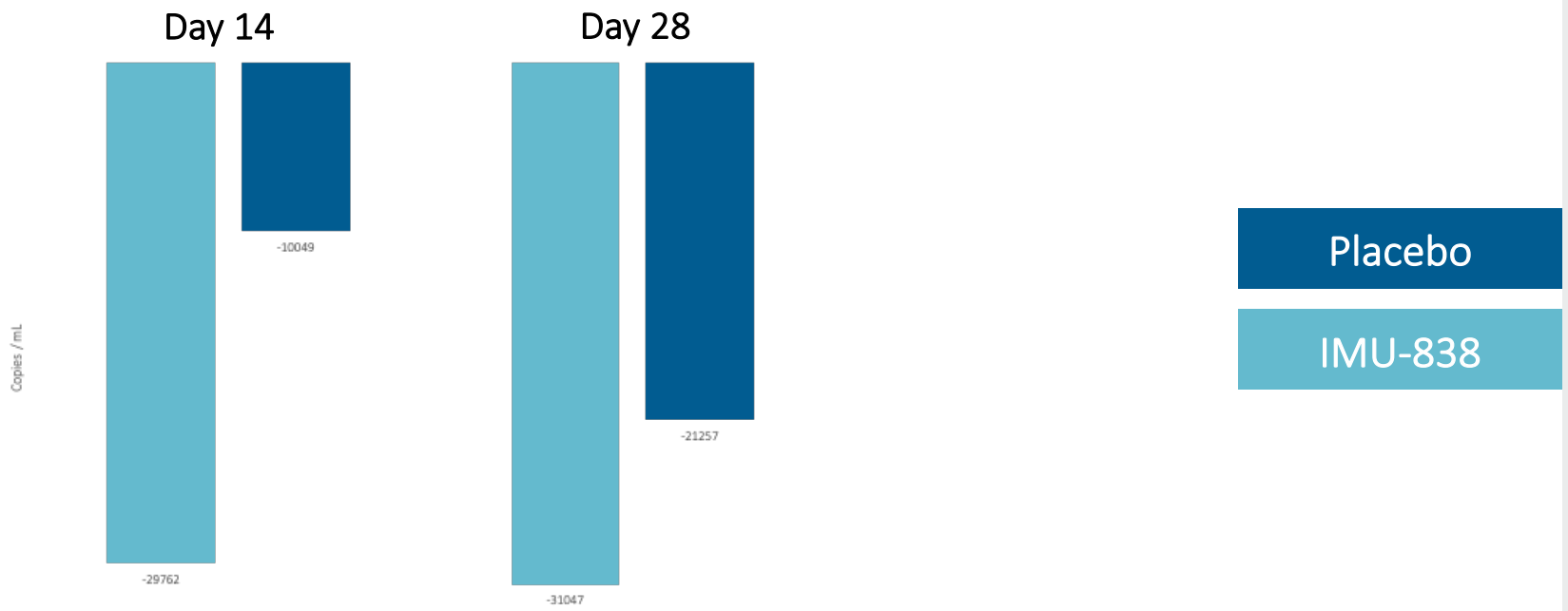
75% Probability of Clinical Improvement (Centrally Calculated)	FAS Population (Days)	
	IMU-838	Placebo
No Combination With Antivirals (Monotherapy)	14.8	15.8
In Combination With Antivirals (Combination Therapy)[1]	14.8	15.7
Difference in Favor of Combination Therapy	0	0.1

The advantage of IMU-838 regarding time to clinical improvement versus placebo does not differ between no combination and combination therapy with direct antivirals.

Clinical improvement is defined as an improvement of at least two points on the derived WHO nine-category ordinal scale, or live discharge from hospital without oxygen supplementation, whichever comes first. The WHO nine-category ordinal scale is derived using SARS-CoV-2 test results provided by the central laboratory (only nasopharyngeal swabs).
Full analysis set (FAS, n=99 for IMU-838, n=103 for Placebo)
[1] n=12 for IMU-838, n=14 for Placebo

Decrease of SARS-CoV-2 Viral Load

Absolute decrease of SARS-CoV-2 viral load (calculated as viral load at Visit Day minus viral load at Baseline Visit)

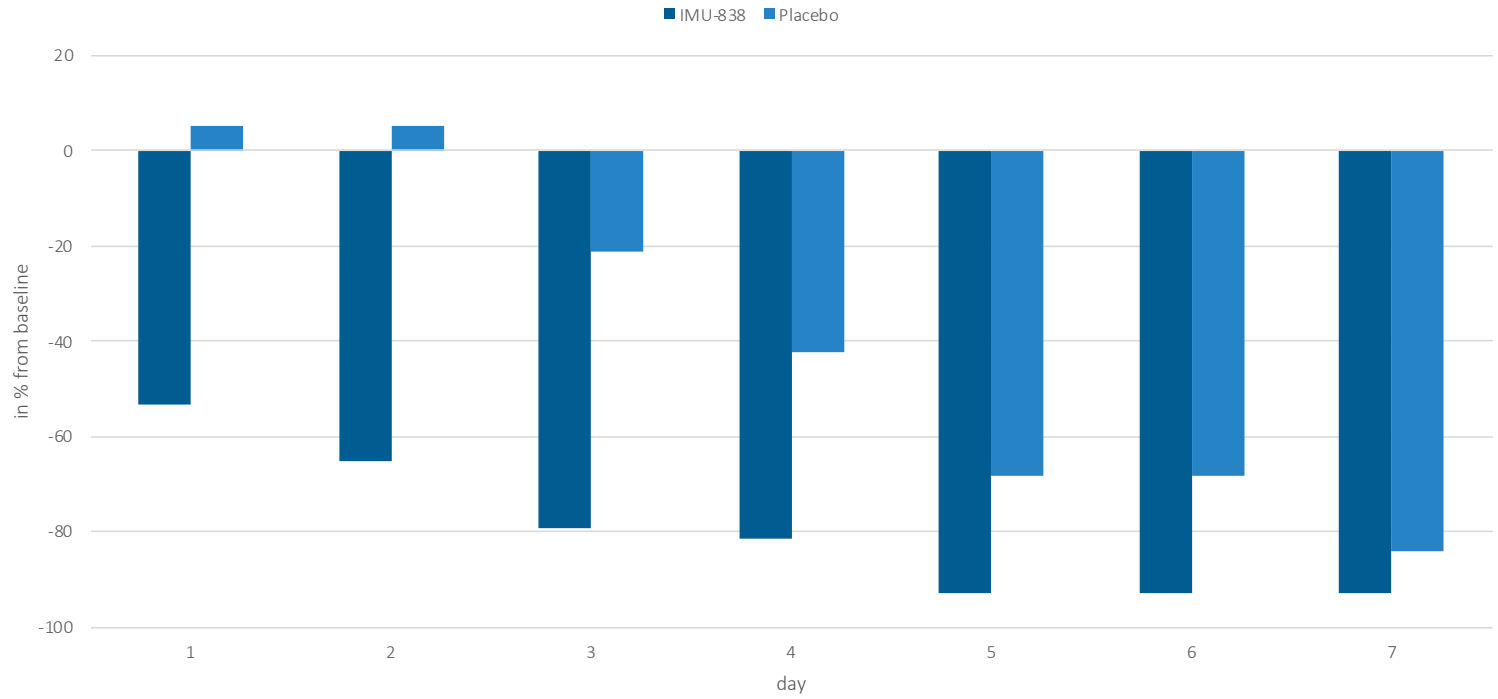


An anti-viral effect of IMU-838 on SARS-CoV-2 was observed as represented by viral titers at the end of the treatment period and at the end of the study.

Modified full analysis set (N = 90 for IMU-838, N = 91 Placebo)
The viral load is set 0 cp/mL if the test result is 'No SARS-CoV2 detected' and set to 1018 cp/mL if the test result is '< 1018 cp/mL SARS-CoV2 detected'.
Only patients with viral load measured from nasopharyngeal swab and results provided by the central laboratory are included. Analysis is based on the median of viral titers (as assessed by the central virology laboratory) on each individual day.

Decrease of C-Reactive Protein (CRP)

Systemic Inflammation Marker Strongly Associated with Patient Outcomes*



An anti-inflammatory effect of IMU-838 was observed, based on a more effective reduction of C-reactive protein (CRP), a well-known marker for systemic inflammation in the blood, in IMU-838 treated patients, as compared to placebo.

*Systemic inflammation, as measured by CRP, is strongly associated with thrombotic events, kidney injury, critical illness, and mortality in COVID-19 patients. (Smilowitz et al. C-reactive protein and clinical outcomes in patients with COVID-19. Eur Heart J. 2021 Jan 15:ehaa1103)
Safety analysis set (n= 99 for IMU-838, n= 103 for Placebo)
Analysis is based on the median of CRP on each individual day

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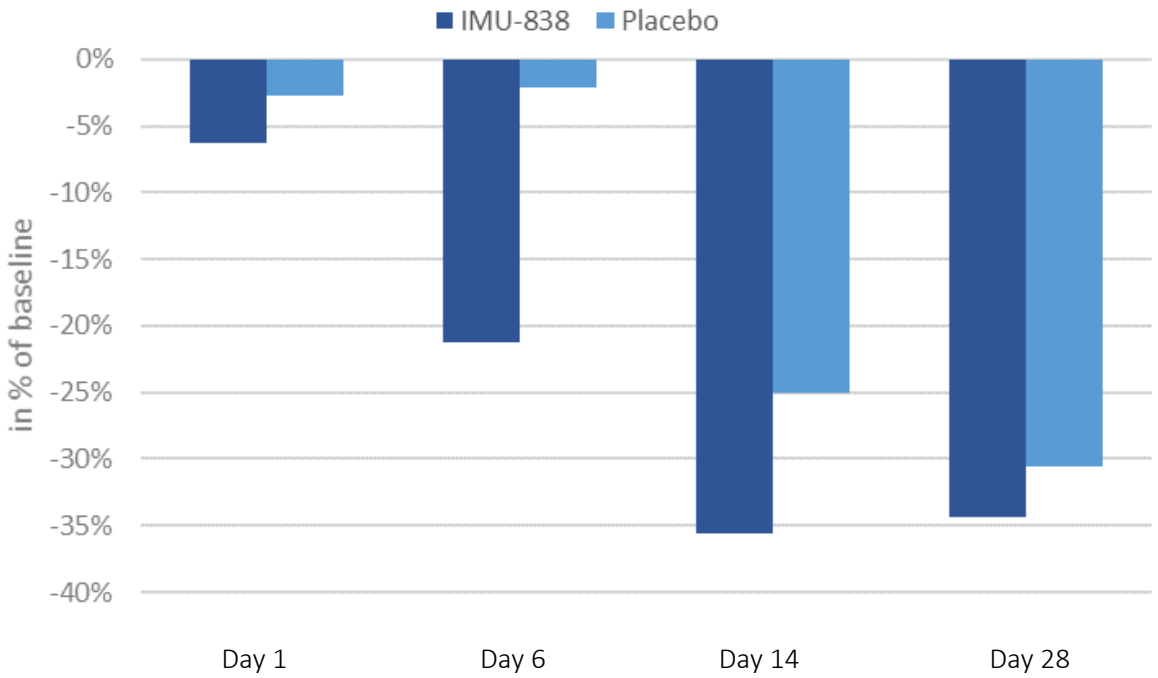
Decrease of D-Dimer

COVID-19 Prognostic Disease Marker Strongly Associated with Patient Outcomes*



A more effective reduction of D-dimer, a well-known prognostic disease marker for COVID-19, was observed in IMU-838 treated patients, as compared to placebo.

*D-dimer is commonly elevated in patients with COVID-19. D-dimer levels correlate with disease severity and are a reliable prognostic marker for in-hospital mortality in patients admitted for COVID-19. (Yao et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. j intensive care 8, 49 (2020)). D-dimer levels are also correlated with thromboembolic events in COVID-19 patients (Vidali et al. D-dimer as an indicator of prognosis in SARS-CoV-2 infection: a systematic review, ERJ Open Research Apr 2020, 6 (2) 00260-2020).
Safety analysis set (n= 99 for IMU-838, n= 103 for Placebo); Analysis is based on the median of D-dimer on each individual day

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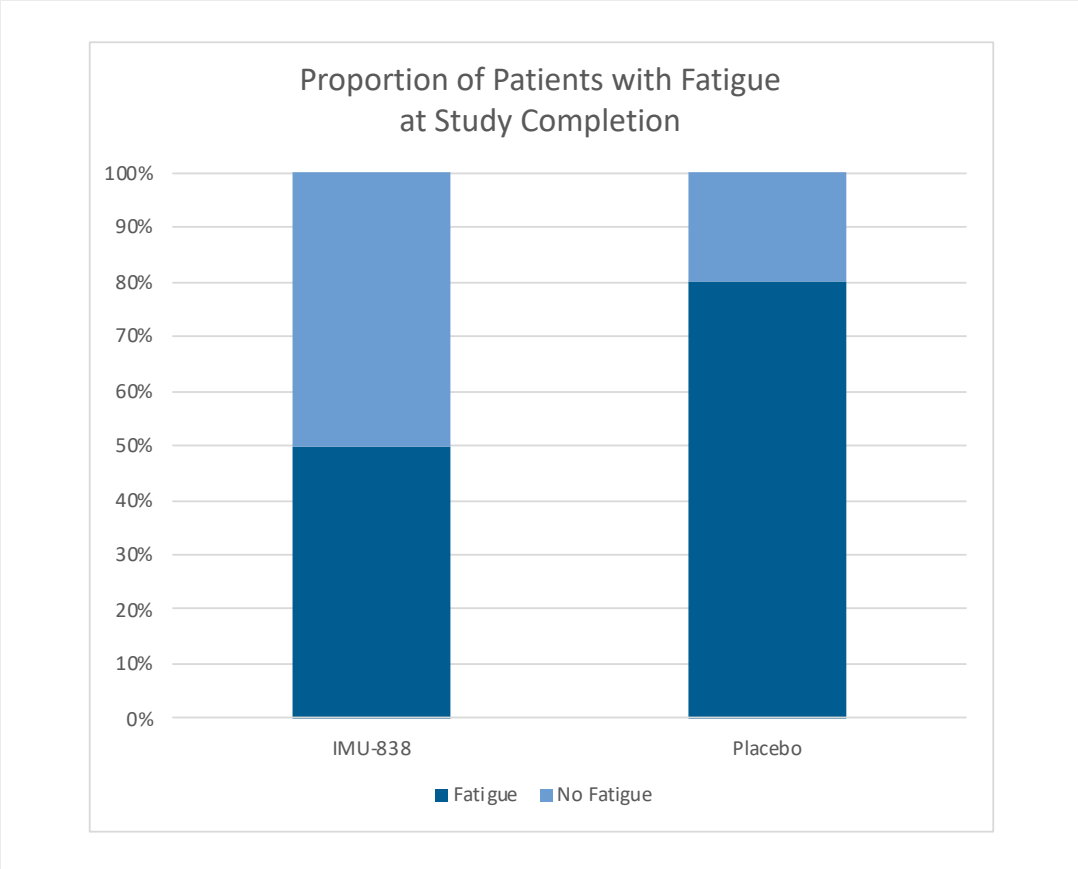
Post Hoc Analysis on 'Long COVID' Symptoms

Initial Signal That IMU-838 May Contribute to Prevention of Long-Term Fatigue

- Questionnaires from 36 patients were returned from investigators who participated in this trial at 3 clinical sites
  - 27 patients are in the MA1 population
  - Additional 9 patients can only be reported at the FA1 analysis (treatment assignment is still blinded)
- Fatigue was the most common 'Long COVID' symptom found in 18 of 27 patients (69.2%)
  - Fatigue in IMU-838 patients: 6/12 (50%)
  - Fatigue in Placebo patients: 12/15 (80%)



This analysis was done by sending a post hoc questionnaire to investigators (who were still blinded to treatment assignments of their patients) in three high enroller sites. The participation was voluntary and a selection bias for participation cannot be fully excluded.
The questionnaire requested the patient status regarding long-term COVID-19 symptoms at the individual study completion for each patient.
Neuroinflammation may trigger impairment of neurotransmitters and, thus, be the mechanism for fatigue on post-COVID-19 patients (Ortelli et al. Neuropsychological and neurophysiological correlates of fatigue in post-acute patients with neurological manifestations of COVID-19: Insights into a challenging symptom. J Neurol Sci. 2021 Jan 15;420:117271).

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CALVID-1: Efficacy Summary

- The rate of serious complications of moderate COVID-19 disease in hospitalized patients is very low:
  - Rates of <1% for invasive ventilation, <2% for 28-day mortality, and <1% of patients requiring an ICU stay
  - These low event rates prevented the primary and key secondary endpoints from being evaluable
- Study showed evidence of clinical activity of IMU-838 on multiple secondary clinical endpoints:
  - Patients with IMU-838 treatment achieve faster clinical recovery (defined as clearance of main COVID-19 symptoms) (FAS).
  - Time to clinical improvement was found to be numerically higher in the IMU-838 treatment arm, as compared to placebo, and the incremental benefit increased over time (mFAS).
  - High-risk patients and patients aged over 65 years experienced a more substantial treatment benefit from IMU-838 (FAS).
  - Clinical improvement observed to be better when IMU-838 was used early in the COVID-19 disease course (within the first 8 days after onset of symptoms) (mFAS).
  - IMU-838 increases the number of patients achieving clinical improvement (FAS).
  - An anti-viral effect of IMU-838 on SARS-CoV-2 was observed by viral titers at the end of the treatment period (Day 14) and at the end of the study (Day 28).
  - An anti-inflammatory effect of IMU-838 was observed, based on a more effective reduction of the systemic inflammation marker CRP in IMU-838 treated patients, as compared to placebo.
  - A more effective reduction of the prognostic disease marker D-dimer was observed in IMU-838 treated patients, as compared to placebo.
  - Initial data from a post hoc analysis of “Long COVID” symptoms indicated that IMU-838 may have the potential to contribute to the prevention of long-term fatigue (subpopulation of 27 patients) .

The study indicates that IMU-838 may be a convenient oral treatment option for patients with moderate COVID-19.

FAS: full analysis set, includes all patients randomized that received at least one dose of study drug (n=99 for IMU-838, n=103 for Placebo)
mFAS: modified full analysis set; CRP: C-reactive protein; ICU: intensive care unit

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CALVID-1 Trial of IMU-838 in Moderate COVID-19

Safety

Summary of the Overall Rate of Adverse Events

No General Safety Signals, as Compared to Placebo

	45 mg IMU-838			Placebo			Total		
	Number of AEs (N#)	No. of patients with AE (N)	Patients with AE (%)	Number of AEs (N#)	No. of patients with AE (N)	Patients with AE (%)	Number of AEs (N#)	No. of patients with AE (N)	Patients with AE (%)
Any TEAE	290	73	73.7	242	67	65.0	532	140	69.3
Any SAE	2	2	2.0	5	4	3.9	7	6	3.0
Any TEAE Related to Study Medication and/or Study Procedure	25	18	18.2	12	10	9.7	37	28	13.9
Any TEAE Leading to Withdrawal of Study Drug	3	2	2.0	3	2	1.9	6	4	2.0
Any TEAE of Increased Severity Related to COVID-19	**9**	**7**	**7.1**	**17**	**13**	**12.6**	**26**	**20**	**9.9**

Safety analysis set (n=99 for IMU-838, n=103 for Placebo)
AE: adverse event; TEAE: treatment-emergent adverse event; SAE: serious adverse event
Adverse events as coded by MedDRA version 23.0

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Adverse Events of Increased Severity Related to COVID-19

Rate of Adverse Events Was Not Increased, as Compared to Placebo

System Organ Class	Preferred Term	45 mg IMU-838			Placebo			Total		
		Number of AEs (N#)	Number of patients with AE (N)	Patients with AE (%)	Number of AEs (N#)	Number of patients with AE (N)	Patients with AE (%)	Number of AEs (N#)	Number of patients with AE (N)	Patients with AE (%)
Cardiac Disorders	Bradycardia	1	1	1.0	2	2	1.9	3	3	1.5
	Total	1	1	1.0	2	2	1.9	3	3	1.5
General Disorders and Administration Site Conditions	Pyrexia	1	1	1.0	4	4	3.9	5	5	2.5
	Total	1	1	1.0	4	4	3.9	5	5	2.5
Infections and Infestations	COVID-19	1	1	1.0	1	1	1.0	2	2	1.0
	COVID-19 Pneumonia	3	3	3.0	4	4	3.9	7	7	3.5
	Total	4	4	4.0	5	5	4.9	9	9	4.5
Respiratory, Thoracic and Mediastinal Disorders	Acute Respiratory Distress Syndrome	1	1	1.0	0	0	0	1	1	0.5
	Acute Respiratory Failure	0	0	0	1	1	1.0	1	1	0.5
	Dyspnoea	1	1	1.0	2	2	1.9	3	3	1.5
	Hypoxia	1	1	1.0	1	1	1.0	2	2	1.0
	Respiratory Distress	0	0	0	1	1	1.0	1	1	0.5
	Respiratory Failure	0	0	0	1	1	1.0	1	1	0.5
	Total	3	3	3.0	6	5	4.9	9	8	4.0
Total		**9**	**7**	**7.1**	**17**	**13**	**12.6**	**26**	**20**	**9.9**

Treatment-emergent adverse events of severity grade 2 or higher. Safety analysis set (n=99 for IMU-838, n=103 for Placebo)
The severity of adverse events (AE) was graded according to the National (US) Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE), Version 5.0
Adverse events as coded by MedDRA version 23.0

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CALVID-1: Safety Summary

- IMU-838 was found to be safe and well-tolerated in hospitalized patients with moderate COVID-19:
  - No general safety signals regarding new or more severe adverse events observed, as compared to placebo
  - Rate of serious adverse events and adverse events leading to treatment discontinuation was not increased, as compared to placebo
  - Fewer COVID-19 related adverse events with increased intensity (grade 2 or higher) in IMU-838 treated patients, as compared to placebo
  - IMU-838 did not intensify any hematological effects of COVID-19, as compared to placebo
  - IMU-838 did not increase the rate of infections and infestations in patients with COVID-19, as compared to placebo
  - IMU-838 did not increase the rate of liver events in patients with COVID-19, as compared to placebo

The study indicates that IMU-838 may be a safe and well tolerated oral treatment option for patients with moderate COVID-19.

Safety analysis set (n=99 for IMU-838, n=103 for Placebo): Includes all patients randomized
The severity of adverse events (AE) was graded according to the National (US) Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE), Version 5.0

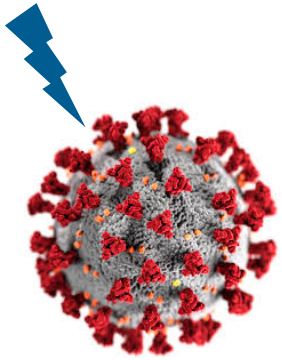
CALVID-1 Trial of IMU-838 in Moderate COVID-19

Conclusions and Outlook

Activity on Clinical Endpoints in Hospitalized COVID-19 Patients

IMU-838 Could Provide Moderate COVID-19 Patients a **Safe and Convenient Oral Treatment Option**

IMU-838



SARS-CoV-2

1. IMU-838 showed evidence of clinical activity on multiple clinical endpoints in hospitalized patients with moderate COVID-19
2. Treatment effect of IMU-838 versus placebo appears to be commensurate with that of other medications successfully tested in COVID-19
3. Effects on preventing “Long COVID” symptoms suggest that IMU-838 could be a promising new therapeutic intervention
4. Immunic will discuss the results with clinical and regulatory experts and plans to explore options for further development and funding support

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IMU-838 in Primary Sclerosing Cholangitis (PSC)

Investigator-Sponsored Trial Performed at Mayo Clinic

IMU-838 for the Treatment of PSC

Top-Line Data Now Available

- Investigator-sponsored trial supported by a grant from the National Institutes of Health (NIH)
- Immunic provided the study medication
- Performed under an investigator IND from the FDA held by the Principal Investigator
- As per agreement between Immunic and Mayo Clinic:
  - Immunic gets access to limited top-line efficacy and safety data at the conclusion of the study
  - Additional and more complete data will be accessible by Immunic only at a later timepoint
  - Immunic is subject to certain restrictions regarding data publication before the full data is published by Mayo Clinic

IMU-838 in PSC: Phase 2 Proof-of-Concept Study

Principal Investigator

Elizabeth Carey, MD (Mayo Clinic)

Study Timelines

- Study started in August 2019
- Enrollment took place between July 2019 and September 2020, but almost all enrollment occurred in 2019 and early 2020
- The ongoing pandemic situation triggered the principal investigator's decision to terminate the study in late 2020

Investigator-Sponsored Trial Conducted at Two Mayo Clinic Sites

- Single-arm, open-label, exploratory study which planned to enroll 30 patients, aged 18 to 75 years
- Supported by National Institutes of Health (NIH) grant
- Study was performed at tertiary referral centers for PSC patients:
  - Mayo Clinic, Phoenix, Arizona (Elizabeth Carey, MD)
  - Mayo Clinic, Rochester, Minnesota (John E. Eaton, MD)
- Immunic provided the study medication
- Dosing: 30 mg of IMU-838 once daily for a period of 24 weeks
- Primary objective: change in serum alkaline phosphatase (ALP) at week 24, as compared to baseline
- Together with the investigators, Immunic determined to readout data of the 18 patients who were enrolled prior to the COVID-19 pandemic*

www.clinicaltrials.gov: NCT03722576

* During the COVID-19 pandemic, recruitment for this study was hampered, as patients with PSC are at a high risk of COVID-19 infections and were advised to avoid travel and unnecessary social contacts such as those required to participate in a clinical trial.

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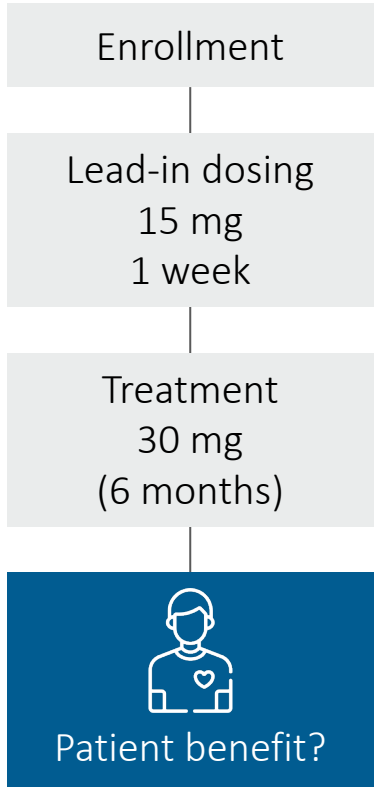
IMU-838 in PSC: Study Flow Chart and Study Population



- Study planned to enroll 30 patients
- Study screened 27 patients
  - 5 patients were screen failures (4 patients did not have ALP elevated of at least 1.5 times ULN, and 1 patient had an excluded condition)
  - 4 patients (in particular during the pandemic period) withdrew consent before receiving any treatment
  - **18 patients** started treatment of once daily 30mg IMU-838 (intent-to-treat population, ITT, n=18)
  - Of these 18 patients, 7 patients discontinued before week 24, and only **11 patients** completed 24-week IMU-838 treatment (per protocol population, PP, n=11)

ALP: alkaline phosphatase; ULN: upper limit of normal

Baseline Characteristics

	PP population (n=11)	ITT population (n=18)
Enrolled Site, n (%)		
Mayo Arizona	3 (27.3%)	9 (50.0%)
Mayo Rochester	8 (72.7%)	9 (50.0%)
Age at Enrollment		
Mean (SD)	48.1 (16.7)	45.7 (15.2)
Median (IQR)	41 (33, 66)	40 (32, 60)
Range	26.0, 69.7	26.0, 69.7
Gender, n (%)		
Male	5 (45.5%)	7 (38.9%)
Female	6 (54.5%)	11 (61.1%)
Race, n (%)		
White	11 (100.0%)	18 (100.0%)
Ethnicity, n (%)		
Not Hispanic or Latino	11 (100.0%)	17 (94.4%)
Hispanic or Latino	0 (0.0%)	1 (5.6%)
Crohn's Disease or Ulcerative Colitis, n (%)		
No	5 (45.5%)	6 (33.3%)
Yes	6 (54.5%)	12 (66.7%)
ALP at Baseline, IU/L		
Mean (SD)	386.2 (147.3)	366.1 (130.4)
Median (IQR)	361 (228, 507)	340 (261, 451)
Range	219.0, 661.0	215.0, 661.0
Total Bilirubin at Baseline, mg/dL		
Mean (SD)	0.9 (0.5)	0.8 (0.5)
Median (IQR)	1 (1, 1)	1 (1, 1)
Range	0.3, 2.1	0.3, 2.1

SD: standard deviation; IQR: interquartile range; ALP: alkaline phosphatase; PP: per-protocol; ITT: intend-to-treat

IMU-838 in Primary Sclerosing Cholangitis (PSC)

Efficacy

Primary Objective: Change in Serum Alkaline Phosphatase

The Primary Objective Was to Determine Whether IMU-838 Reduces Serum ALP in Adult Patients Diagnosed With PSC

Definition of the primary objective:

- Patients who achieve a reduction of ALP at week 24
  - greater or equal to 25%, as compared to baseline,
  - while the AST increase at week 24 is no more than 33%, as compared to baseline.

	Positive Outcome N (%)	95% CI
ALP Reduction ≥25% and AST Increase ≤33% Between Baseline and Week 24 (ITT, N=18)	3/18 (16.7%)	3.6%, 41.4%
ALP Reduction ≥25% and AST Increase ≤33% Between Baseline and Week 24 (PP, N=11)	**3/11 (27.3%)**	**6.0%, 61.0%**

ALP: alkaline phosphatase; AST: aspartate aminotransferase; PP: per-protocol; ITT: intend-to-treat, CI: confidence interval

Study Results: Statistically Significant Reduction in Serum ALP

IMU-838's Reduction in Serum ALP Levels Compares Well to Other Medications in Development for PSC

	IMU-838	norUDCA[1]	OCA[1]	Cilofexor[1]
Administration	Oral	Oral	Oral	Oral
Daily Dose	30 mg QD	1500 mg QD	5 to 10 mg QD	(30 and) 100 mg QD
Endpoint ("Positive Outcome" in %)	ALP reduction >=25% **and** AST increase <= 33% at week 24	≥ 25% ALP reduction	≥ 25% ALP reduction	≥ 25% ALP reduction
Treatment Duration	24 weeks	12 weeks	24 weeks	12 weeks
Number of Patients With a "Positive Outcome" in %	**27%***	**na**	**na**	**5% for 30 mg and 35% for 100 mg**

[1] Gerussi et al., Annals of Hepatology 19 (2020) 5-16
ALP: alkaline phosphatase; AST: aspartate aminotransferase; QD: quaque die = once-daily
*ALP reduction (PP, LS means)

Quantitative Change in Serum Alkaline Phosphatase

The Primary Objective Was to Determine Whether IMU-838 Reduces Serum ALP in Adult Patients Diagnosed With PSC

- Time from baseline: calculated as continuous variable and treated as the primary predictor using a random intercept model which was adjusted for age at baseline and gender
  - **ALP value statistically significantly (p=0.041) decreased** by an average of 5.76 IU/L every 30 days (95% CI: -11.29, -0.23; statistical model) in the PP population (N=11)
  - Not statistically significant in the ITT analysis (p=0.578; N=18)

	Estimate of Change Every 30 Days (95% CI)	p-value
ALP Change Between Baseline and Week 24 (ITT, N=18)	-2.11 (-9.62, 5.40)	0.578
ALP Change Between Baseline and Week 24 (PP, N=11)	**-5.76 (-11.29, -0.23)**	**0.041**

Model adjusted for age at baseline and gender

ALP: alkaline phosphatase; AST: aspartate aminotransferase; PP: per-protocol; ITT: intend-to-treat, CI: confidence interval

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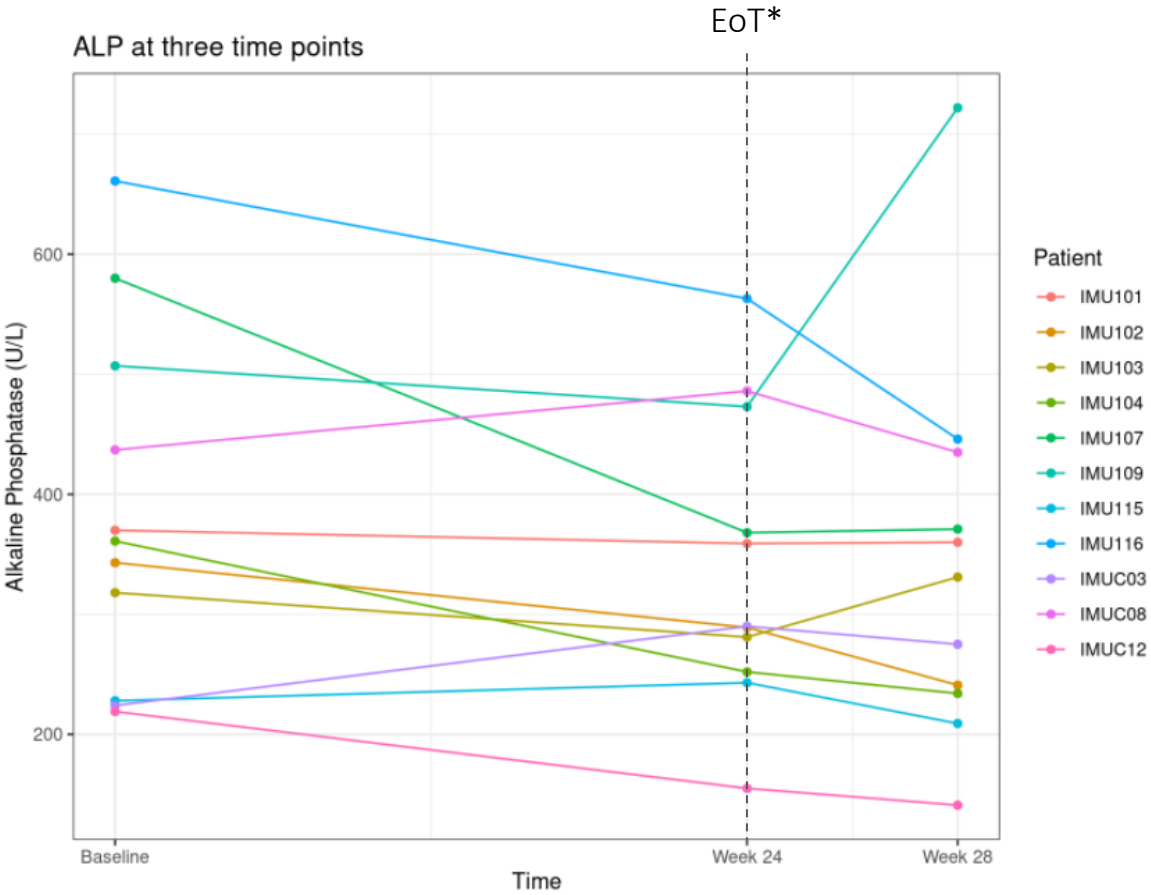
Individual ALP Changes Over Treatment Period



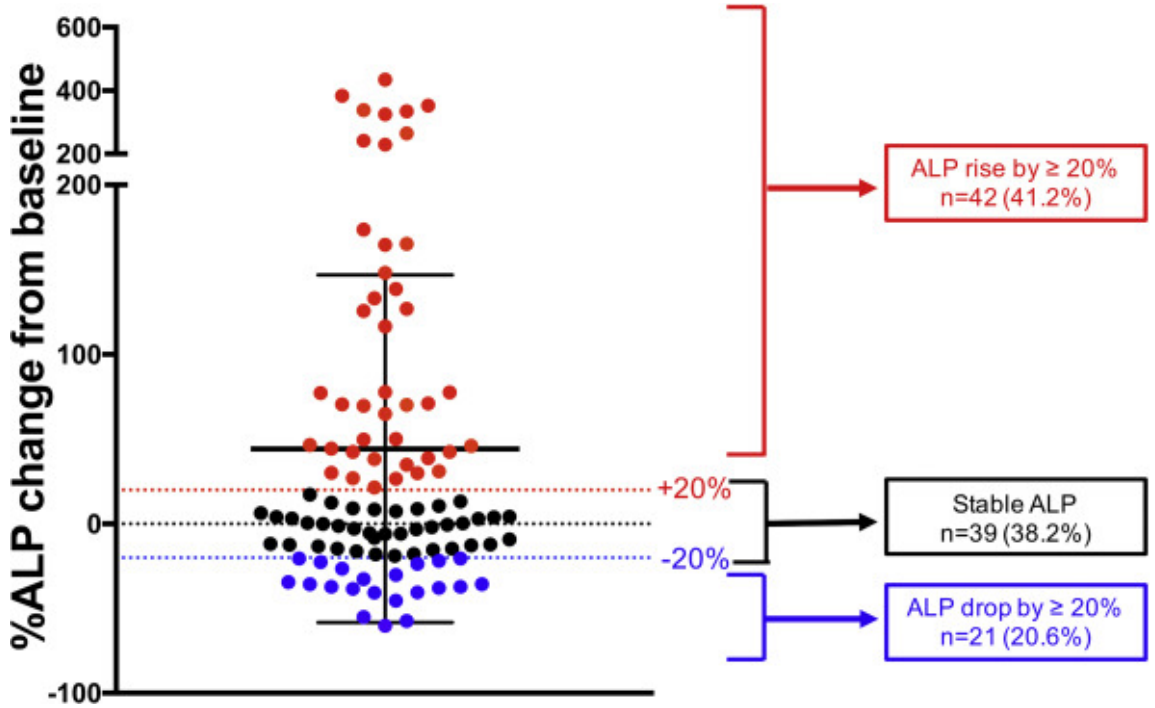
- Consistent individual pattern of a stable decrease in ALP values between baseline and Week 24 (24-week treatment period)
- While the decrease in ALP values was moderate, no patient of the PP population showed an increase of more than 20% of ALP at Week 24, as compared to baseline
- After treatment cessation at Week 24, a total of 2 patients showed a strong rebound effect at Week 28

ALP: alkaline phosphatase, Treatment period between baseline and Week 24. Follow-up period (without treatment) between Week 24 and Week 28, Per Protocol (PP) Population (n=11)
*EoT: End of Treatment

Example of Variability of Alkaline Phosphatase in PSC

Longitudinal Analysis of Vedolizumab in PSC-IBD

Vedolizumab, n=102; median treatment duration, 412 days



Almost half of the patients showed a progression by more than 20% in alkaline phosphatase

Serum levels of alkaline phosphatase decreased by more than 20% in only 20.6% of patients

Lynch et al. Effects of Vedolizumab in Patients With Primary Sclerosing Cholangitis and Inflammatory Bowel Diseases. Clin Gastroenterol Hepatol. 2020 Jan;18(1):179-187

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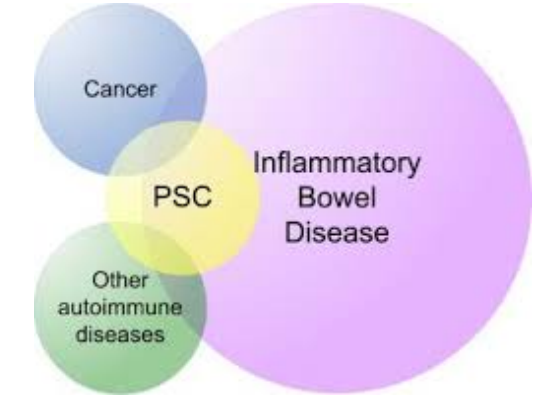
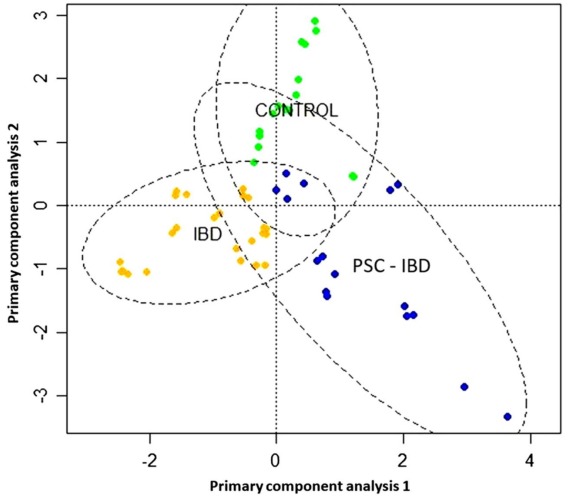
IMU-838 in Primary Sclerosing Cholangitis (PSC)

Patients with Existing Comorbidity: IBD Assessments

PSC and Ulcerative Colitis

Overlap and Differences in Epidemiology and Biology





- Whereas PSC occurs in about 5% of patients with inflammatory bowel disease (IBD), approximately 70% of patients with PSC have IBD[1]
- The gut-adherent microbiota in patients with PSC-IBD and IBD without PSC are significantly different[2]

[1] Maurice JB, Thorburn D. Precision medicine in primary sclerosing cholangitis. J Dig Dis. 2019 Jul;20(7):346-356
[2] Quraishi et al. Probing the microbiota in PSC: the gut adherent microbiota of PSC-IBD is distinct to that of IBD and controls. Hepatology 2014, Vol. 60, p. 267A

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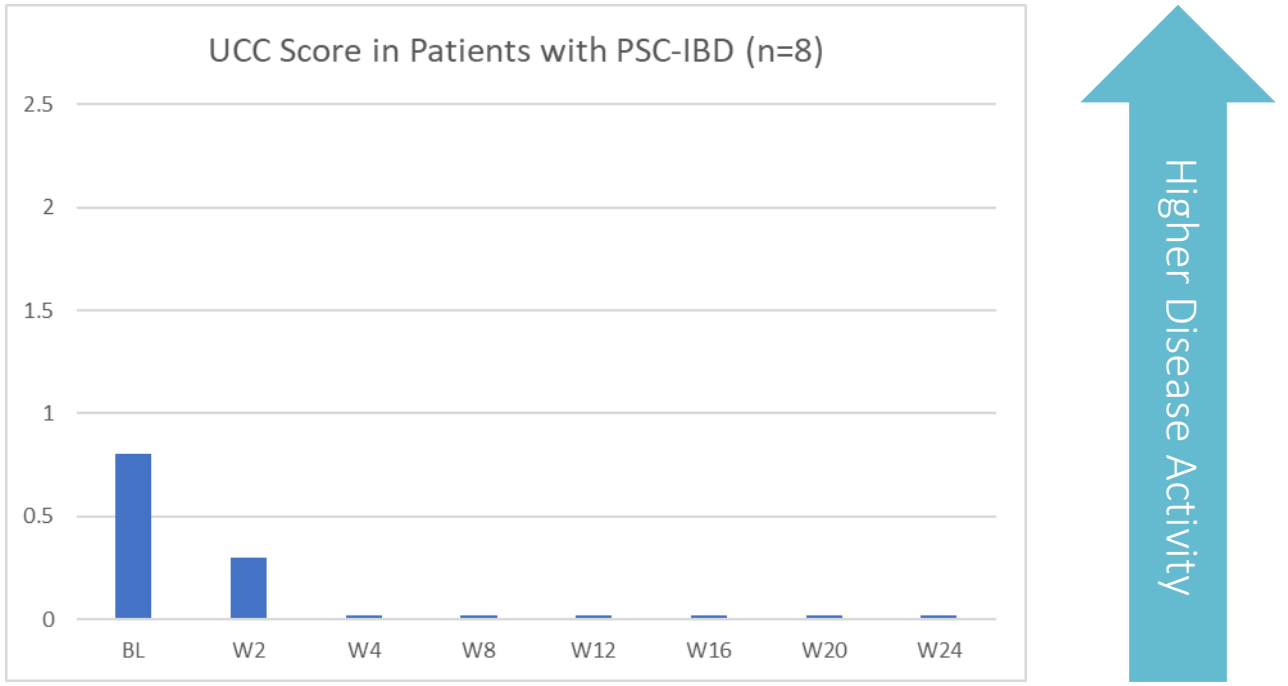
Ulcerative Colitis Clinical (UCC) Score

Physician Assessment of Ulcerative Colitis Activity

The UCC score, a modification and simplification of the well-known Mayo Score, consists of four items:

- stool frequency,
- rectal bleeding,
- subject's functional assessment, and
- physician's global assessment.

Scores Range From 0 to 12 Points, With Higher Scores Meaning Higher Colitis-Related Active Disease



Mean of UCC Score of patients with comorbidity PSC-IBD

Between baseline (BL) up to end of treatment at Week (W) 24

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Short Inflammatory Bowel Disease Questionnaire (SIBDQ)

Patient-Reported Questionnaire for Health-Related Quality of Life

The SIBDQ consists of questions scored in four domains:

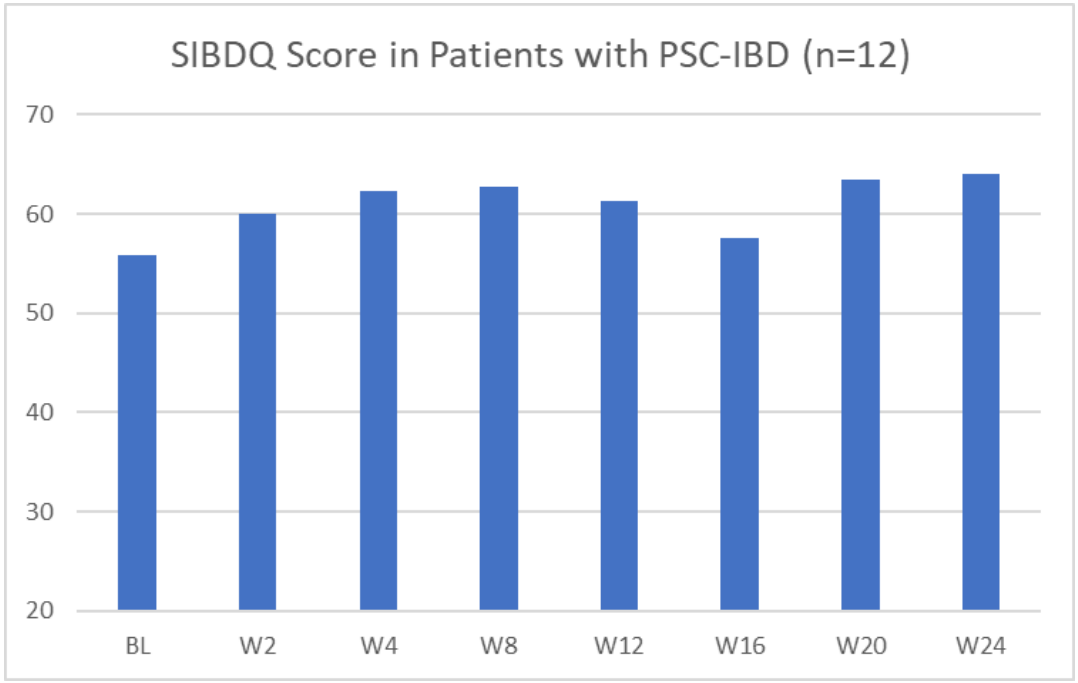
- bowel symptoms,
- emotional health,
- systemic systems, and
- social function.

Respondents are asked to provide a rating from 1 to 7 on quality-of-life measures during the last two weeks.

Typical SIBDQ scores: [1]

- Remission 50-64
- Mild relapse 35-50
- Moderate relapse 22-35
- Severe relapse 15-30

Questionnaire Provides a Score Ranging From 10 (Lowest Score) to 70 (Highest Score)



Mean of SIBDQ Score of patients with comorbidity PSC-IBD

Between baseline (BL) up to end of treatment at Week (W) 24

[1] Jowett et al. The short inflammatory bowel disease questionnaire (SIBDQ) is reliable and responsive to clinically important change in UC. Gastroenterology 2001 Vol120 (5) S1, p. A273-A274

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IMU-838 in Primary Sclerosing Cholangitis (PSC)

Safety

Study Results: Safety

IMU-838's Favorable Safety and Tolerability Profile Was Confirmed in This Patient Population

- **SAE:** There were no SAE or on-study deaths.
- **Treatment Emergent Adverse Events:**
  - A total 36 AE were reported in 12 of the 18 patients that received any dose of IMU-838:
    - 2 patients had one AE
    - 1 patient had two AE
    - 6 patients had 3 AE
    - 2 patients had 4 AE
    - 1 patient had 6 AE
- **Severity:** The majority of the AE was grade 1 (n=33) and only 3 AE were grade 2.
- **Relatedness:** Only 4 AE were possibly, probably or definitely attributed to the study drug by the investigators (n=1 ALP increased, n=1 fever, n=1 hematuria, n=1 liver enzymes worsened) while all the other 32 AE were not attributed to the study drug.

SAE: serious adverse events; AE: adverse events, ALP: alkaline phosphatase

IMU-838 in Primary Sclerosing Cholangitis (PSC)

Outlook

IMU-838 in PSC: Outlook

As an Orally Available DHODH Inhibitor With a Prominent Influence on Th17 Induced Inflammatory Processes, IMU-838 is a Promising Approach for the Treatment of PSC

- The encouraging results regarding biochemical parameters and safety suggest that IMU-838 merits further clinical testing in PSC
- Immunic is in discussions with investigators and leading clinical experts to further evaluate the data set and to explore potential next steps
- Immunic believes that dose optimization would be needed for potential future trials, which would also require assessment of pharmacokinetics in hepatic impaired patients

Thank You!

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