Immunic Therapeutics

Main Phase 2 Analysis CALVID-1 Trial of IMU-838 in Moderate COVID-19

NASDAQ: IMUX | February 18, 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	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

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IMU-838: Preparations for Broad Market Access

- Safety database contains more than 800 individuals (healthy volunteers and several patient populations)
- Commercial-scale production in place; material from this production ready to be used in future clinical trials and potentially for expanded access schemes
- Significant amounts of API available, quick upscaling to market scale possible

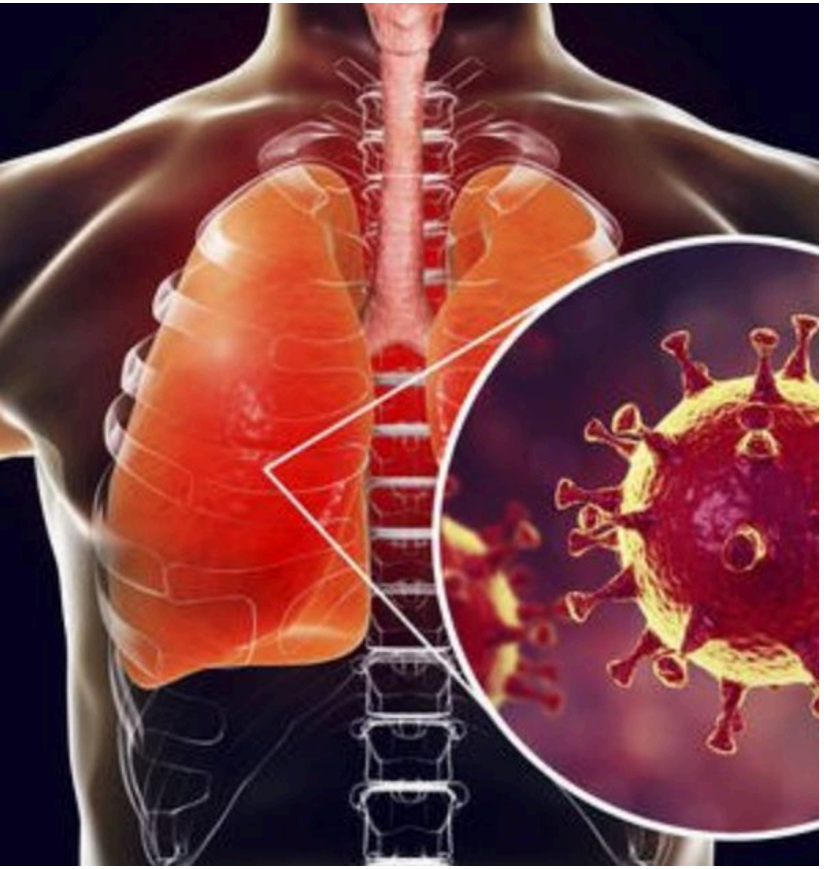
API: active pharmaceutical ingredient

IMU-838 Fighting COVID-19

Leveraging DHODH's Broad-Spectrum Antiviral Activity

IMU-838: Triple Attack on COVID-19

IMU-838 is an Advanced Clinical Oral Drug Candidate With a Favorable Pharmacokinetic, Safety and Tolerability Profile With More Than **800 Individuals Exposed to Date**



IMU-838 Attacks COVID-19 by Three Complementary Mechanisms:

1. Inhibition of **virus replication** by depletion of nucleotide pool
2. Insufficient first immune response due to SARS-CoV-2 encoded interferon antagonists. Induction of **innate immune response** by DHODH inhibition independent of interferon signaling
3. Excessive activation of adaptive immune response – “cytokine storm”. Inhibition of “overreacting”, **cytokine high** producing immune cells

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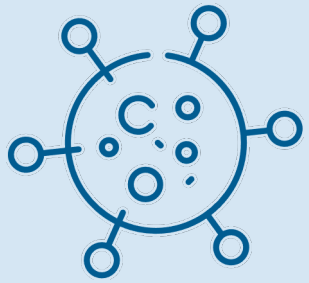
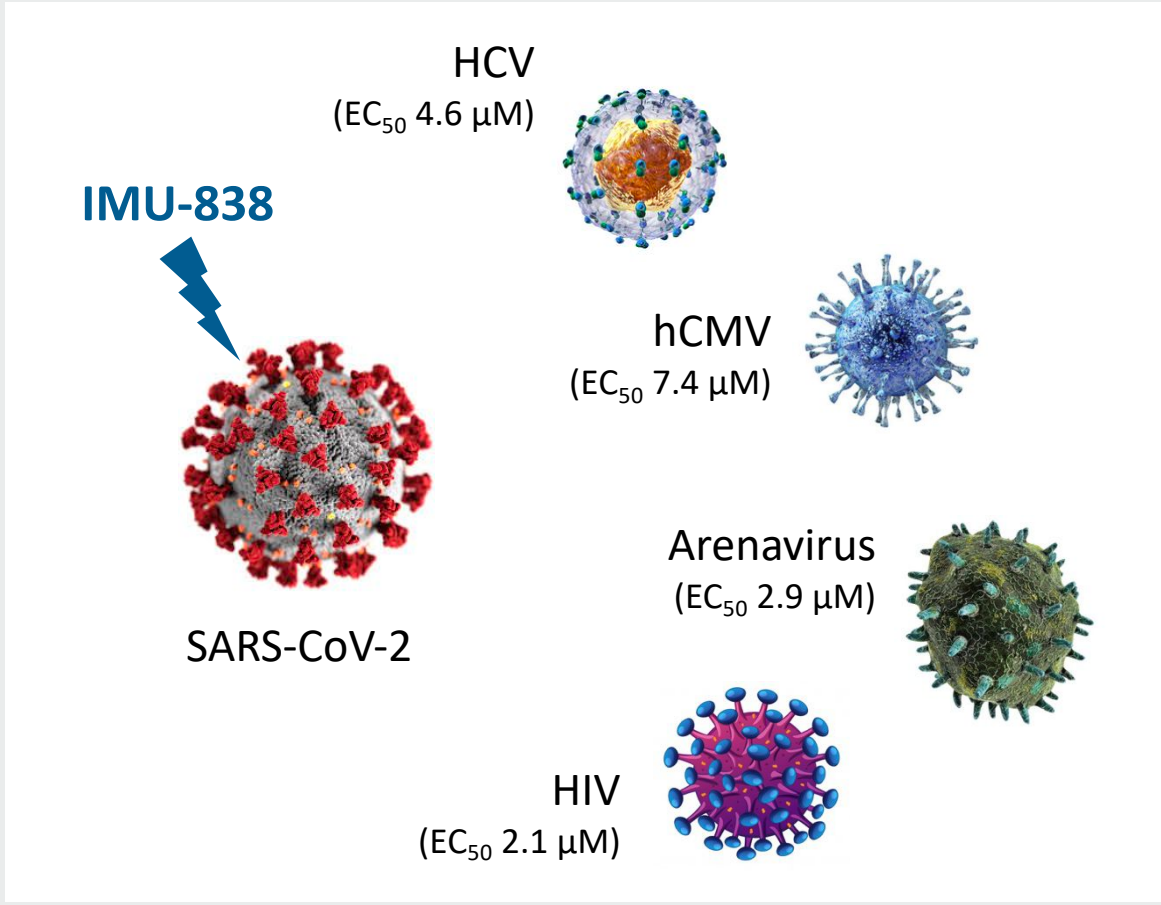
IMU-838 Antiviral Activity Against SARS-CoV-2 and Other Viruses



- 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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Publication: Summary of Antiviral Effects of IMU-838

viruses

MDPI OPEN ACCESS

Article

IMU-838, a Developmental DHODH Inhibitor in Phase II for Autoimmune Disease, Shows Anti-SARS-CoV-2 and Broad-Spectrum Antiviral Efficacy In Vitro

Friedrich Hahn [1], Christina Wangen [1], Sigrun Häge [1], Antonia Sophia Peter [1], Gerhard Dobler [2], Brett Hurst [3], Justin Julander [3], Jonas Fuchs [4], Zsolt Ruzsics [4], Klaus Überla [1], Hans-Martin Jäck [5], Roger Ptak [6], Andreas Muehler [7], Manfred Gröppel [7], Daniel Vitt [7], Evelyn Peelen [7], Hella Kohlhof [7,†] and Manfred Marschall [1,*,†]

Viruses. 2020 Dec 5;12(12):1394

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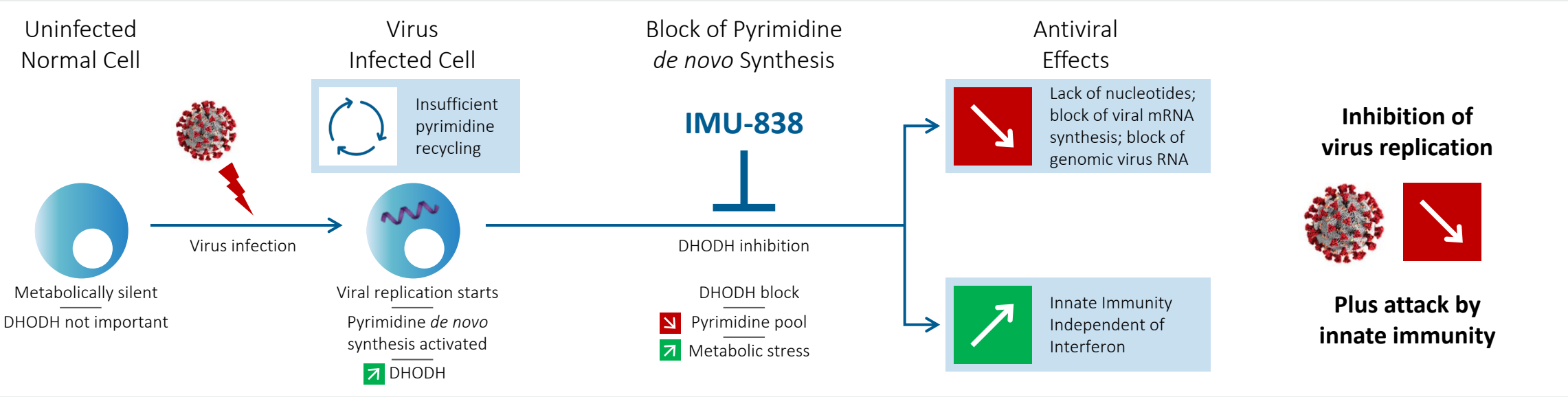
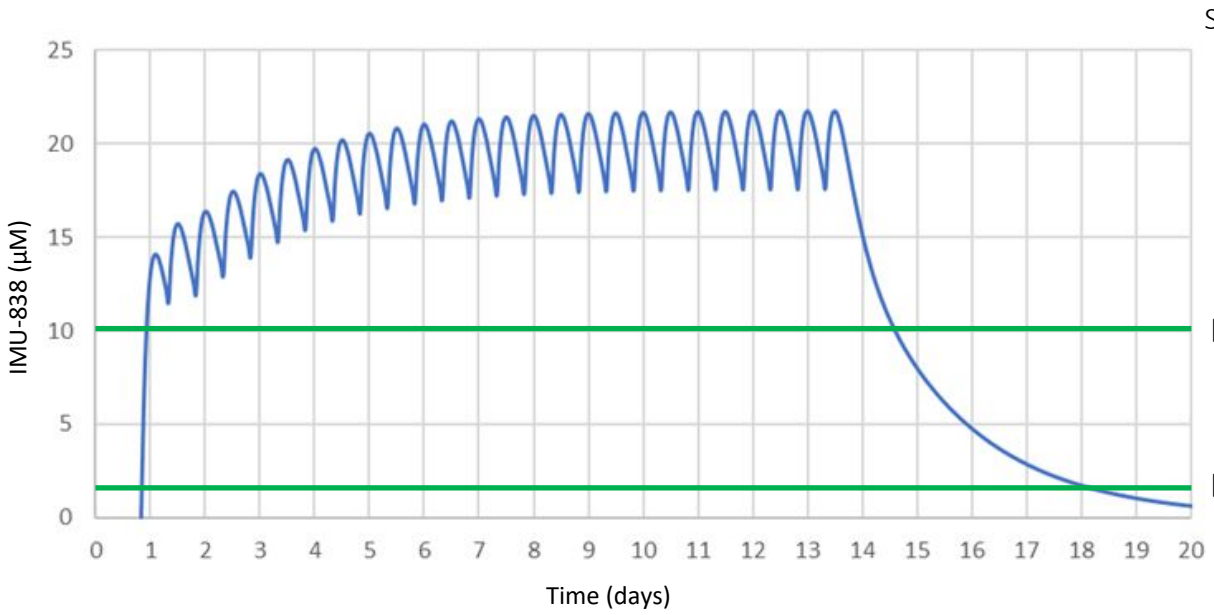
Summary of Rationale for IMU-838 in COVID-19

Triple mode of action: orally available DHODH inhibitor with both antiviral and anti-inflammatory effects plus activation of innate immune response

Host-based mechanism: avoids dependence on specific viral proteins and, therefore, offers broad-spectrum antiviral activity

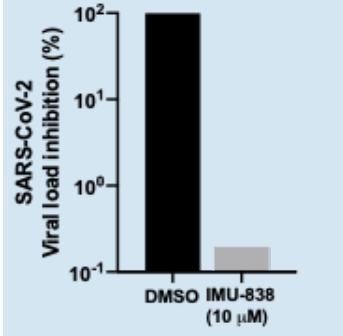


Anticipated Pharmacokinetic Profile 22.5 mg BID 14-day Treatment in Phase 2 IMU-838 in COVID-19 Patients



SARS-CoV-2

A549-ACE2



Proposed dosing regimen ensures that therapeutic levels of IMU-838 are reached starting from first dose.

Based on Population Pharmacokinetic Model for IMU-838 as described in the following publication: Muehler et al. Eur J Drug Metab Pharmacokinet. May 2, 2020
BID: bis in die = two times daily

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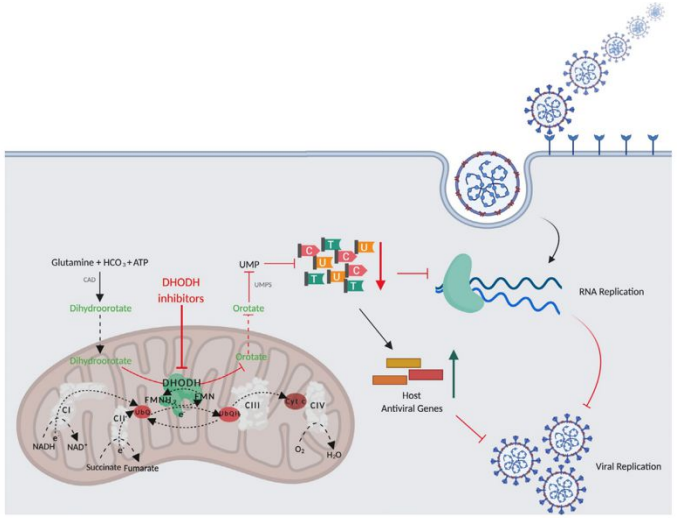
IMU-838: Host Cell Based Approach Active Against Different Virus Variants



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

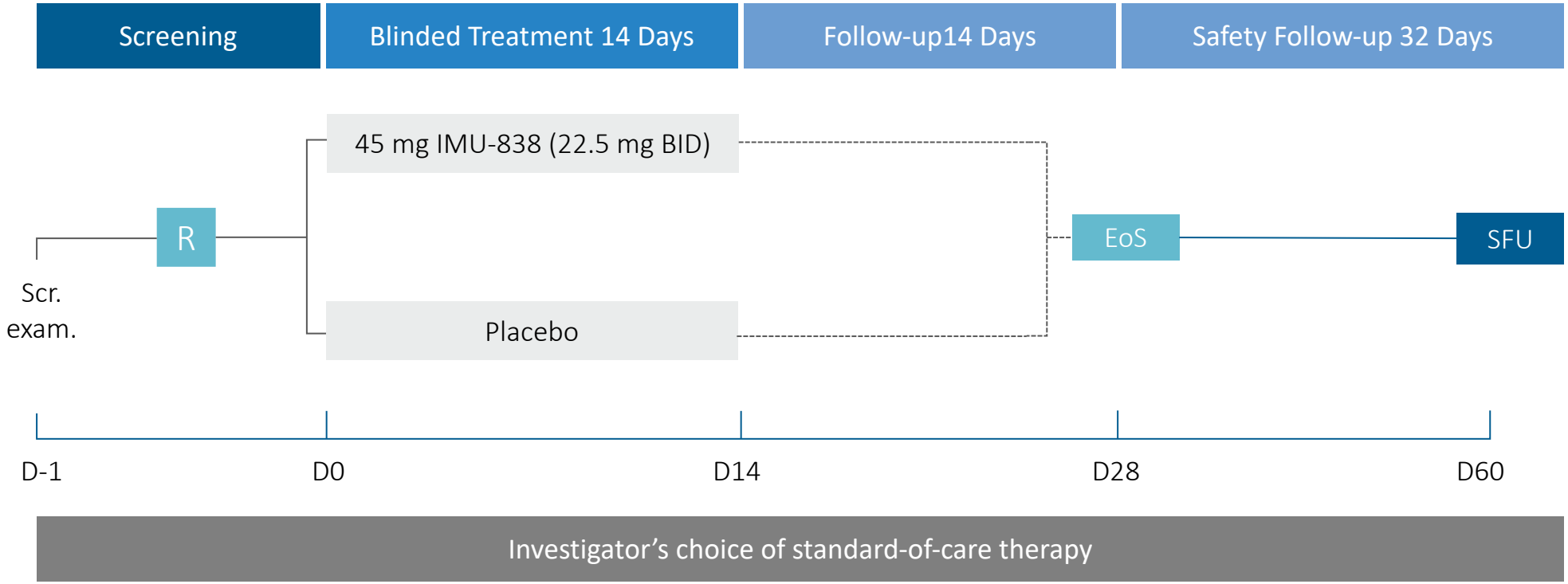
Eur J Clin Invest. 2020;50:e13366

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

Study Background

CALVID-1: Study Flow Chart

NCT04379271



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

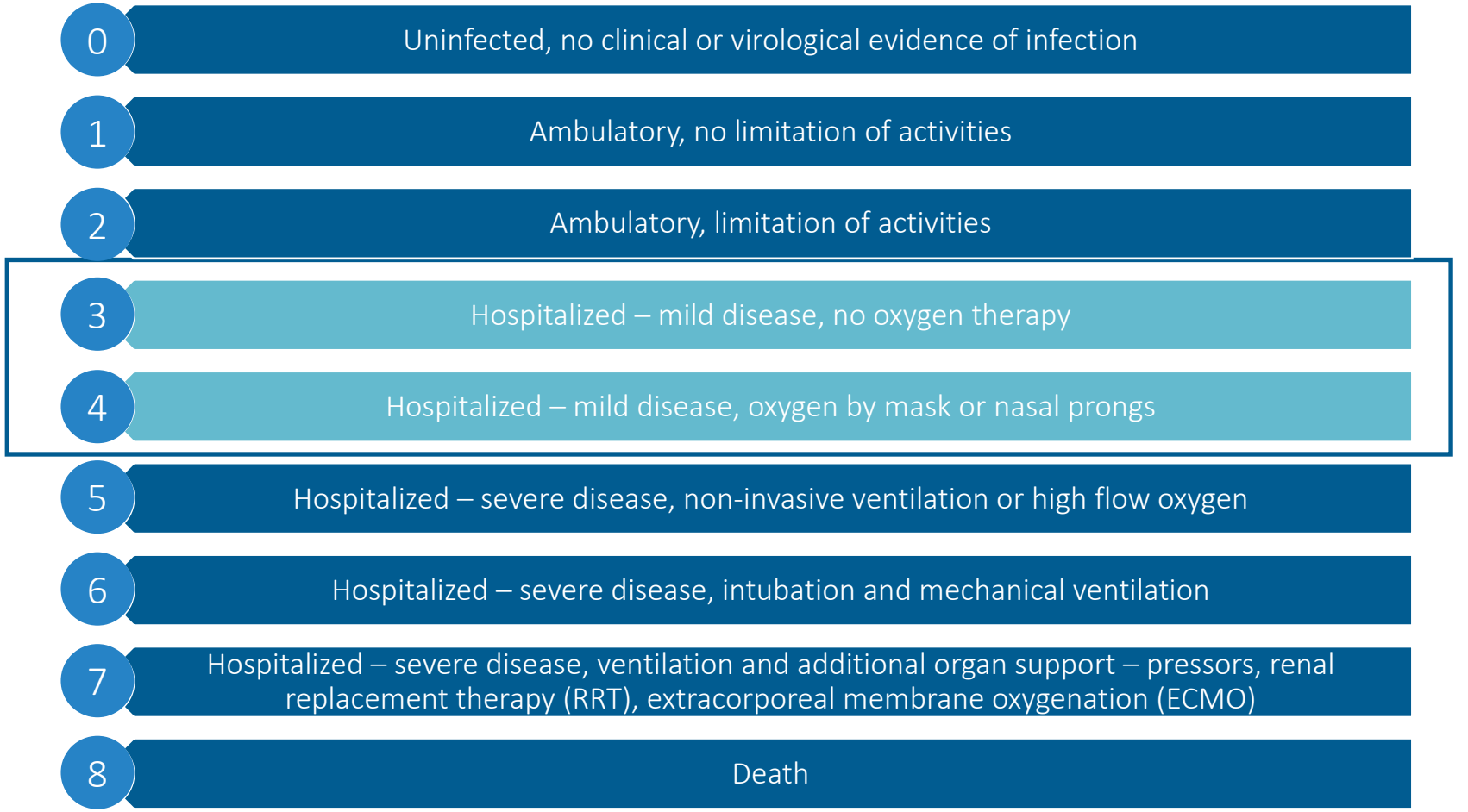
- USD 29 million EIB venture loan accessible for further phase 2/3 development

CALVID-1: Inclusion Criteria

- Male or female patients at least 18 years old
- Admitted to the hospital or other medical in-patient treatment facility for treatment of COVID-19
- SARS-CoV-2 infection confirmed by reverse transcriptase polymerase chain reaction (RT-PCR) test in a nasopharyngeal, oropharyngeal or respiratory sample at ≤4 days before randomization
- Moderate COVID-19 disease defined as fulfilling clinical status category 3 or 4 on the WHO nine-category ordinal scale:
  - Category 3: Hospitalized, virus-positive, no oxygen therapy with the following disease criteria
  - Category 4: Hospitalized, virus-positive, oxygen by mask or nasal prongs (excluding high-flow oxygen therapy) with the following disease criteria
- Fulfilling certain disease criteria:
  - Peripheral capillary oxyhemoglobin saturation (SpO2) >92% at maximum of 6 liters oxygen flow per minute
  - Stable respiratory rate ≤30 breaths/min at maximum of 6 liters oxygen flow per minute
  - Presence of at least 1 symptom characteristic for COVID-19 disease, i.e., fever, cough or respiratory distress

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

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: Main Exclusion Criteria

- Presence of respiratory failure, shock, and/or combined failure of other organs that requires ICU monitoring in the near foreseeable future
- History or presence of serious or acute heart disease such as uncontrolled cardiac dysrhythmia or arrhythmia, uncontrolled angina pectoris, cardiomyopathy, or uncontrolled congestive heart failure (NYHA class 3 or 4)
- Patients on dialysis or in end-stage liver disease (Child Pugh B and C score)
- Hospitalization primarily for reasons other than COVID-19 (including for concomitant conditions)
- Treatment exclusions:
  - Chloroquine and Hydroxychloroquine during the entire trial unless taken for indicated use before entering the trial
  - Concurrent use of any mycophenolate mofetil or of methotrexate exceeding 17.5 mg weekly
  - Current treatments for any malignancy
- Allowed standard of care treatment included antivirals, including medications approved under Emergency Use Authorizations or similar mechanisms

NYHA: New York Heart Association; ICU: intensive care unit

CALVID-1: Database Outline

Main Analysis (MA1) Includes Data From 204 Randomized Patients

- MA1 was intended to provide decision point for further development
- 202 patients received at least one dose of study drug (efficacy and safety sets for MA1)
- Contains most data for treatment period until Day 14 and follow-up period until Day 28
- Includes top-line efficacy data only; additional and more detailed efficacy data will be reported at FA1
- Includes full safety data until Day 28

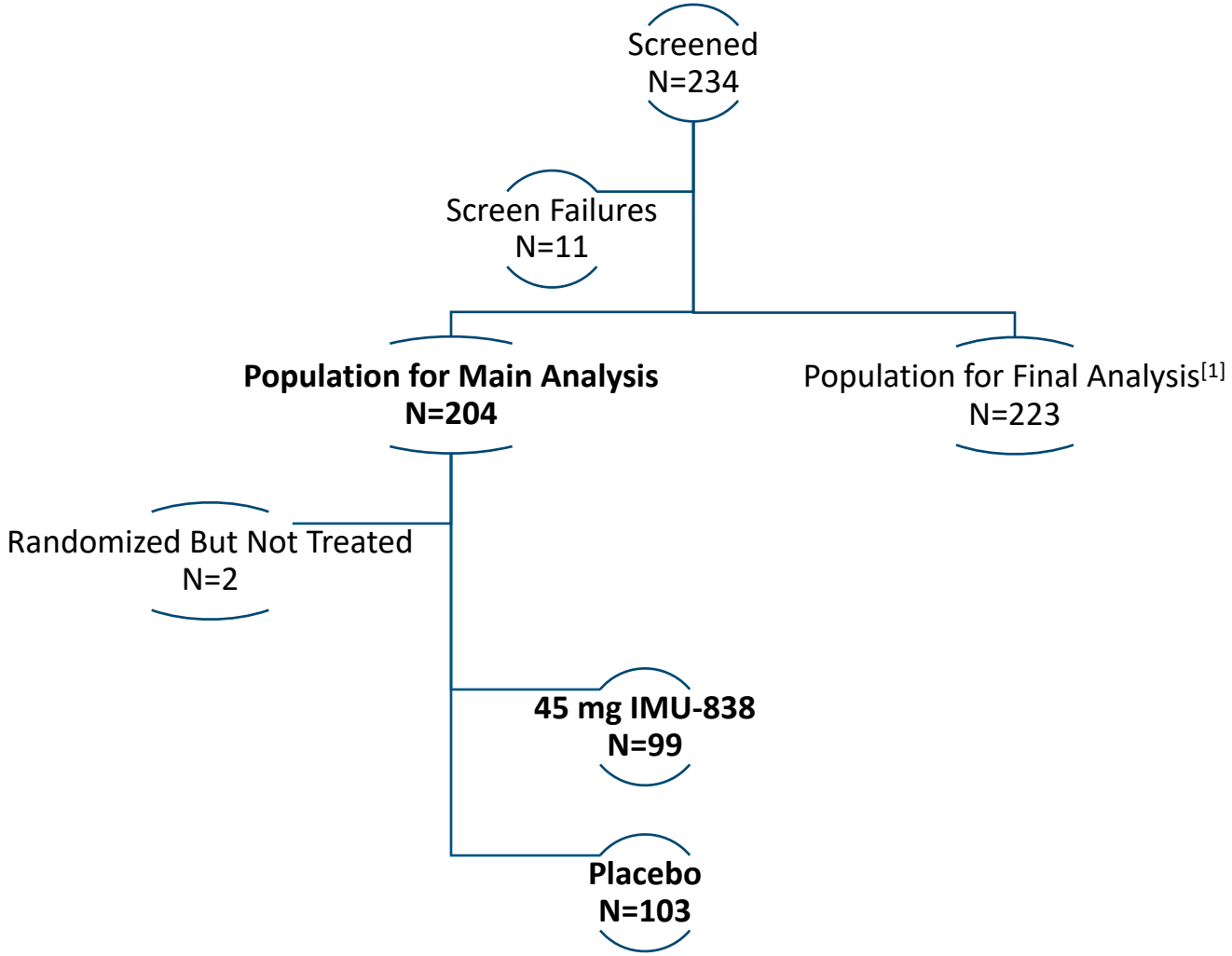
Full Analysis (FA1) Will Comprise Data From All 223 Randomized Patients

- Will contain data from all randomized patients including safety follow-up until Day 60
- Will include full efficacy data, including subgroup and sensitivity analyses
- Will include full virology data
- Will include drug trough level data
- Expected to be available in Q2/2021

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.

Patient Demographics

		Planned Treatment				Total	
		45 mg IMU-838		Placebo			
		N	%	N	%	N	%
Sex	Female	48	48.5	43	41.7	91	45.0
	Male	51	51.5	60	58.3	111	55.0
Race	Asian	0	0.0	1	1.0	1	0.5
	Black or African American	0	0.0	1	1.0	1	0.5
	Other	0	0.0	1	1.0	1	0.5
	White	99	100.0	100	97.1	199	98.5
Ethnicity	Not Hispanic or Latino	99	100.0	103	100.0	202	100.0
Age Category	< 65 Years	75	75.8	79	75.7	153	75.7
	>= 65 Years	24	24.2	24	23.3	49	24.3
Antiviral Therapy at Randomization	All Antivirals	14	14.1	16	15.5	30	14.9
	No Antivirals	85	85.9	87	84.5	172	85.1

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

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

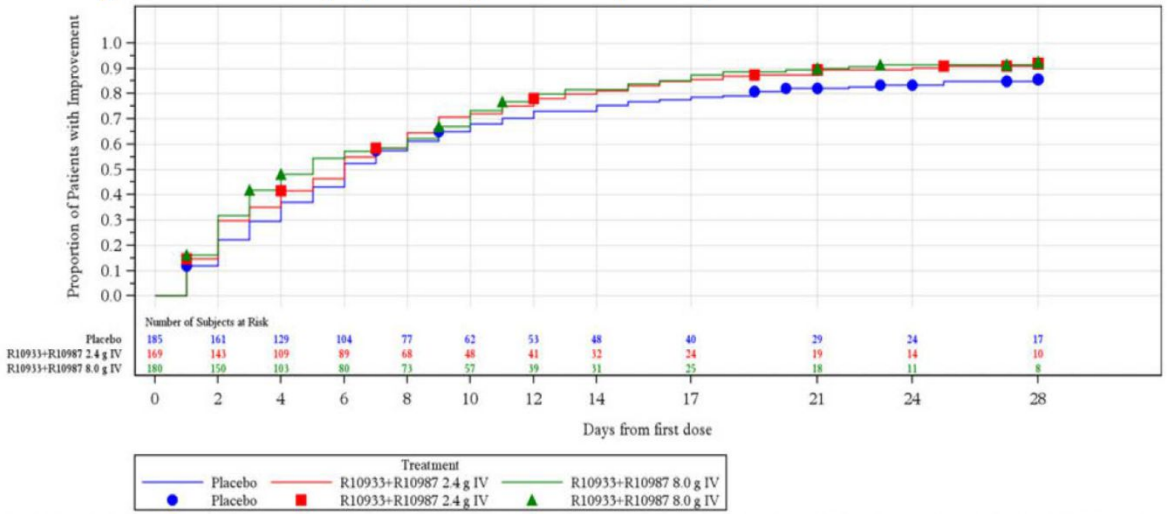
Full analysis set (FAS, n=99 for IMU-838, n=103 for Placebo)
Clinical recovery is defined as as axillary temperature <= 36.6 °C, or oral temperature <= 37.2 °C, or rectal or tympanic temperature <= 37.8 °C, and respiratory frequency <= 24 times/min without oxygen inhalation and oxygen saturation >= 98%.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

Time to Clinical Recovery / Symptom Resolution

Results of Other Medications Tested in COVID-19 Patients

Casirivimab-Imdevimab[1]

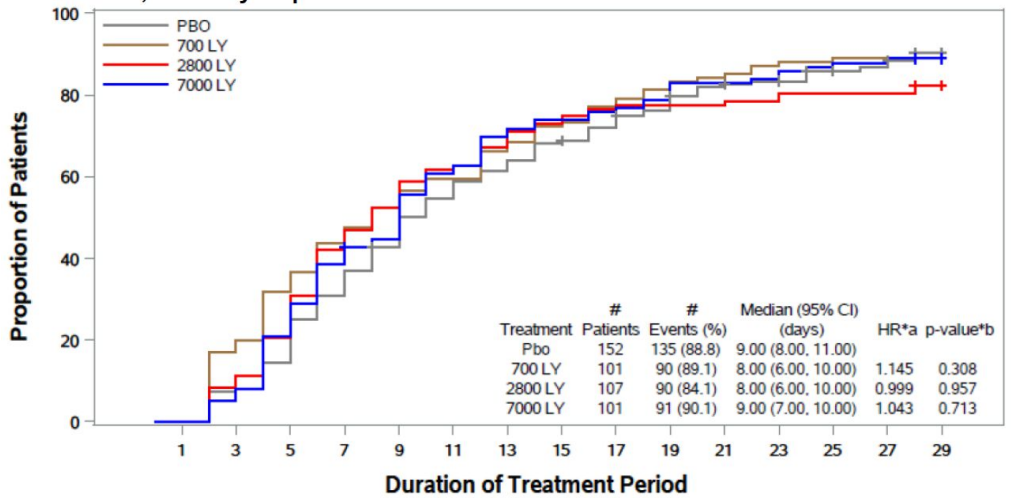
Figure 4: Time to Symptom Improvement (mFAS)



The median time to first day of symptom resolution was **14 days** for casirivimab and imdevimab, **as compared to 16 days for placebo**. Symptom resolution was defined as all symptoms rated by participants to be absent.

Bamlanivimab[2]

Figure 3: Time to First Symptomatic Resolution, Kaplan Meier Product Limit Curve, Efficacy Population in Trial PYAB



The overall symptom burden was generally lower through Day 11 in active treatment groups. Times to resolution appeared relatively similar between the placebo group (9-day median) and active treatment groups **(8/9-day median for each arm).**

[1] Emergency Use Authorization (EUA) for casirivimab and imdevimab. CDER Review. Available at: https://www.fda.gov/media/144468/download
[2] Emergency Use Authorization (EUA) for bamlanivimab 700mg IV. CDER Review. Available at: https://www.fda.gov/media/144118/download

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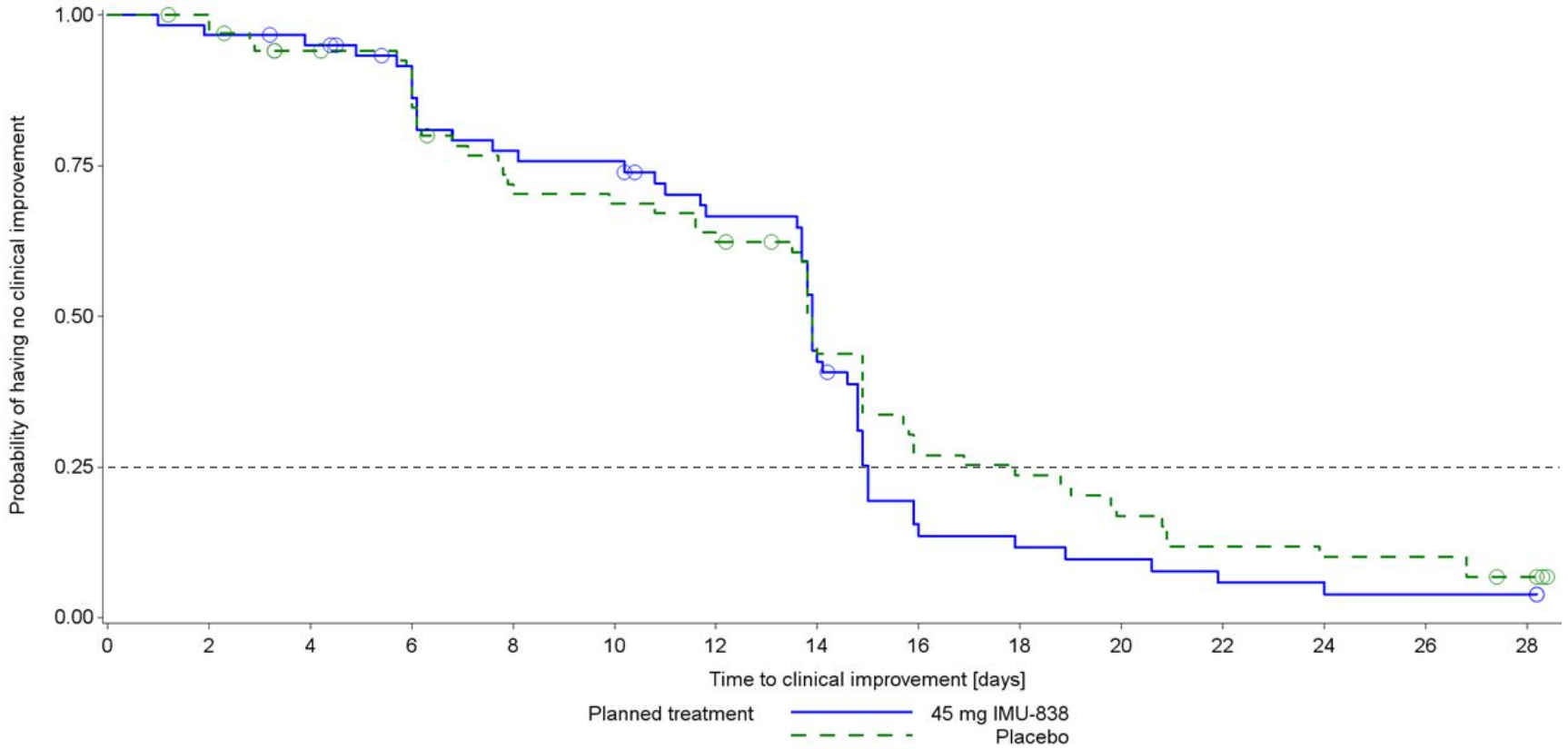
Time to Clinical Improvement

IMU-838 Shows Acceleration of Time to Clinical Improvement



Duration of Hospitalization (FAS):

- Median: 14.0 days
- Third patient quartile:[1]
  - 16.0 days for IMU-838
  - 19.4 days for Placebo

Note: The endpoint time to clinical improvement is largely driven by hospitalization. The study design included required visits at Day 6 and Day 14. This study design may explain that investigators in the early phase of therapy made most decisions regarding hospitalization after these visits (hence the large drop in the Kaplan Meier curve at this visits). This study bias may mask any treatment differences up to Day 14 and Immunic believes that, for this reason, the benefit of IMU-838 on clinical improvement should only be evaluated after Day 14 and median may not be appropriate.

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 virology laboratory (only nasopharyngeal swabs).

The Kaplan Meier curve depicts the 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. the trial design, on the advice of regulatory agencies and clinical experts, included mandatory study visits at days 6 and 14, mainly for evaluation of safety, which we believe led investigators in many cases to wait for the completion of these visits before discharging patients. 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.

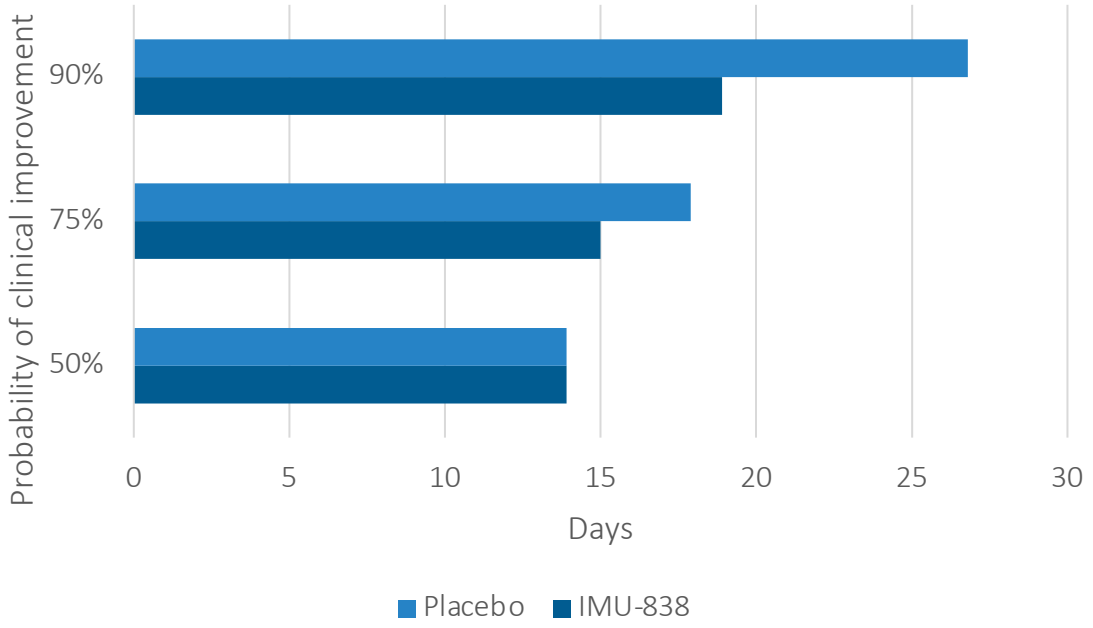
FAS: full analysis set (included all randomized patients that received at least 1 dose of study drug (n=99 for IMU-838, n=103 for Placebo). This included patients with mandatory hospital stay for the entire 14-day treatment period in Bulgaria.

[1] The third patient quartile means that 75% of patients have a shorter hospitalization duration and 25% have a longer duration of hospitalization.

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).

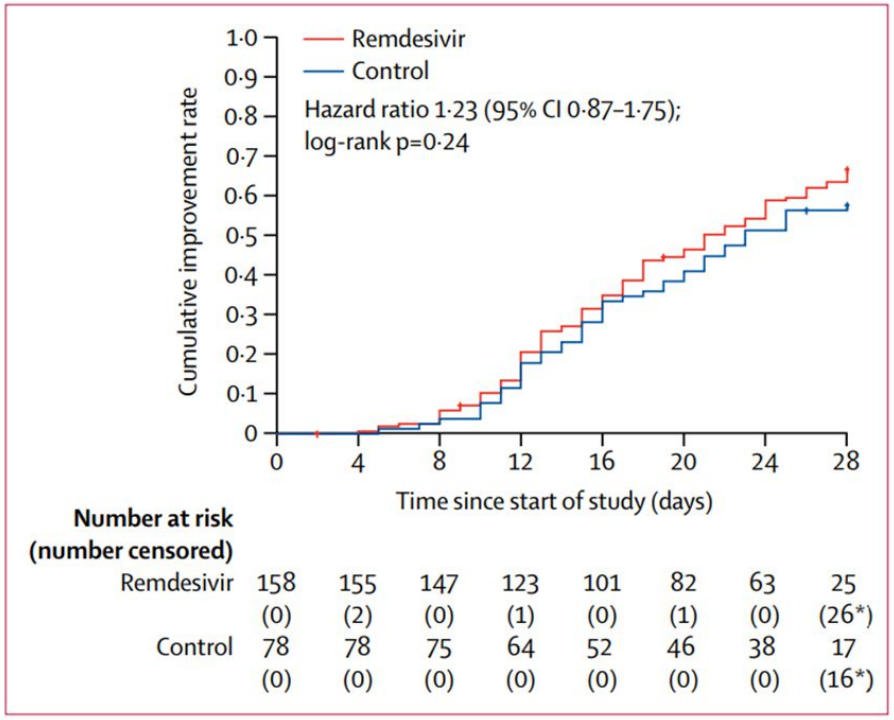
[1] Modified full analysis (mFAS) set (n=61 for IMU-838, n=69 for Placebo): In centers in Bulgaria, as per request by the regulatory agency, patients must be hospitalized during the entire treatment period until Day 14. Thus, these patients are excluded from this analysis, as the derived WHO status includes 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.

Immunic THERAPEUTICS

Time to Clinical Improvement

Results of Other Medications Tested in COVID-19

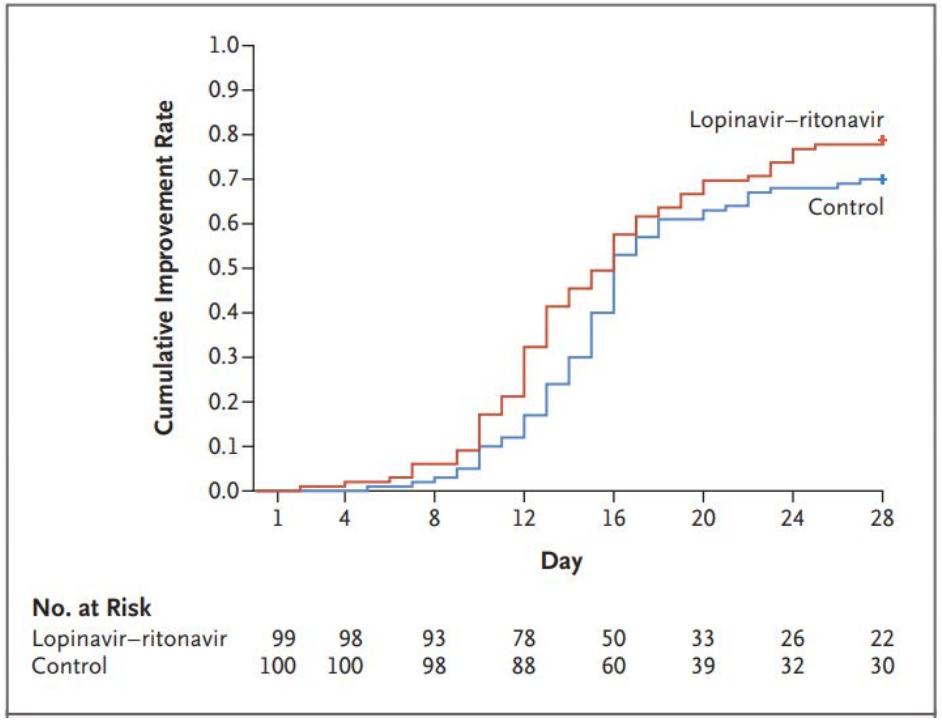
Remdesivir[1]



Number at risk (number censored)								
Remdesivir	158	155	147	123	101	82	63	25
	(0)	(2)	(0)	(1)	(0)	(1)	(0)	(26*)
Control	78	78	75	64	52	46	38	17
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(16*)

Remdesivir group (n=158)	Placebo group (n=78)	Difference*
21·0 (13·0 to 28·0)	23·0 (15·0 to 28·0)	1·23 (0·87 to 1·75)†

Lopinavir–Ritonavir[2]



No. at Risk								
Lopinavir–ritonavir	99	98	93	78	50	33	26	22
Control	100	100	98	88	60	39	32	30

Lopinavir–Ritonavir (N=99)	Standard Care (N=100)	Difference†
16.0 (13.0 to 17.0)	16.0 (15.0 to 18.0)	1.31 (0.95 to 1.80)

[1] Wang Y, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet. 2020 May 16;395(10236):1569-1578

[2] Cao B, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med. 2020 May 7;382(19):1787-1799

Immunic THERAPEUTICS

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

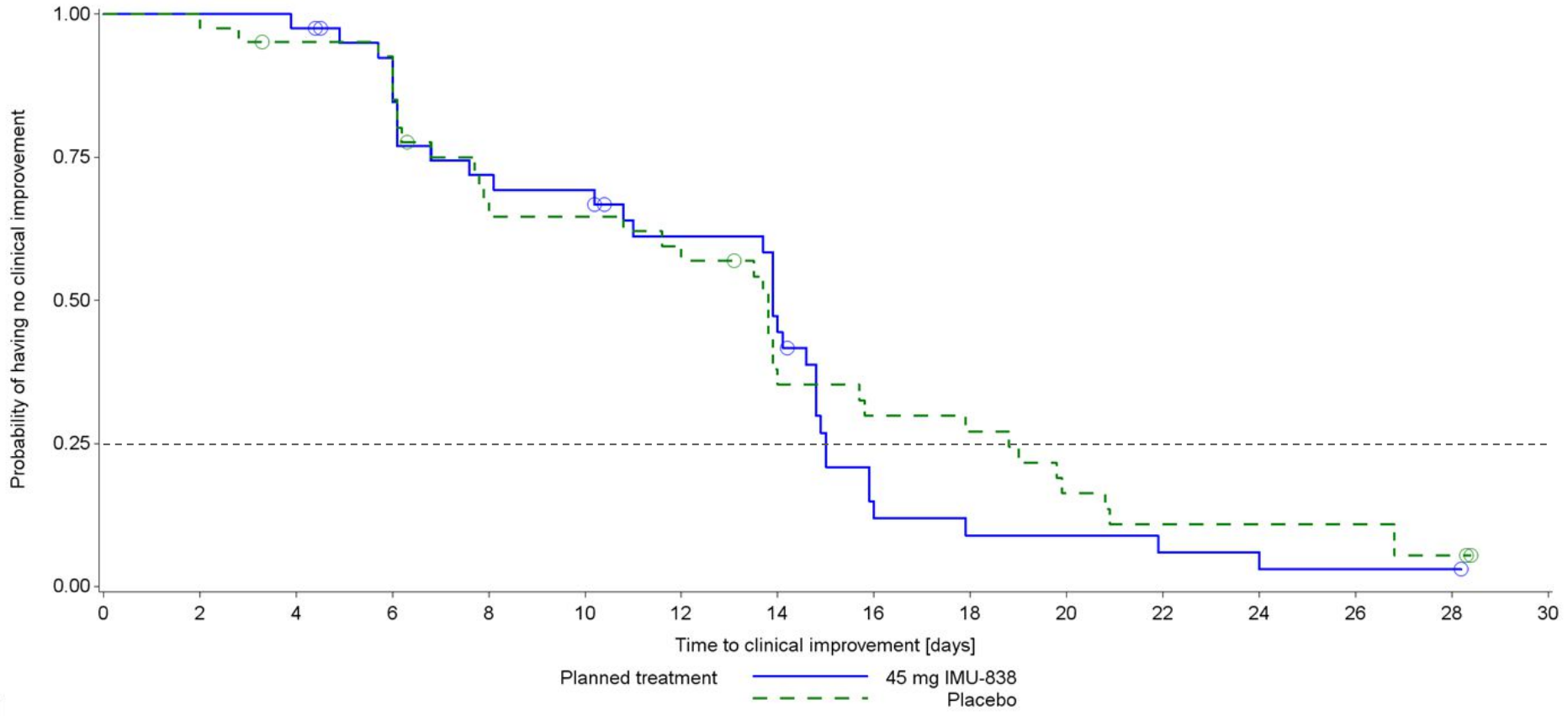
[1] High-risk factors are age ≥65 years, cardiovascular disease (including hypertension), pre-existing pulmonary disease, diabetes, malignancy, medical conditions leading to immunodeficiency, current or recent (within three months) immunosuppressive treatment.

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.

Immunic THERAPEUTICS

Time to Clinical Improvement

Kaplan Meier Assessment of High-Risk Population



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
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). This is a post hoc analysis not pre-specified in the statistical analysis plan.

Immunic THERAPEUTICS

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).

Immunic THERAPEUTICS

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.

Immunic THERAPEUTICS

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..

Immunic THERAPEUTICS

Proportion of Patients with Clinical Improvement

Results of Other Medications Tested in COVID-19 Patients

Remdesivir[1]

Clinical improvement rates	Remdesivir group (n=158)	Placebo group (n=78)
Day 7	4 (3%)	2 (3%)
Day 14	42 (27%)	18 (23%)
Day 28	103 (65%)	45 (58%)

Lopinavir–Ritonavir[2]

Clinical improvement — no. (%)	Lopinavir–Ritonavir (N=99)	Standard Care (N=100)
Day 7	6 (6.1)	2 (2.0)
Day 14	45 (45.5)	30 (30.0)
Day 28	78 (78.8)	70 (70.0)

[1] Wang Y, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet. 2020 May 16;395(10236):1569-1578
[2] Cao B, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med. 2020 May 7;382(19):1787-1799

Immunic THERAPEUTICS

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

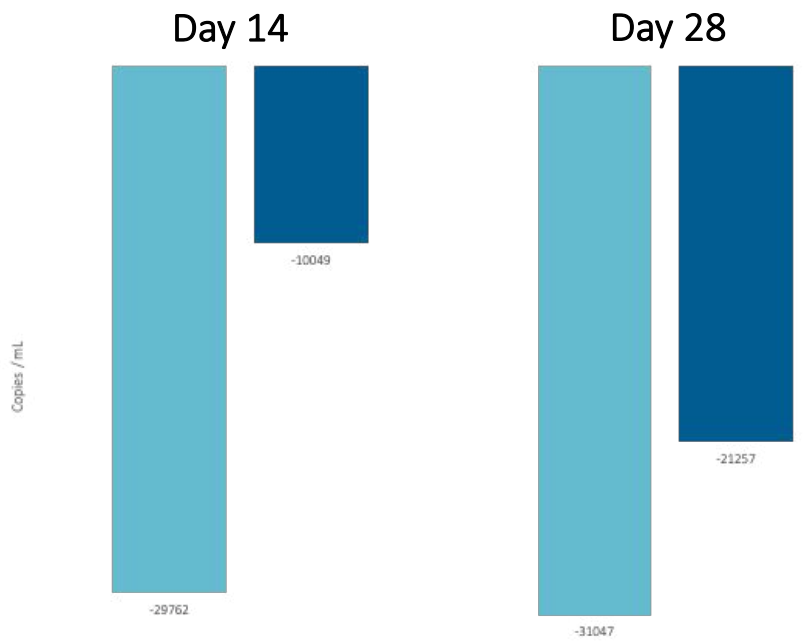
The advantage of IMU-838 regarding time to clinical improvement versus placebo does not differ between no combination and combination therapy with direct antivirals.

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

Immunic THERAPEUTICS

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)



Placebo

IMU-838

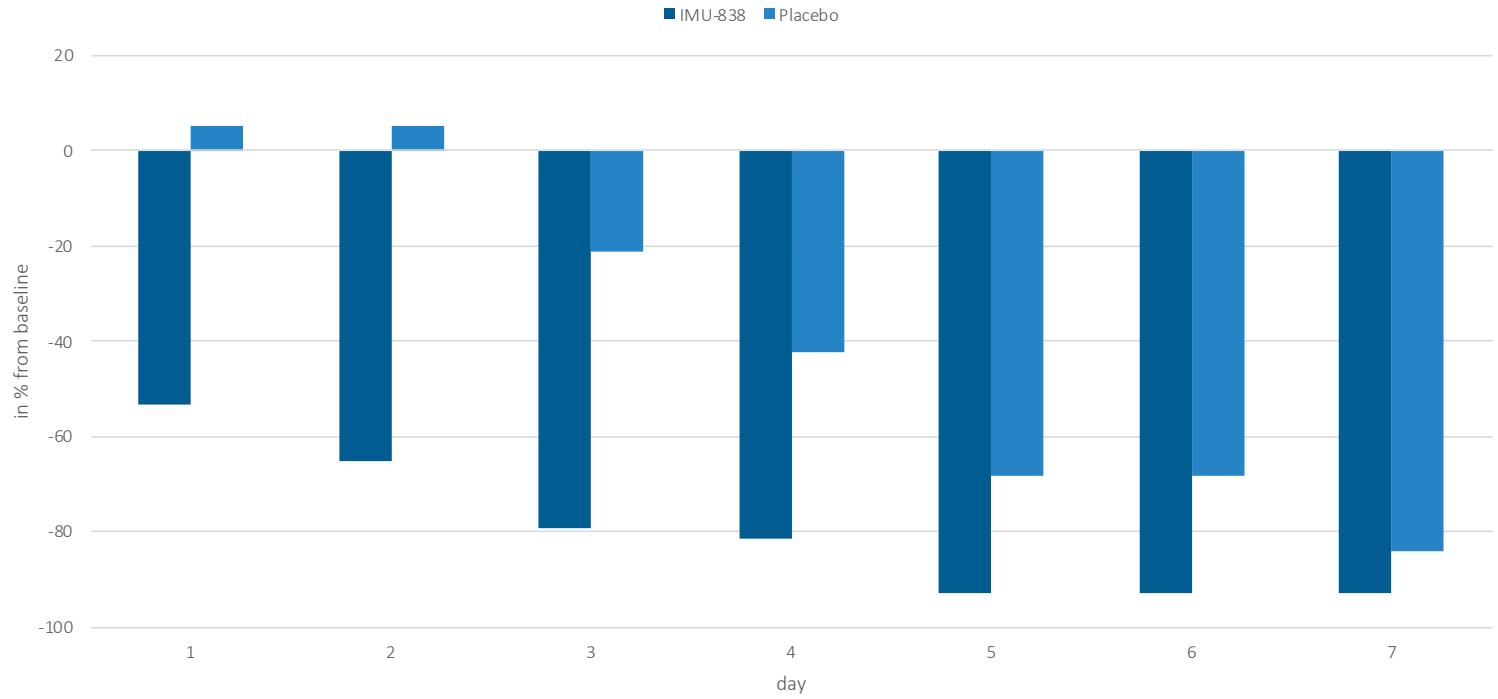
An anti-viral effect of IMU-838 on SARS-CoV-2 was observed as represented by viral titers at the end of the treatment period and at the end of the study.

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.

Immunic THERAPEUTICS

Decrease of C-Reactive Protein (CRP)

Systemic Inflammation Marker Strongly Associated with Patient Outcomes*



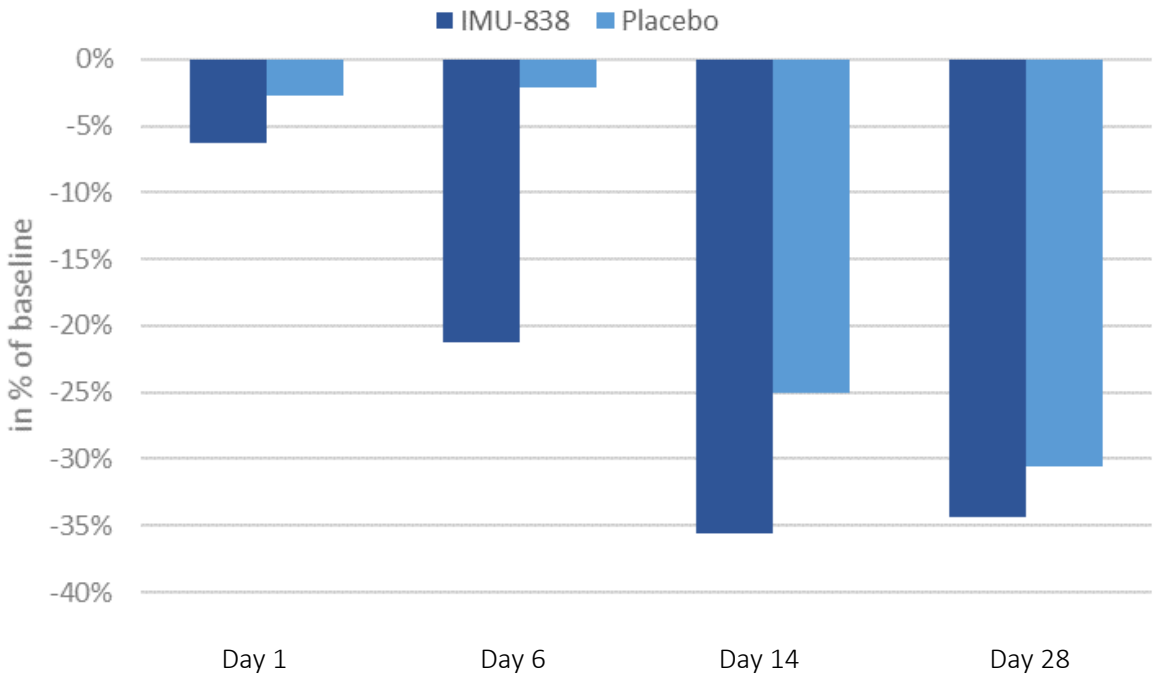
An anti-inflammatory effect of IMU-838 was observed, based on a more effective reduction of C-reactive protein (CRP), a well-known marker for systemic inflammation in the blood, in IMU-838 treated patients, as compared to placebo.

*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

Immunic THERAPEUTICS

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.

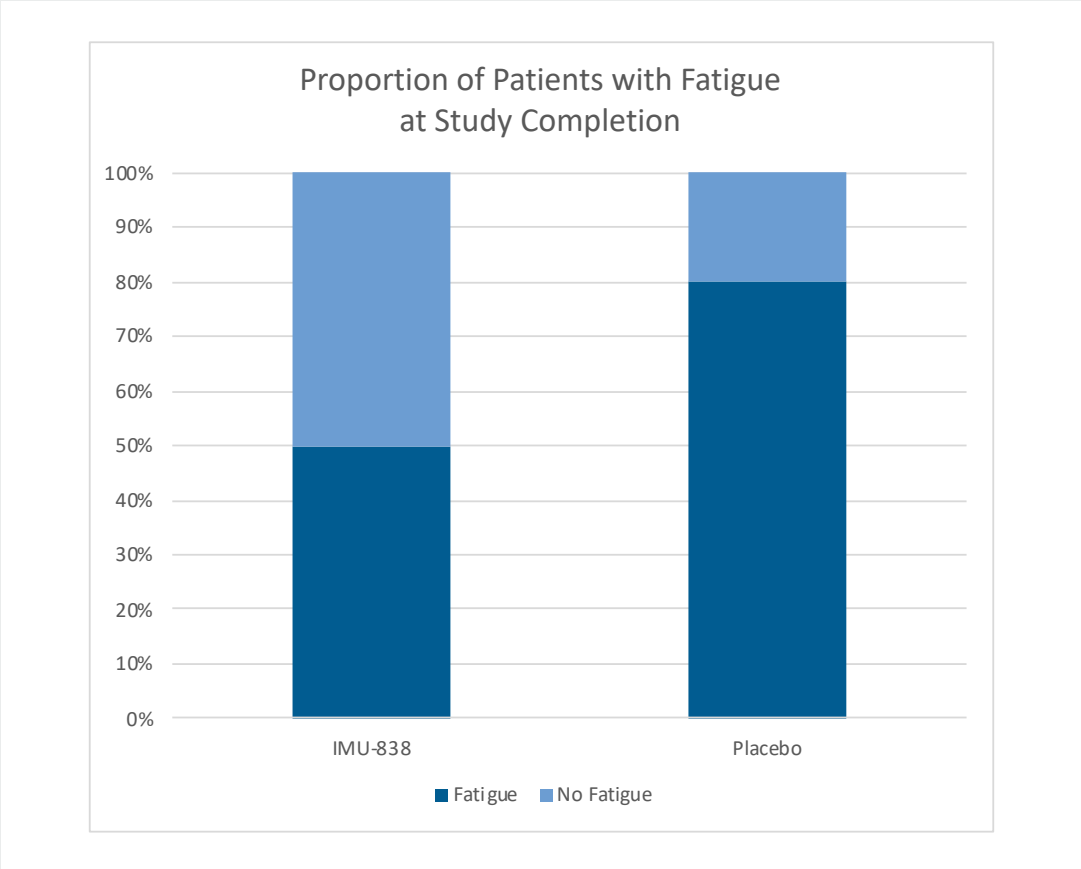
*D-dimer is commonly elevated in patients with COVID-19. D-dimer levels correlate with disease severity and are a reliable prognostic marker for in-hospital mortality in patients admitted for COVID-19. (Yao et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case 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

Immunic THERAPEUTICS

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).

Immunic THERAPEUTICS

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

Immunic THERAPEUTICS

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

Immunic THERAPEUTICS

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

Immunic THERAPEUTICS

Summary of Hematologic Adverse Events

IMU-838 Did Not Intensify Any Hematological Effects, 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 (%)
Blood and Lymphatic System Disorders	Anaemia	4	4	4.0	6	6	5.8	10	10	5.0
	Anaemia Macrocytic	0	0	0	1	1	1.0	1	1	0.5
	Iron Deficiency Anaemia	0	0	0	1	1	1.0	1	1	0.5
	Leukocytosis	4	4	4.0	2	2	1.9	6	6	3.0
	Leukopenia	1	1	1.0	2	2	1.9	3	3	1.5
	Lymphopenia	2	2	2.0	1	1	1.0	3	3	1.5
	Neutropenia	1	1	1.0	3	3	2.9	4	4	2.0
	Neutrophilia	5	4	4.0	3	3	2.9	8	7	3.5
	Normocytic Anaemia	1	1	1.0	0	0	0	1	1	0.5
	Secondary Thrombocytosis	1	1	1.0	1	1	1.0	2	2	1.0
	Thrombocytopenia	2	2	2.0	1	1	1.0	3	3	1.5
	Thrombocytosis	6	6	6.1	8	8	7.8	14	14	6.9
	Total	**27**	**14**	**14.1**	**29**	**17**	**16.5**	**56**	**31**	**15.3**

Treatment-emergent adverse events of System Organ Class blood and lymphatic system. Safety analysis set (n=99 for IMU-838, n=103 for Placebo)
AE: adverse event
Adverse events as coded by MedDRA version 23.0

Immunic THERAPEUTICS

Summary of Adverse Events of Infections

IMU-838 Did Not Increase the Rate of Infections and Infestations, 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 (%)
Infections and Infestations	Ascariasis	0	0	0	1	1	1.0	1	1	0.5
	Bacterial Disease Carrier	4	2	2.0	0	0	0	4	2	1.0
	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
	Candida Infection	1	1	1.0	1	1	1.0	2	2	1.0
	Clostridium Difficile Colitis	1	1	1.0	2	2	1.9	3	3	1.5
	Conjunctivitis	1	1	1.0	0	0	0	1	1	0.5
	Encephalitis Viral	0	0	0	1	1	1.0	1	1	0.5
	Giardiasis	0	0	0	1	1	1.0	1	1	0.5
	Oral Candidiasis	1	1	1.0	1	1	1.0	2	2	1.0
	Oropharyngeal Candidiasis	0	0	0	1	1	1.0	1	1	0.5
	Pharyngitis	1	1	1.0	0	0	0	1	1	0.5
	Pneumonia Chlamydial	3	3	3.0	1	1	1.0	4	4	2.0
	Pneumonia Moraxella	0	0	0	1	1	1.0	1	1	0.5
	Pneumonia Mycoplasmal	3	3	3.0	1	1	1.0	4	4	2.0
	Q Fever	0	0	0	1	1	1.0	1	1	0.5
	Staphylococcal Sepsis	0	0	0	1	1	1.0	1	1	0.5
	Toxocariasis	0	0	0	1	1	1.0	1	1	0.5
	Urinary Tract Infection	4	4	4.0	4	4	3.9	8	8	4.0
	Viral Infection	1	1	1.0	0	0	0	1	1	0.5
	Total	**24**	**17**	**17.2**	**23**	**16**	**15.5**	**47**	**33**	**16.3**

Treatment-emergent adverse events of System Organ Class infections and infestations. Safety analysis set (n=99 for IMU-838, n=103 for Placebo)
AE: adverse event
Adverse events as coded by MedDRA version 23.0

Immunic THERAPEUTICS

Summary of Hematologic Adverse Events

IMU-838 Did Not Increase the Rate of Liver Events, 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 (%)
Hepatobiliary Disorders	Cholestasis	1	1	1.0	0	0	0	1	1	0.5
	Drug-Induced Liver Injury	1	1	1.0	0	0	0	1	1	0.5
	Hepatic Steatosis	0	0	0	1	1	1.0	1	1	0.5
	Hepatitis	2	2	2.0	3	3	2.9	5	5	2.5
	Hepatitis Toxic	3	3	3.0	3	3	2.9	6	6	3.0
	Hepatocellular Injury	4	3	3.0	7	7	6.8	11	10	5.0
	Total	**11**	**10**	**10.1**	**14**	**14**	**13.6**	**25**	**24**	**11.9**

Treatment-emergent adverse events of System Organ Class hepatobiliary disorders. Safety analysis set (n=99 for IMU-838, n=103 for Placebo)
AE: adverse event
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

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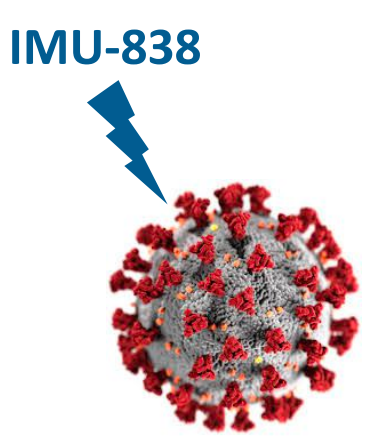
CALVID-1 Trial of IMU-838 in Moderate COVID-19

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**



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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Thank You!

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