- Clinical Activity of IMU-838 Confirmed Based on Multiple Secondary Endpoints, Including Clinically Meaningful Improvements in Time to Clinical Recovery and Clinical Improvement -

- Primary and Key Secondary Endpoints Were Not Evaluable Due to the Very Low Rates of Serious Complications in the Population of Hospitalized Patients With Moderate COVID-19 -

- High-Risk Patients and Patients Aged Over 65 Years Experienced a More Substantial Treatment Effect of IMU-838 -

- Robust Anti-Inflammatory Effect Observed, Based on a More Effective Reduction of C-Reactive Protein (CRP) in IMU-838 Treated Patients, as Compared to Placebo -

- Initial Data From a Post Hoc Analysis of "Long COVID" Symptoms Indicates That IMU-838 May Have the Potential to Contribute to the Prevention of Long-Term Fatigue -

- Conference Call and Webcast to be Held on February 18, 2021 at 8:00am ET -

NEW YORK, Feb. 17, 2021 /PRNewswire/ -- **Immunic, Inc.** (Nasdaq: IMUX), a clinical-stage biopharmaceutical company developing a pipeline of selective oral immunology therapies aimed at treating chronic inflammatory and autoimmune diseases, today announced that its lead asset, IMU-838, the company's selective oral DHODH inhibitor, has shown evidence of clinical activity in hospitalized patients with moderate coronavirus disease 2019 (COVID-19). This planned main analysis of the company's phase 2 CALVID-1 trial is based on data from 204 randomized patients and includes top-line clinical efficacy, safety, disease marker, and virology data. Although no formal statistical analysis was pre-specified for this main analysis, endpoints have been analyzed descriptively. A final analysis of the complete randomized patient population of 223, which will comprise data on all endpoints, including subgroup and sensitivity analyses, is expected to be available in the second quarter of 2021.

The primary endpoint of the randomized, placebo-controlled, double-blind trial was defined as the proportion of patients without any need for invasive ventilation through day 28. In contrast to the relatively high rates of ventilation reported in the first COVID-19 wave in early 2020, the CALVID-1 trial found an actual rate of less than 1% of invasive ventilation for hospitalized patients with moderate COVID-19. This very low event rate, consistent with the findings of many recent third-party trials in COVID-19, prevented the primary endpoint from being evaluable.

Regarding the key secondary endpoints, the trial was 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, and probability of use of intensive care unit (ICU) treatment. Similar to the low ventilation rates discussed above, the trial found a rate of less than 2% for 28-day mortality, balanced between the two arms, and less than 4.5% of patients required an ICU stay. Based on the very 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.

Despite the low mortality and invasive ventilation rates observed in this trial, clinical activity of IMU-838 was confirmed based on the assessment of multiple secondary clinical endpoints:

Time to clinical recovery[1]: The proportion of patients reaching clinical recovery at day 7 was 18.5% (N=15) in IMU-838 treated patients, compared with only 12.8% (N=10) in the placebo arm. At day 28, 71.3% (N=57) of the IMU-838 treated patients had recovered compared with only 66.7% (N=58) in the placebo arm (FAS[2]).

Time to clinical improvement[3]: Time to clinical improvement was found to beshorter in the IMU-838 treatment arm, as compared to placebo, and the incremental benefit increased over time (mFAS[4]).

- The proportion of patients reaching clinical improvement (as assessed by the investigators) at day 14 was 42.7% (N=38) in IMU-838 treated patients compared with only 38.5% (N=35) in the placebo arm (FAS). At day 28, the numbers were 90.9% (N=90) and 87.4% (N=90), respectively. The relative proportion of patients not improving was 6.8% greater in the placebo arm than the IMU-838 treatment arm at 14 days, and 27.7% greater at 28 days.
- Following day 14[5], patients treated with IMU-838 experienced a numerically higher probability of clinical improvement (centrally calculated) compared with those on placebo. For instance, the 75% probability[5] to reach clinical improvement was accelerated by 2.9 days in IMU-838 treated patients, as compared to placebo (mFAS).

- The third patient quartile[5] for duration of hospitalization (75% of patients have a shorter hospitalization duration and 25% have a longer duration of hospitalization) was shortened by 3.4 days in IMU-838 treated patients, as compared to placebo (mFAS). Meanwhile, Immunic believes that trial design issues and regulatory requirements may obscure any potential differences in the median (50^{th} percentile) itself[5].
- Clinical improvement (centrally calculated) was 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).
- Initial data from a post hoc analysis of what is called "Long COVID" symptoms, the frequently remaining symptoms of COVID-19 after elimination of the virus, indicated that IMU-838 may have the potential to contribute to the prevention of long-term fatigue.

	mFAS Population[4] (Days)		
Probability of Clinical Improvement *(Centrally Calculated)*	IMU-838	Placebo	**Difference in Favor of IMU-838**
50%	13.9	13.9	**0.0**
75%	15.0	17.9	**2.9**
90%	18.9	26.8	**7.9**

Table: IMU-838 Shows Acceleration of Time to Clinical Improvement

High-risk patients and patients aged over 65 years experienced a more substantial treatment benefit from IMU-838 than in the general patient population:

- The 75% probability[5] to reach clinical improvement (based on investigator assessment) was accelerated by 3.8 days in IMU-838 treated high-risk patients[6], as compared to placebo (FAS).
- The 75% probability[5] to reach clinical improvement (based on investigator assessment) was accelerated by 4.8 days in IMU-838 treated elderly patients (65 years or older), as compared to placebo (FAS).
- In the group of elderly patients (65 years or older), IMU-838 contributed to a faster improvement in WHO scores by at least two points, as compared to placebo (mFAS). At day 14, 36.4% (N=8/22) of the elderly patients reached a WHO score improvement by two points following treatment of IMU-838, whereas only 22.2% (N=4/18) of the elderly patients reached such improvement following placebo treatment at day 14.

Viral burden as well as biochemical inflammation and disease markers:

- 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 C-reactive protein (CRP), a well-known marker for inflammation in the blood, in IMU-838 treated patients, as compared to placebo.
- 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.

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 were observed for IMU-838 in this patient population, as compared to placebo. In addition, IMU-838's rate of serious adverse events and adverse events leading to treatment discontinuation was not increased, as compared to placebo. The trial also found fewer COVID-19 related adverse events with increased intensity in IMU-838 treated patients (7.1%), as compared to placebo (12.6%) and IMU-838 did not intensify any hematological effects of COVID-19. In addition, IMU-838 did not increase the rate of infections and infestations as well as the rate of liver events in patients with COVID-19, as compared to placebo.

"I am truly excited to report that our CALVID-1 trial showed clinical activity of IMU-838 in hospitalized patients with moderate COVID-19 and also reproduced in this patient population the drug's already established favorable safety and tolerability profile," stated **Daniel Vitt, Ph.D., Chief Executive Officer and President of Immunic**. "The reductions in hospitalization and clinical recovery times observed thus far in our CALVID-1 trial are clinically meaningful, and particularly interesting in the high-risk and elderly populations. In addition, we have seen effects on preventing long-term COVID-19 symptoms which suggest that IMU-838 could be a promising new therapeutic intervention that could provide meaningful clinical benefit. I strongly believe that this trial underlines the potential of IMU-838 to be a convenient, safe and well-tolerated oral treatment option for patients with moderate COVID-19 and may even pave the way for testing IMU-838 in earlier stage COVID-19 patients in the future. We look forward to analyzing the final data on the full 223 patient population, but we are also mindful of the rapidly changing COVID-19 landscape for decisions on future plans. In the meantime, we look forward to discussing the results of this main analysis as well as the upcoming full analysis with clinical and regulatory experts. In parallel, we plan to explore options for the further development of IMU-838 in this indication and for funding support."

"The Immunic team is forever indebted to the countless physicians, nurses, study coordinators and other healthcare

personnel who participated in this trial while, at the same, working under challenging conditions in this pandemic situation, in order to improve lives and outcomes for patients infected with the SARS-CoV-2 virus," added **Andreas Muehler, M.D., Chief Medical Officer of Immunic**. "With the help of our collaborators, we were able to show clinical activity of IMU-838 in COVID-19 patients and, consistent with prior data sets in other patient populations, administration of IMU-838 in this trial was observed to be safe and well-tolerated, thereby providing evidence of an attractive target profile for IMU-838 as a convenient oral treatment option in the moderate COVID-19 patient population. The treatment effect of IMU-838 versus placebo appears to be commensurate with that of other medications which were successfully tested in COVID-19. Based on these promising clinical data from the main analysis of our CALVID-1 trial, later also complemented by the more detailed efficacy and virology data from the full analysis of all randomized patients, we will evaluate the way forward for IMU-838 as a potential treatment option for COVID-19 patients."

A total of 204 patients were included in the main analysis of the CALVID-1 trial, as per the protocol requirement of approximately 200 patients. 202 patients received at least one dose of study drug, of whom 99 patients received 45 mg/day of IMU-838 and 103 patients received placebo. The main analysis contains top-line data for the treatment period until day 14 and the follow-up period until day 28 as well as the full safety data until day 28. Additional data will be reported after the full analysis of all 223 randomized patients, which is expected to be available in the second quarter of 2021. This supplemental data set will contain full efficacy, virology, and drug trough level data, as well as the safety follow-up until day 60.

The aim of the CALVID-1 trial was to investigate IMU-838 as an oral treatment option for COVID-19 and to support potential use of IMU-838 as a treatment for current and potential future viral pandemic threats. The prospective, multicenter, randomized, placebo-controlled, double-blind phase 2 trial was designed to evaluate efficacy, safety and tolerability of IMU-838 in patients with moderate COVID-19. Patients were enrolled at 20 sites in eleven countries, including the United States, Germany, and a range of other European countries. Patients were randomized to receive either 22.5 mg of IMU-838 twice daily (45 mg/day), or placebo twice daily, for 14 consecutive days. Patients in both arms were also eligible to receive investigator's choice of standard-of-care therapy throughout the duration of the study. Inclusion criteria called for hospitalized adult patients with a confirmed SARS-CoV-2 infection fulfilling clinical status category 3 or 4, as assessed with the nine-category ordinal scale proposed by the World Health Organization (WHO) COVID-19 Therapeutic Trial Synopsis, as well as certain additional clinical and laboratory criteria.

For more information on this clinical trial, please visit:www.clinicaltrials.gov, NCT04379271.

Conference Call and Webcast Information

Immunic's management team will host a public conference call and webcast onFebruary 18, 2021 at 8:00 a.m. Eastern Time to discuss the data from the main phase 2 analysis of the CALVID-1 trial of IMU-838 in hospitalized patients with moderate COVID-19.

To participate in the conference call, dial 1-877-870-4263 (USA) or 1-412-317-0790 (International) and ask to be joined into the Immunic, Inc. call. A live, listen-only webcast of the conference call can be accessed at https://www.webcaster4.com/Webcast/Page/2301/39950 or on the "Events and Presentations" section of Immunic's website at ir.imux.com/events-and-presentations.

An archived replay of conference call and webcast will be available approximately one hour after the completion for one year on Immunic's website at: ir.imux.com.

[1] Time to recovery is defined 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).
[2] FAS: full analysis set: Includes all patients randomized who received at least one dose of study drug (n=99 for IMU-838, n=103 for Placebo).
[3] Time to clinical improvement is defined as as an improvement of at least two points on the derived nine-category ordinal WHO scale, or live discharge from hospital without oxygen supplementation, whichever comes first.
[4] mFAS: modified full analysis set: Patients who had positive local virus tests during the screening period, but no positive confirmation was possible by centralized virology laboratory (presumably due to sampling and storage issues) at a later timepoint, were excluded because the virus status for the WHO score was not assessable. Thus, the mFAS analysis was used for endpoints (such as centrally calculated WHO scores) that included data from the central virology laboratory, whereas any endpoint that was independent from the central virology laboratory and used local virology results (such as WHO score based on investigator assessment) were analyzed in the FAS population. Additionally, for endpoints that included the variable hospitalization (such as time to clinical improvement), the mFAS population also excluded patients randomized in Bulgaria. The national regulatory agency required that all patients at Bulgarian centers be hospitalized during the entire 14-day treatment period. Because assessment of the WHO status includes hospitalization status, Bulgarian patients were excluded from centralized calculations of the WHO score. Immunic believes that this avoids the bias of mandatory hospitalization (see also footnote 5 below) independent of COVID-19 status. For endpoints that are independent of hospitalization duration or that are based on the investigator assessment of

need for hospitalization, the FAS population has been reported.

[5] Although the most common presentation of data generally focuses on the median, or 50th percentile, Immunic believes that the third quartile/75th percentile is more appropriate in this case. The median for the hospitalization time for both IMU-838 and placebo arms in this trial was 14.0 days in the FAS population, which is likely due to several factors relating to regulatory guidance and trial design. First, the Bulgarian regulatory agency required that all trial participants in that country be hospitalized for the entire 14-day treatment period of the trial, and not be discharged during that period independent of health or viral status. Second, 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. The study results show a large proportion of patients who discharged from hospital immediately after these two required visits. Such behavior has introduced an evaluation bias for all hospitalization-related endpoints, such as central calculation of time to clinical improvement where the hospitalization status is part of the calculated WHO score, and may have masked treatment-related differences between treatment groups up to day 14. To counteract this evaluation bias, all clinical endpoints relying on hospitalization status presented in this analysis focus on the third quartile data, which in statistical terms represents the 25% of patients group right after the median. For proportion of patients between treatment groups, this correlates to the 75% probability which is also presented here. Immunic believes that this provides the most unbiased assessment for clinical endpoints given the evaluation bias of hospitalization status.

[6] 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.

About IMU-838

IMU-838 is an orally available, next-generation selective immune modulator that inhibits the intracellular metabolism of activated immune cells by blocking the enzyme dihydroorotate dehydrogenase (DHODH). IMU-838 acts on activated T and B cells while leaving other immune cells largely unaffected and allows the immune system to stay functioning, e.g. in fighting infections. In previous trials, IMU-838 did not show an increased rate of infections compared to placebo. In addition, DHODH inhibitors, such as IMU-838, are known to possess a host-based antiviral effect, which is independent with respect to specific virus proteins and their structure. Therefore, DHODH inhibition may be broadly applicable against multiple viruses. IMU-838 was successfully tested in two phase 1 clinical trials in 2017 and is currently being tested in a phase 2 trial in patients with ulcerative colitis. In the third quarter of 2020, the company reported positive results from its phase 2 EMPhASIS trial of IMU-838 in relapsing-remitting multiple sclerosis, achieving both primary and key secondary endpoints with high statistical significance. In the first quarter of 2021, Immunic announced that IMU-838 has shown evidence of clinical activity in its phase 2 CALVID-1 trial in hospitalized patients with moderate COVID-19. Furthermore, Immunic's collaboration partner, the Mayo Clinic, has started an investigator-sponsored proof-of-concept clinical trial testing IMU-838 activity in patients with primary sclerosing cholangitis. To date, IMU-838 has been tested in about 800 individuals and has shown an attractive pharmacokinetic, safety and tolerability profile. IMU-838 is not yet licensed or approved in any country.

About Immunic, Inc.

Immunic, Inc. (Nasdaq: IMUX) is a clinical-stage biopharmaceutical company with a pipeline of selective oral immunology therapies aimed at treating chronic inflammatory and autoimmune diseases, including relapsing-remitting multiple sclerosis, ulcerative colitis, Crohn's disease, and psoriasis. Immunic is developing three small molecule products: its lead development program, IMU-838, is a selective immune modulator that inhibits the intracellular metabolism of activated immune cells by blocking the enzyme DHODH and exhibits a host-based broad-spectrum antiviral effect; IMU-935 is an inverse agonist of RORγt; and IMU-856 targets the restoration of the intestinal barrier function. For further information, please visit: www.imux.com.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains "forward-looking statements" that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this press release regarding strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives of management are forward-looking statements. Examples of such statements include, but are not limited to, statements relating to Immunic's three development programs and the targeted diseases; the potential for IMU-838 to safely and effectively target diseases; the timing of current and future clinical trials; the potential for IMU-838 as a treatment for SARS-CoV-2 infections associated with COVID-19 that may be supported by the company's phase 2 CALVID-1 trial data, and any clinical trials, collaborations and approvals relating to such potential treatment; the nature, strategy and focus of the company; and the development and commercial potential of any product candidates of the company. Immunic may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in the forward-looking statements and you should not place undue reliance on these forward-looking statements. Such statements are based on management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation, the COVID-19 pandemic, risks and uncertainties associated with the ability to project future cash utilization and reserves needed for contingent future liabilities and business operations, the availability of sufficient resources to meet business objectives and operational requirements, the

fact that the results of earlier studies and trials may not be predictive of future clinical trial results, the protection and market exclusivity provided by Immunic's intellectual property, risks related to the drug development and the regulatory approval process and the impact of competitive products and technological changes. A further list and descriptions of these risks, uncertainties and other factors can be found in the section captioned "Risk Factors," in the company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC onMarch 16, 2020, the company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed with the SEC onNovember 6, 2020, and in the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov or ir.imux.com/sec-filings. Any forward-looking statement made in this release speaks only as of the date of this release. Immunic disclaims any intent or obligation to update these forward-looking statements to reflect events or circumstances that exist after the date on which they were made. Immunic expressly disclaims all liability in respect to actions taken or not taken based on any or all the contents of this press release.

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