Immunic, Inc. Announces Positive Top-Line Data From Investigator-Sponsored Phase 2 Proof-of-Concept Clinical Trial of IMU-838 in Primary Sclerosing Cholangitis

– Statistically Significant Decrease in Serum Alkaline Phosphatase (ALP) Levels in the Per-Protocol Population After 24-Week IMU-838 Treatment, as Compared to Baseline –

– Primary Objective of Therapeutic Benefit Achieved in 27.3% of the Patients of the Per-Protocol Population at Week 24 –

– Other Liver Biochemistry Parameters Remained Stable –

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

– Study Conducted in Collaboration with Investigators at Mayo Clinic in Arizona and Minnesota –

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

NEW YORK, February 18, 2021 – 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 positive top-line data from an investigator-sponsored phase 2 proof-of-concept clinical trial of IMU-838 in primary sclerosing cholangitis (PSC). This single-arm, open-label, exploratory study was designed to investigate IMU-838's potential to improve various biochemical parameters in PSC patients and help determine whether any such activity warrants further investigation in randomized PSC trials. As previously announced, due to the COVID-19 pandemic, only 18 of the targeted 30 patients were enrolled in the study (intent-to-treat population, ITT), of whom only 11 patients completed the full IMU-838 treatment course and were evaluable over the 24-week treatment period (per-protocol population, PP).

The PP population experienced a statistically significant decrease in serum alkaline phosphatase (ALP) levels (p=0.041) after 24 weeks of treatment using 30 mg IMU-838 once daily, as compared to baseline. A consistent individual pattern of a stable decrease in ALP values was observed in the PP population between baseline and week 24, without any single patient showing an increase of more than 20% of ALP. As per the definition of the primary objective of the study, 27.3% of the patients in the PP population had a clinically relevant reduction of serum ALP higher than 25% at week 24, without an increase in liver biochemistry of more than 33%, as compared to baseline. Biochemical endpoints, such as changes in serum ALP, have been used in PSC trials performed by third parties.

Regarding the secondary objectives of the study, no changes in aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total, direct or indirect bilirubin were observed in the ITT or PP populations, as compared to baseline. In addition, despite the limited scope of the data, encouraging results were

observed regarding symptoms of inflammatory bowel disease, a common comorbidity for PSC patients, and patient assessments of health-related quality of life. The study also found that IMU-838 is a safe and well-tolerated oral drug for PSC patients and treatment-emergent adverse events were rare and generally mild.

"I am very excited about the effects we have seen in this highly underserved patient population where there is only a small number of cases worldwide and where no pharmaceutical treatment option is currently available," noted **Daniel Vitt, Ph.D., Chief Executive Officer and President of Immunic**. "We are also very pleased to see that IMU-838's safety and tolerability profile was confirmed in this patient group. The results from this small, open-label study suggest that IMU-838 merits further clinical testing in PSC. We are in discussions with investigators and leading clinical experts to further evaluate the data set and to explore potential next steps for this indication."

"Currently, no effective treatment options are available for PSC patients and the hepatology community is very keen to see new approaches and clinical programs for the investigation of promising new approaches. I am grateful that Mayo Clinic and Immunic are collaboratively exploring this underserved indication for which liver transplantation is often the only effective option," stated **Keith Lindor, M.D., Professor of Medicine Emeritus and former President of the American Association for the Study of Liver Diseases**. "Although we are mindful of the small size of this dataset, I do believe the results are noteworthy and merit further exploration. Notable in this small patient cohort is the absolute consistency with which these patients experienced decreases in serum alkaline phosphatase at the 24-week time point."

Study Background and Baseline Characteristics

The single-arm, open label, exploratory study was an investigator-sponsored trial led by Elizabeth Carey, M.D., Professor of Medicine, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Mayo Clinic, who had received Investigator Investigational New Drug (IND) approval from the U.S. Food & Drug Administration (FDA) and had been granted Institutional Review Board (IRB) approval to conduct the study. The study was supported by a grant from the National Institutes of Health (NIH) and was conducted at two sites: Mayo Clinic, Phoenix, Arizona (Dr. Carey) and Mayo Clinic, Rochester, Minnesota (John E. Eaton, M.D.), both of which are tertiary referral centers for PSC patients.

The study, for which Immunic provided the study medication, planned to enroll 30 patients with PSC, aged 18 to 75 years, who received 30 mg of IMU-838 once daily for a period of 24 weeks. Enrollment for the study took place between July 2019 and September 2020, but almost all enrollment occurred in 2019 and early 2020. 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. Together with the investigators, Immunic determined to readout data of the 18 patients who were enrolled prior to the COVID-19 pandemic. The ongoing COVID-19 pandemic also triggered the principal investigator's decision to terminate the study in late 2020, before the intended recruitment goal of 30 patients was reached.

A total of 18 patients started treatment of 30 mg IMU-838 once daily (intent-to-treat population, ITT, n=18). Of these 18 patients, 11 patients received the full 24-week treatment with IMU-838 (per-protocol population, PP, n=11). Due to the high number of discontinued patients during the COVID-19 pandemic and the fact that all discontinued patients in an ITT statistical analysis will be counted as treatment failures at week 24, this analysis focuses mainly on the 11-patient PP population.

Primary Objective

The primary objective of this study was to determine whether IMU-838 reduces serum ALP in adult patients diagnosed with PSC. The main analysis for the primary objective was whether patients could achieve a reduction of ALP at week 24 which is 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. This positive primary outcome was achieved by 3 of 11 patients in the PP population (27.3%, 95% CI: 6-61%). By virtue of inclusion criteria, patients at baseline had to have an elevated ALP value of at least 1.5 times upper limit of normal (ULN).

In addition, time from baseline was calculated as a continuous variable and treated as the primary predictor using a random intercept model which was adjusted for age at baseline and gender. For this longitudinal analysis of ALP from baseline to week 24 in the PP population, the 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). The time trend was not statistically significant in the ITT analysis (p=0.578) due to missing data following the high rate of treatment discontinuations during the COVID-19 pandemic.

Secondary Objectives

Secondary objectives were to investigate the liver biochemistry parameters, AST, ALT, and total/direct/indirect bilirubin, as well as the concentrations of proinflammatory cytokines, as compared to baseline. The longitudinal analysis of both AST and ALT as well as total, direct and indirect bilirubin values showed a stable pattern in the PP population with no statistically significant change over time and the confidence interval to include the no-change scenario (AST: average 30 day change 1.22 IU/L, 95% CI: -0.53, 2.97, p=0.170; ALT: average 30 day change 0.85 IU/L, 95% CI -1.46, 3.15, p=0.467, total bilirubin: average 30 day change 0.00 mg/dL, 95% CI -0.01, 0.02, p=0.561, direct bilirubin: average 30 day change 0.00 mg/dL, 95% CI -0.01, 0.01, p=0.861, indirect bilirubin: average 30 day change 0.00 mg/dL, 95% CI -0.01, 0.01, p=0.556). Similar results were found in the ITT population. In addition, a decrease in the Ulcerative Colitis Clinical score was observed in evaluated patients, although the number of assessed patients was limited.

“This was a feasibility study to explore activity of IMU-838 in PSC patients based on biochemical parameters. IMU-838 was found to lead to a statistically significant reduction of serum ALP over time in the PP population, while no trend for increases in ALT, AST or bilirubin was observed,” commented **Andreas Muehler, M.D., Chief Medical Officer of Immunic**. “Despite the challenges we faced due to COVID-19, which severely hindered the enrollment at the two Mayo Clinic sites and which led to an unusually high discontinuation rate and an early termination of the study, we have seen encouraging activity signals for IMU-838 in this patient population. Based on these promising data and, in particular, the improvement in biochemical liver parameters, we will continue to evaluate the potential of IMU-838

as a treatment option for PSC patients. It may also be worthwhile to optimize dose levels of IMU-838 in PSC patients in the future."

For more information on this clinical trial, please visit: www.clinicaltrials.gov, NCT03722576.

Conference Call and Webcast Information

As previously announced, Immunic's management team will host a public conference call and webcast today, February 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, as well as data from the investigator-sponsored phase 2 clinical trial of IMU-838 in primary sclerosing cholangitis.

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.

About Primary Sclerosing Cholangitis (PSC)

PSC is a rare liver disease with a prevalence of approximately 4.15 per 100,000 in the United States, in which the bile ducts in the liver become inflamed, narrow and prevent bile from flowing properly. The exact cause and disease mechanism of PSC are still unknown, but an autoimmune mechanism may play a role. There is an association with inflammatory bowel diseases, most often with ulcerative colitis and less commonly with Crohn's disease. PSC is a progressive disease and, other than liver transplantation, there are currently no approved therapies that have been shown to improve survival in patients with PSC. The estimated time from diagnosis of PSC to death or liver transplant has been shown to be less than 15 years.

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. Also, in the first quarter of 2021, the company reported positive top-line data from an investigator-sponsored phase 2 proof-of-concept clinical trial of IMU-838 in primary

sclerosing cholangitis which was conducted in collaboration with Mayo Clinic. To date, IMU-838 has been tested in more than 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 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 proof-of-concept study of IMU-838 for the treatment of patients with primary sclerosing cholangitis; the timing of current and future clinical trials; the potential for IMU-838 as a treatment for primary sclerosing cholangitis that may be supported by the investigator-sponsored phase 2 proof-of-concept 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 on March 16, 2020, the company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed with the SEC on November 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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