Immunic, Inc. InvestorRoom

– Trial Did Not Achieve Primary Endpoint in the Ulcerative Colitis (UC) Population Caused by Unexpected Interference Between Vidofludimus Calcium and Concurrent Use of Corticosteroids –

– In UC Population Without Concurrent Steroid Use, Pooled Vidofludimus Calcium Data Suggest Activity in Clinical Remission Over Placebo; Counterbalanced by Interference Observed in the UC Population with Concurrent Steroid Use –

– Company Does Not Plan Further Development Activities in Ulcerative Colitis Without a Partner –

– Focus to Remain on Ongoing Phase 3 Development of Vidofludimus Calcium in Multiple Sclerosis, and Ongoing IMU-935 and IMU-856 Programs with Clinical Data for Both Expected in 2022 –

– $93.1 Million in Cash and Cash Equivalents as of May 31, 2022 Expected to Fund Immunic Into the Fourth Quarter of 2023 –

– Conference Call and Webcast, Including a Corporate Update, to be Held today, June 2, 2022 at 8:00 am ET –

NEW YORK, June 2, 2022 /PRNewswire/ -- **Immunic, Inc. (Nasdaq: IMUX)**, a clinical-stage biopharmaceutical company developing a pipeline of selective oral immunology therapies focused on treating chronic inflammatory and autoimmune diseases, today reported top-line data from its phase 2 CALDOSE-1 trial of lead asset, vidofludimus calcium (IMU-838), the company's selective oral DHODH inhibitor, in patients with moderate-to-severe ulcerative colitis (UC) (clinicaltrials.gov: NCT03341962).

The trial did not achieve the primary endpoint of clinical remission for the pooled 30 and 45 mg/day active dose groups of vidofludimus calcium versus placebo at week 10. In addition, no meaningful differences were observed between the three active dose groups for the overall intent-to-treat patient population (10 mg/day: 14.9%, 30 mg/day: 10.6%, 45 mg/day: 13.6%, placebo: 12.5%) or for the trial's other secondary endpoints, including symptomatic remission, or endoscopic healing.

Consistent with prior data sets in other patient populations, administration of vidofludimus calcium in this trial was observed to be safe and well-tolerated. No new safety signals were observed. As compared to placebo, there were no increased rates of infections and infestations, no elevated rates of liver events or liver enzyme elevations, and no elevated rates for changes in hematology-related laboratory variables. The most common adverse events in this trial were anemia (15/263 patients, 5.7%), headache (9/263 patients, 3.4%) and COVID-19 (7/263 patients, 2.7%). Most adverse events were generally mild in severity.

As is common for the design of clinical trials in UC, the use of oral systemic corticosteroids (≤20 mg/day prednisolone equivalent) was allowed in CALDOSE-1 in patients who had been treated with corticosteroids for at least four weeks before randomization. Doses of corticosteroids were required to be kept constant throughout the induction phase (weaning was not allowed in this phase of the trial), and the distribution of patients using corticosteroids was equal throughout all treatment groups.

Surprisingly, CALDOSE-1 data suggest a previously unknown treatment interference between the efficacy of vidofludimus calcium and the concurrent use of corticosteroids in the UC patient population. More specifically, the non-steroid patient population showed an 11.4% advantage in clinical remission for vidofludimus calcium over placebo (pooled vidofludimus calcium treatment groups at week 10: 14.7%, placebo: 3.3%). Such a difference in clinical remission between active treatment and placebo would traditionally be considered as confirming therapeutic activity. In contrast, patients concomitantly taking vidofludimus calcium and corticosteroids during induction treatment had a lower rate of clinical remission at week 10 (11.5%) than placebo patients (20.6%) and also lower than the group of vidofludimus calcium monotherapy without concurrent use of steroids (14.7%). This treatment interference between vidofludimus calcium and corticosteroids was not expected by currently available preclinical or clinical data.

"We are disappointed with the results of the CALDOSE-1 trial. The interference of vidofludimus calcium with concurrent corticosteroid use is surprising, and we will further explore the mechanism behind this unexpected observation. We believe that this finding has no consequences for our ongoing program in multiple sclerosis as corticosteroids are not used chronically in this patient population," stated Andreas Muehler, M.D., Chief Medical Officer of Immunic. "We are also happy to see that, once again, the study data confirm the very favorable safety and tolerability profile of vidofludimus calcium observed in other trials. Importantly, we want to thank all of the investigators, study personnel, patients and caretakers involved in this trial for their participation and tremendous contributions."

"Putting the CALDOSE-1 data in context with the wealth of compelling opportunities we have across our clinical development portfolio, we do not intend to move forward with phase 3 development of vidofludimus calcium in UC on our own," commented Daniel Vitt, Ph.D., Chief Executive Officer and President of Immunic. "We will use this opportunity to focus our vidofludimus calcium-related efforts around the ongoing multiple sclerosis program, including the phase 3 trials in relapsing multiple sclerosis (RMS) and the phase 2 trial in progressive multiple sclerosis (PMS). As evidenced by data from our phase 2 EMPhASIS trial, we believe vidofludimus calcium holds the potential for meaningful differentiation based on anticipated strong efficacy, unprecedented safety and tolerability, oral delivery, and neuroprotective effects. We also eagerly await further clinical data for IMU-935 and IMU-856 later this year, including phase 1b data of IMU-935 in moderate-to-severe psoriasis patients in the second half, and phase 1 safety data of IMU-856 in healthy human subjects in the third quarter. Both of these investigational medicines hold tremendous potential in their intended indications and beyond. Despite our disappointment with the overall CALDOSE-1 data, the second half of 2022 remains an exciting time for Immunic, and we hope to share successful data in the near future."

Corporate Update

Vidofludimus Calcium in Multiple Sclerosis

With completion of analysis from the Cohort 2 dataset, final data for the phase 2 EMPhASIS trial of vidofludimus calcium in relapsing-remitting multiple sclerosis (RRMS) are available. In the final data set combining patients from both Cohort 1 (30 mg, 45 mg and placebo) and Cohort 2 (10 mg and placebo), placebo adjusted reductions in gadolinium-enhancing lesions at 24 weeks for the 10 mg, 30 mg, and 45 mg dose groups of vidofludimus calcium were 13%, 78%, and 74%, respectively. The company believes this data provides further corroboration for the selection of the 30 mg dose for the ongoing phase 3 program in RMS.

In addition, the final data also provide evidence of dose-proportional neuroprotective activity. For instance, the baseline adjusted decreases in the biomarker serum neurofilament light chain (NfL) at 24 weeks for the 10 mg, 30 mg, and 45 mg dose groups of vidofludimus calcium were 9%, 18%, and 26%, respectively, as compared to placebo. The company believes this observation suggests that higher doses, such as 45 mg vidofludimus calcium, may be preferrable in indications where neuroprotective effects are most important, such as in PMS.

Patient enrollment in both the phase 3 ENSURE program of vidofludimus calcium in patients with RMS and the phase 2 CALLIPER trial of vidofludimus calcium in patients with PMS remain ongoing.

IMU-935 in Psoriasis

The phase 1b clinical trial of IMU-935, the company's highly potent and selective oral IL-17 inhibitor, is ongoing in patients with moderate-to-severe psoriasis. This week, the company received regulatory approval to proceed with the trial in Europe, which should expedite enrollment of the high dose cohort, which is currently being started. Initial results from the psoriasis portion of the phase 1 clinical trial are targeted for the second half of 2022.

IMU-856 in Healthy Human Subjects and Celiac Disease

The company continues to expect a third quarter 2022 release of data from both the single and multiple ascending dose parts of the ongoing phase 1 clinical trial of IMU-856, an orally available and systemically acting small molecule shown preclinically to regulate intestinal barrier function and regenerate bowel epithelium. Recently, Immunic also started the third part of this phase 1 clinical trial in patients with celiac disease, which is currently ongoing.

Cash and Cash Runway

Cash and cash equivalents as of May 31, 2022 were $93.1 million. The company expects to have funding into the fourth quarter of 2023.

Webcast Information
Immunic will host a webcast today at 8:00 am ET. To participate in the webcast, please register in advance at: https://imux.zoom.us/webinar/register/WN_XgdotnImTHKxQiLFa958mA or on the "Events and Presentations" section of Immunic's website at: ir.imux.com/events-and-presentations. Registrants will receive a confirmation email containing a link for online participation or a telephone number for dial in access.

An archived replay of the webcast will be available approximately one hour after completion on Immunic's

website at: ir.imux.com/events-and-presentations.

About the CALDOSE-1 Trial
The phase 2 CALDOSE-1 trial was a multicenter, randomized, double-blind, placebo-controlled, dose-finding study which included 263 UC patients from 78 study sites in the United States, Western, Central and Eastern Europe. The trial was designed to evaluate the efficacy and safety of vidofludimus calcium in patients with moderate-to-severe UC. The primary endpoint comprised a composite of a patient-reported outcome and endoscopy-assessed outcome, also referred to as clinical remission, both evaluated following ten weeks of induction treatment. Patients were randomized into four arms: three active dosing arms of 10 mg, 30 mg and 45 mg of vidofludimus calcium, as well as placebo.

CALDOSE-1 was the first trial of vidofludimus calcium that allowed chronic co-medication with corticosteroids. Explanation for the observed interference is not yet available and this finding was not predicted based on any prior preclinical or clinical data. The company does intend to explore this potential topic scientifically. In the meantime, the company plans to only develop vidofludimus calcium in indications, such as multiple sclerosis, where chronic corticosteroid administration does not play a role in routine treatment.

About Vidofludimus Calcium (IMU-838)
Vidofludimus calcium is an investigational drug in development as an orally available, next-generation selective immune modulator that is designed to inhibit the intracellular metabolism of activated immune cells by blocking the enzyme dihydroorotate dehydrogenase (DHODH). Vidofludimus calcium has been observed to act 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, vidofludimus calcium did not show an increased rate of infections compared to placebo. In addition, DHODH inhibitors, such as vidofludimus calcium, 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. To date, vidofludimus calcium has been tested in more than 1,100 individuals and has shown an attractive pharmacokinetic, safety and tolerability profile. Vidofludimus calcium 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 focused on treating chronic inflammatory and autoimmune diseases. The company is developing three small molecule products: its lead development program, vidofludimus calcium (IMU-838), 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, is currently being developed as a treatment option for multiple sclerosis, and primary sclerosing cholangitis. IMU-935, a selective inverse agonist of the transcription factor RORγ/RORγt, is targeted for development in psoriasis, castration-resistant prostate cancer and Guillain-Barré syndrome. IMU-856, which targets the restoration of the intestinal barrier function, is targeted for development in diseases involving bowel barrier dysfunction. 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, expected timing and results of clinical trials, 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 vidofludimus calcium to safely and effectively target diseases; preclinical and clinical data for vidofludimus calcium; the timing of current and future clinical trials and anticipated clinical milestones; the nature, strategy and focus of the company and further updates with respect thereto; 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 substantial 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 financial and other resources to meet business objectives and operational requirements, the fact that the results of earlier preclinical studies and clinical 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, 2021, filed with the SEC on February 24, 2022, 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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