Immunic Reports Positive Results From Phase 1b Clinical Trial of IMU-856 in Celiac Disease, Providing Clinical Proof-of-Concept for New Therapeutic Approach to Gastrointestinal Disorders

– Positive Effects Demonstrated Over Placebo in Four Key Dimensions of Celiac Disease Pathophysiology: Protection of Gut Architecture, Improvement of Patients' Symptoms, Biomarker Response, and Enhancement of Nutrient Absorption –

– Corroborates Hypothesized Ability of IMU-856 to Renew Gut Wall and Restore Gut Health –

– No Safety or Tolerability Issues Detected –

– Conference Call and Webcast to be Held Today, May 4, 2023 at 8:00 am ET –

NEW YORK, May 4, 2023 – Immunic, Inc. (Nasdaq: IMUX), a biotechnology company developing a clinical pipeline of orally administered, small molecule therapies for chronic inflammatory and autoimmune diseases, today announced positive results from the part C portion of its phase 1 clinical trial of IMU-856 in patients with celiac disease. The company believes that this data set provides initial clinical proof-of-concept for an entirely new therapeutic approach to gastrointestinal disorders by promoting regeneration of bowel architecture.

Data from four key dimensions of celiac disease pathophysiology and outcomes are summarized as follows:

- **Protection of gut architecture and reduction of gluten-induced intestinal damage**: Over the course of the trial, the placebo group (N=11) experienced a 60.3 µm reduction in villous height in response to four weeks of treatment and two weeks of 6 g/day gluten challenge. In contrast, this reduction was only 20.9 µm and 22.5 µm for the 80 mg (N=11) and 160 mg (N=13) IMU-856 groups, respectively (p=0.04*). Villi are small finger-like projections found in the lumen of the small intestine, which play a key role in the absorption of digested nutrients necessary for health and growth. Decrease in villous height is a well-recognized measure of gluten-induced damage in celiac disease and a main reason for signs and symptoms of malabsorption. Of particular interest, during the course of the trial, two IMU-856 treated patients demonstrated a 1-category improvement in Q-Marsh histology scores despite 15 consecutive days of exposure to gluten challenge. No analogous improvement was seen with placebo treatment.

- **Improvement of patients' symptoms related to gluten exposure**: On the first day of gluten challenge, the placebo group (N=12) experienced a marked average increase in symptoms, as assessed by the Celiac Disease Symptom Diary using a 5-point scale, of 0.8 for nausea, 0.8 for abdominal pain, and 0.8 diarrhea. In contrast, among the pooled IMU-856 arms (N=26), these average increases were only 0.4 for nausea, 0.5 for abdominal pain and 0.6 for diarrhea. Continued treatment with IMU-856 during gluten challenge also resulted in improvement or reversal of disease-related symptoms, such as bloating and tiredness.

- **Dose-dependent changes in biomarker responses**: Following the initiation of gluten challenge on day 14, patients treated with IMU-856 exhibited a dose-dependent lessening of acute immune response, as measured by serum interleukin-2 (IL-2) release, compared with placebo. IL-2 is a well-recognized biomarker of acute gluten exposure which has been correlated by independent third parties with timing and severity of symptoms after gluten exposure. In addition, average levels of citrulline, a biomarker for the proper function of gut wall cells, were increased in both active treatment arms while decreasing levels were observed in placebo-treated patients, reflecting a positive effect of IMU-856 on the function of gut lining cells.

- **Enhancement of nutrient absorption**: Over the course of the trial, the placebo group (N=11) experienced a 31.0 pmol/L *reduction* in levels of vitamin B12. In contrast, the 80 mg (N=11) and 160 mg (N=13) IMU-856 groups experienced a 45.8 pmol/L and 74.2 pmol/L *increase* in vitamin B12 levels, respectively. Vitamin B12 is a nutrient essential for the formation of red blood cells, and the normal functioning of the brain and nervous system, whose absorption from the gastrointestinal tract is frequently impaired in patients with celiac disease. Similar responses to treatment were observed for zinc- and iron-related measures.

Immunic believes that this data provides first clinical evidence that IMU-856's ability, observed in preclinical studies, to re-establish proper gut cell renewal translates into clinical benefits for patients with celiac disease. Most importantly, the observed protection of intestinal villi from gluten-induced destruction, independent of targeting immune mechanisms involved specifically in celiac disease, appears to be unique among proposed therapeutic approaches and may be applicable to other gastrointestinal diseases.

IMU-856 was observed to be safe and well-tolerated in this trial. There were no investigational medicinal product-related serious or treatment-emergent adverse events nor was there any dose-dependency in adverse events. Moreover, the rates of treatment-emergent adverse events in non-disease-related parameters were comparable between the active treatment groups and placebo.

"We believe today's data strongly corroborates IMU-856's potential to regenerate the gut wall as measured through a variety of key parameters," commented Daniel Vitt, Ph.D., Chief Executive Officer and President of Immunic. "IMU-856 was designed to restore a healthy gut without targeting the immune system, thus avoiding the immune dysfunction inherent in current approaches. Ultimately, IMU-856 could represent a possible game-changer in not only celiac disease, but also other gastrointestinal disorders with high unmet needs such as ulcerative colitis, Crohn's disease, or irritable bowel syndrome with diarrhea. We are eagerly preparing clinical phase 2b testing of IMU-856 in ongoing active celiac disease, while also considering other potential clinical applications for this first-in-class and orally available molecule."

"For a study designed to provide initial clinical proof-of-concept in a 28-day treatment setting, the resulting data set significantly exceeded our expectations," stated Andreas Muehler, M.D., Chief Medical Officer of Immunic. "The study demonstrated consistent and meaningful improvements for IMU-856 treatment over placebo in four key dimensions of celiac disease. We were delighted to see the dose-dependency, the consistency of improvement over placebo in a wide array of key histologic, symptomatic, nutritional and immunologic parameters, as well as a clean safety and tolerability profile. We were particularly excited to see the level of protection against histological deterioration by IMU-856 during gluten challenge, with some actively treated patients even displaying histologic improvements despite

repeated daily exposure to gluten. Moreover, the data on malabsorption testing and the enterocyte health marker citrulline are also striking as they address mechanisms known to be relevant for potential future medical complications in celiac disease patients. Given the large unmet need in celiac disease, along with the recognized inadequacy of strict gluten avoidance for many patients, we believe that IMU-856 represents a particularly promising clinical approach for this serious health condition."

Part C of the phase 1 clinical trial of IMU-856 was structured as a double-blind, randomized, placebo-controlled trial designed to assess the safety and tolerability of IMU-856 in patients with celiac disease during periods of gluten-free diet and gluten challenge. The trial was conducted at sites in Australia and New Zealand. A total of 43 patients were enrolled in two consecutive cohorts with 80 mg or 160 mg of IMU-856 or placebo given once-daily over 28 days. Secondary objectives included pharmacokinetics as well as acute and chronic disease markers, including those evaluating gastrointestinal architecture and inflammation.

Additional data from the phase 1b clinical trial of IMU-856 in celiac disease will be filed on a Form 8-K and discussed during the management presentation to be held today at 8:00 am ET.

*Exploratory post-hoc statistical analysis, Exact Wilcoxon Two-Sample Test comparison between IMU-856 (80 mg and 160 mg pooled) and placebo for villous height absolute changes between baseline and Day 29 (Disease Analysis Set, n=35).

Webcast Information

Immunic will host a webcast today, May 4, 2023, at 8:00 am ET to discuss these results. To participate in the webcast, please register in advance at: https://imux.zoom.us/webinar/register/WN_EbVhqfsaTGCXeAromYvIcA 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 Celiac Disease

Celiac disease is a multifactorial, complex autoimmune disease caused by an inappropriate immune reaction against a degradation product of gluten in genetically susceptible individuals. It is characterized by epithelial injury of the small intestine, elevated intestinal permeability, and nutrient malabsorption. Celiac disease causes debilitating signs and symptoms of malabsorption such as diarrhea, steatorrhea, fatigue, weight loss, anemia, and osteopenia, and can lead to serious complications such as enteropathy-associated T-cell lymphoma. In children, nutrient malabsorption can affect growth and development, in addition to causing the symptoms seen in adults. There is currently no known cure or treatment for celiac disease and patients must adhere to a strict, life-long gluten-free diet which can help manage symptoms and avoid disease flareups. Celiac disease is estimated to affect 1 in 100 people, worldwide. In the United States, alone, it is estimated that approximately one million people are undiagnosed and are, therefore, at risk for long-term health complications.

About IMU-856

IMU-856 is an orally available and systemically acting small molecule modulator that targets a protein which serves as a transcriptional regulator of intestinal barrier function and regeneration of bowel epithelium. Based on preclinical data, the compound may represent a unique treatment approach, as the mechanism of action targets the restoration of the intestinal barrier function and bowel wall architecture in patients suffering from gastrointestinal diseases such as celiac disease, inflammatory bowel disease, irritable bowel syndrome with diarrhea and other intestinal barrier function associated diseases. Immunic believes that, because IMU-856 has been shown in preclinical investigations to avoid suppression of immune cells, it may therefore have the potential to maintain immune surveillance for patients during therapy, an important advantage versus immunosuppressive medications. IMU-856 demonstrated positive results in a phase 1b clinical trial in celiac disease patients in four key dimensions of the disease's pathophysiology: histology, disease symptoms, biomarkers and nutrient absorption. Currently, the company is preparing for phase 2 clinical testing in this patient population. IMU-856 is an investigational drug product that has not been approved in any jurisdiction.

About Immunic, Inc.

Immunic, Inc. (Nasdaq: IMUX) is a biotechnology company developing a clinical pipeline of orally administered, small molecule therapies for chronic inflammatory and autoimmune diseases. The company's lead development program, vidofludimus calcium (IMU-838), currently in phase 3 clinical trials for the treatment of multiple sclerosis and which has shown therapeutic activity in phase 2 clinical trials in patients suffering from relapsing-remitting multiple sclerosis and moderate-to-severe ulcerative colitis, selectively inhibits activated immune cells and shows combined anti-inflammatory, anti-viral and neuroprotective effects. IMU-856 is targeted to restore intestinal barrier function and regenerate bowel epithelium, which would be applicable in numerous gastrointestinal diseases, such as celiac disease, where it is currently in preparations for a phase 2 clinical trial. 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, sufficiency of cash, 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 IMU-856 to safely and effectively target diseases; interpretation of preclinical and clinical data for IMU-856 and potential effects; 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,

impacts of the Ukraine – Russia conflict on clinical trials, 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, 2022, filed with the SEC on February 23, 2023, 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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