Immunic Reports Positive Interim Data from Phase 2 CALLIPER Trial of Vidofludimus Calcium in Progressive Multiple Sclerosis

– 24-Week Data from First Half of Patients Shows Improvements in Biomarker NfL, Consistent Throughout the Overall Progressive Multiple Sclerosis Population as well as All Subtypes –

– NfL Effect in Non-Active Subpopulation Reinforces Vidofludimus Calcium's Neuroprotective Potential –

– Brain Volume Data of the Full 467 CALLIPER Patient Cohort Expected in April 2025 –

– Phase 3 ENSURE Program in Relapsing Multiple Sclerosis Ongoing –

– Conference Call and Webcast to be Held Tomorrow, October 10, 2023 at 8:00 am ET –

NEW YORK, October 9, 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 interim data from its phase 2 CALLIPER trial of nuclear receptor related 1 (Nurr1) activator, vidofludimus calcium (IMU-838), in patients with progressive multiple sclerosis (PMS). The Company believes that this data shows biomarker evidence that vidofludimus calcium's activity extends beyond the previously observed anti-inflammatory effects, thereby further reinforcing its neuroprotective potential.

The predefined interim analysis examined the change from baseline to 24 weeks in serum neurofilament light chain (NfL) and glial fibrillar acidic protein (GFAP) levels among approximately the first half of patients enrolled in this trial. Serum NfL results are as follows:

		Total N	45 mg vidofludimus calcium versus placebo
Change in serum NfL at 24 weeks in % of baseline as compared to placebo	**All PMS**	**N=203**	**-22.4%**
	PPMS*	N=59	-18.8%
	Non-Active SPMS	N=124	-20.1%
	Active SPMS	N=20	-43.3%

PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis

* The only approved drug for PPMS, Ocrevus® (ocrelizumab), showed a 12.4% reduction versus placebo in 24-week serum NfL levels in the phase 3 ORATORIO trial (Bar-Or A. et al., EBioMedicine. 2023 Jul;93:104662).

Serum NfL responses were consistently observed for vidofludimus calcium across progressive MS disease and all subpopulations. In the overall PMS population at 24 weeks (N=203), vidofludimus calcium was associated with a 6.7% reduction from baseline in serum NfL, compared to a 15.8% increase over baseline in placebo (p=0.01, post hoc). At 48 weeks (N=79), vidofludimus calcium reduced serum NfL by 10.4% from baseline, compared to a 6.4% increase in placebo. Substantial reductions were also seen across all PMS subtypes, as well as in patients that show or do not show disease and/or magnetic resonance imaging (MRI) activity.

Although early, interim GFAP data also showed a promising signal: at 24 weeks (N=203), GFAP increased by 3.7% for vidofludimus calcium, and 4.4% for placebo. At 48 weeks (N=79), the change was only 2.7% for vidofludimus calcium, with a 6.4% increase for placebo. Progression of GFAP response is generally thought to evolve more slowly than NfL, and the Company believes that a longer follow-up may further strengthen this signal.

“Serum NfL has been consistently shown to capture disease activity and to predict future disability in MS. Vidofludimus calcium shows a separation in serum NfL over placebo in this interim analysis, an effect also seen across different subgroups,” stated Prof. Jens Kuhle, M.D., Ph.D., Senior Physician, Head of Neuroimmunology Unit and Multiple Sclerosis Centre, University Hospital Basel, Switzerland. “Particularly remarkable, the non-active progressive MS population, which represents the highest unmet medical need in MS, also showed differences in NfL levels over this relatively short observation period in favor of vidofludimus calcium. Meanwhile, although longer follow-up is needed, the GFAP data set also shows a potential promising early signal. Overall, the interim biomarker data further support vidofludimus calcium’s possible activity beyond an anti-inflammatory effect, which may be related to its potent Nurr1 activation.”

“The clear separation observed in serum NfL for vidofludimus calcium over placebo in the PMS patient population represents another major step forward for, what potentially could be, a first-in-class Nurr1 activator for MS,” commented Daniel Vitt, Ph.D., Chief Executive Officer and President of Immunic. “Although no head-to-head data is available, it is encouraging to see that vidofludimus calcium's improvement in NfL over placebo appears at least as good as, and is in fact numerically higher than that observed with historical studies of other therapeutic approaches for PMS. We believe that, if the top-line CALLIPER data, expected in April of 2025, continue to show a neuroprotective effect, we may be able to position vidofludimus calcium as the first oral treatment option for non-active SPMS. Additionally, the drug’s first-in-class ability to activate Nurr1, a known neuroprotective target, should also significantly benefit our ongoing phase 3 ENSURE program in relapsing MS where prevention of disability progression independent of relapse activity (PIRA), serves as a key outcome.”

“We are very pleased to see such strong improvements in serum NfL for vidofludimus calcium over placebo in the overall PMS population of this interim analysis, as well as across all PMS subtypes and in patients with and without disease activity, and with and without MRI activity. We even saw evidence in non-active SPMS, a population where the medical need for new therapies is high as there is currently no relevant treatment available in the US,” added Andreas Muehler, M.D., Chief Medical Officer of Immunic. “Finally, we were also excited to see an encouraging early signal with GFAP. This is a newer biomarker which is thought to evolve more slowly and with lower amplitude than NfL, and longer follow-up will hopefully allow us to see even stronger results.”

The Company believes that these results corroborate separate findings from its phase 2 EMPhASIS trial in relapsing-remitting multiple sclerosis (RRMS), where vidofludimus calcium was associated with a decrease in serum NfL at 24 weeks (-17.0% for 30 mg and -20.5% for 45 mg) as compared to baseline values, as contrasted with a 6.5% increase in serum NfL over baseline among placebo patients.

CALLIPER is a multicenter, randomized, double-blind, placebo-controlled phase 2 trial which enrolled 467 patients with primary PMS or active or non-active secondary PMS at more than 70 sites throughout North America as well as Western, Central and Eastern Europe. Patients were randomized to either 45 mg daily doses of vidofludimus calcium or placebo, and the trial’s primary endpoint is the annualized rate of

percent brain volume change up to 120 weeks. Key secondary endpoints include the annualized rate of change in whole brain atrophy and time to 24-week confirmed disability progression based on the expanded disability status scale (EDSS).

Anticipated MS Clinical Milestones

- Top-line data from the phase 2 CALLIPER trial of vidofludimus calcium in PMS is expected in April of 2025.
- Data from the interim analysis of the phase 3 ENSURE program of vidofludimus calcium in relapsing MS is expected in late 2024, with the top-line readout of the first of the ENSURE trials at the end of 2025.

For more information on the phase 2 CALLIPER trial, please visit: www.clinicaltrials.gov, NCT05054140.

The interim data of the phase 2 CALLIPER trial of vidofludimus calcium in PMS will be filed on a Form 8-K and discussed during the management presentation to be held tomorrow at 8:00 am ET. The presentation will also be accessible on the "Events and Presentations" section of Immunic's website at: https://ir.imux.com/events-and-presentations.

Webcast Information

Immunic will host a webcast tomorrow, October 10, 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_evpnpdOKQX2AKEXpCacoUA 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 Progressive Multiple Sclerosis

Multiple sclerosis (MS) is an autoimmune disease that affects the brain, spinal cord and optic nerve. In MS, myelin, the coating that protects the nerves, is attacked and damaged by the immune system. Thus, MS is considered an immune-mediated demyelinating disease of the central nervous system. Progressive multiple sclerosis (PMS) includes both primary progressive MS (PPMS) and secondary progressive MS (SPMS). PPMS is characterized by steadily worsening neurologic function from the onset of symptoms without initial relapse or remissions. SPMS is identified following an initial relapsing-remitting course, after which the disease becomes more steadily progressive, with (active SPMS) or without (non-active SPMS) other disease activity present.

About Vidofludimus Calcium (IMU-838)

Vidofludimus calcium is a small molecule investigational drug in development as an oral next-generation treatment option for patients with multiple sclerosis and other chronic inflammatory and autoimmune diseases. The selective immune modulator activates the neuroprotective transcription factor nuclear receptor related 1 (Nurr1), which is associated with direct neuroprotective properties. Additionally, vidofludimus calcium is a known inhibitor of the enzyme dihydroorotate dehydrogenase (DHODH), which

is a key enzyme in the metabolism of overactive immune cells and virus-infected cells. This mechanism is associated with the anti-inflammatory and anti-viral effects of vidofludimus calcium. Vidofludimus calcium has been observed to selectively act on hyperactive T and B cells while leaving other immune cells largely unaffected and enabling normal immune system function, e.g., in fighting infections. To date, vidofludimus calcium has been tested in more than 1,400 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 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), is currently in phase 3 and phase 2 clinical trials for the treatment of relapsing and progressive multiple sclerosis, respectively, and has shown therapeutic activity in phase 2 clinical trials in patients suffering from relapsing-remitting multiple sclerosis and moderate-to-severe ulcerative colitis. Vidofludimus calcium combines neuroprotective effects, through its mechanism as a first-in-class nuclear receptor related 1 (Nurr1) activator, with additional anti-inflammatory and anti-viral effects, by selectively inhibiting the enzyme dihydroorotate dehydrogenase (DHODH). IMU-856, which targets the protein Sirtuin 6 (SIRT6), is intended to restore intestinal barrier function and regenerate bowel epithelium, which could potentially be applicable in numerous gastrointestinal diseases, such as celiac disease, where it is currently in preparations for a phase 2 clinical trial. IMU-381, which currently is in preclinical testing, is a next generation molecule being developed to specifically address the needs of gastrointestinal diseases. 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, development 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 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, increasing inflation, impacts of the Ukraine – Russia conflict on planned and ongoing 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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