Immunic Therapeutics

Positive Outcome of Interim Analysis of Phase 3 ENSURE Program of Vidofludimus Calcium in Relapsing Multiple Sclerosis

NASDAQ: IMUX | October 22, 2024

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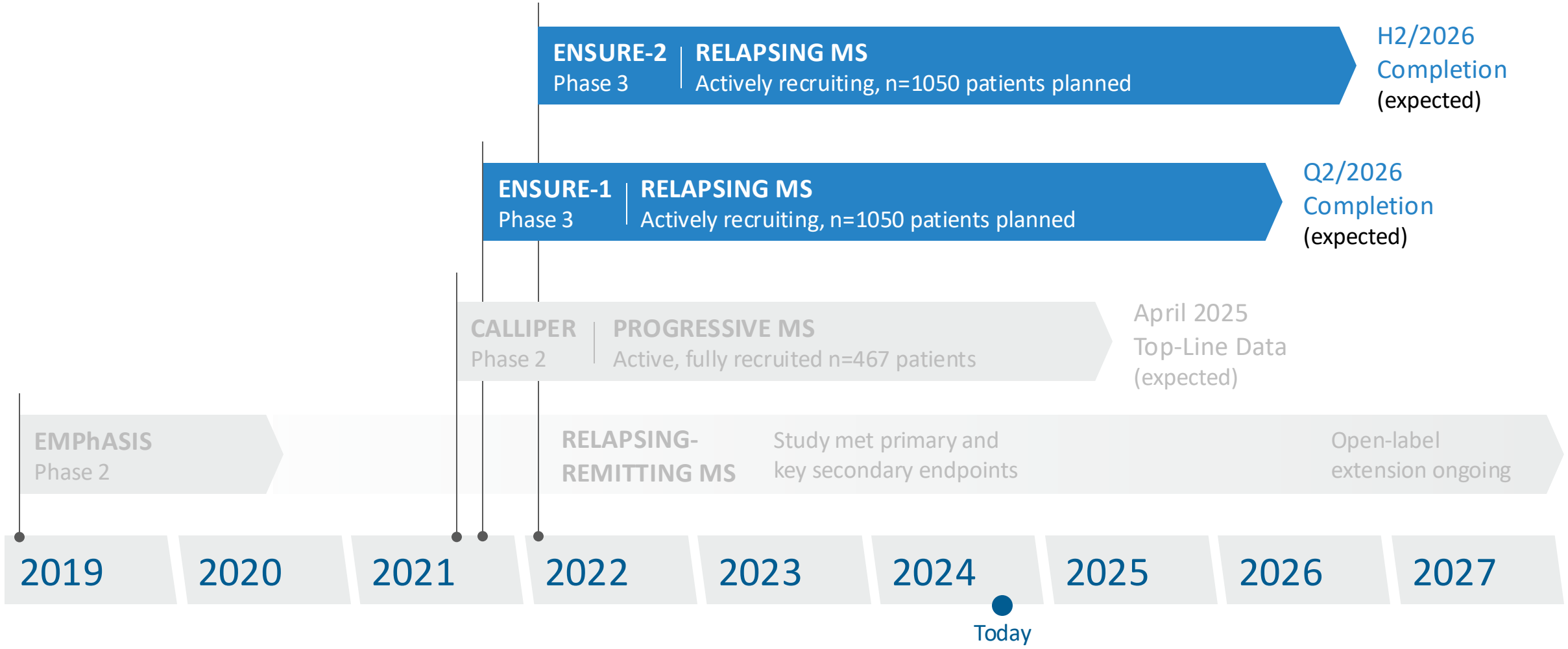
Forward-looking statements included in this presentation are based on information available to Immunic as of the date of this presentation. Immunic does not undertake any obligation to update such forward-looking statements except as required by applicable law.

Vidofludimus Calcium: Clinical Trials Overview in Multiple Sclerosis (MS)



Vidofludimus Calcium Has the Potential to Transform the Oral Multiple Sclerosis DMT Market

Anticipated Profile

First-in-class, dual mode of action approach designed to address the **full spectrum of disease:**

- Nurr1 activation provides **direct neuroprotective effects**
- DHODH inhibition is associated with **anti-inflammatory effects**

Oral DMT category: Achieves **best-in-class benefit / risk profile** by combining **strong efficacy** with **safety**, **tolerability**, and **once-daily** convenience

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No first-dose or on-treatment monitoring makes it an **easy start or switch to therapy**

No anticipated black box warnings or serious infection risk (e.g., PML, malignancies, etc.)

If approved, peak sales potential for vidofludimus calcium of $2-6 billion[1]

DMT: disease-modifying therapy; Nurr1: nuclear receptor related 1; DHODH: dihydroorotate dehydrogenase; PML: progressive multifocal leukoencephalopathy [1] Based on Immunic internal market research

Immunic THERAPEUTICS

Vidofludimus Calcium in Relapsing Multiple Sclerosis

Positive Outcome of Interim Analysis of Phase 3 ENSURE Program

ENSURE: Ongoing Pivotal Phase 3 Trials in Relapsing MS
NCT05134441 & NCT05201638

Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic

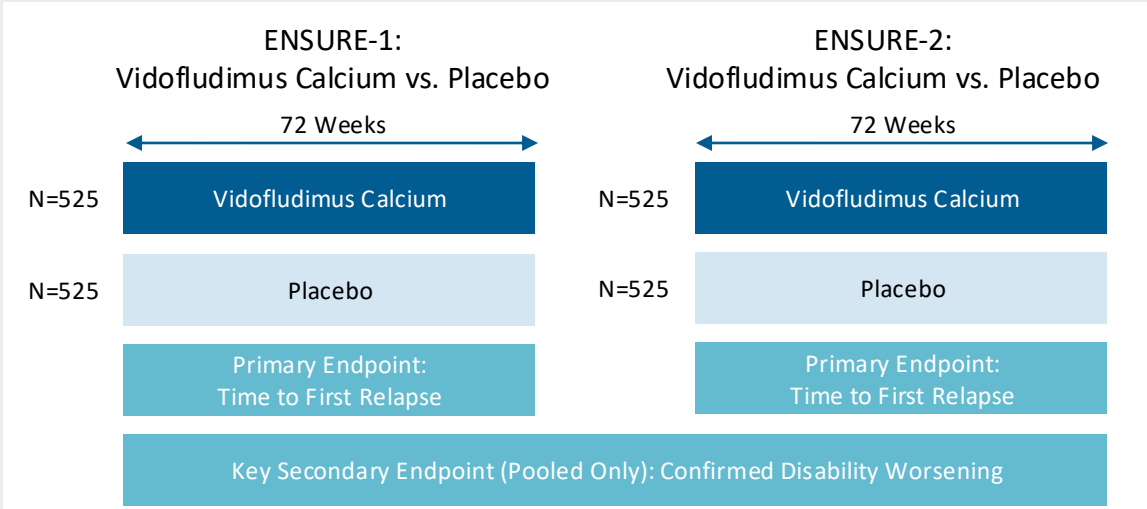
Included Patient Population: Relapsing Forms of MS

- Adult patients aged 18 to 55 years
- Established diagnosis of MS (revised McDonald criteria 2017)
- Confirmed relapsing MS (1996 Lublin criteria[1])
- Active disease as defined by Lublin 2014
- EDSS score at screening between 0 to 5.5

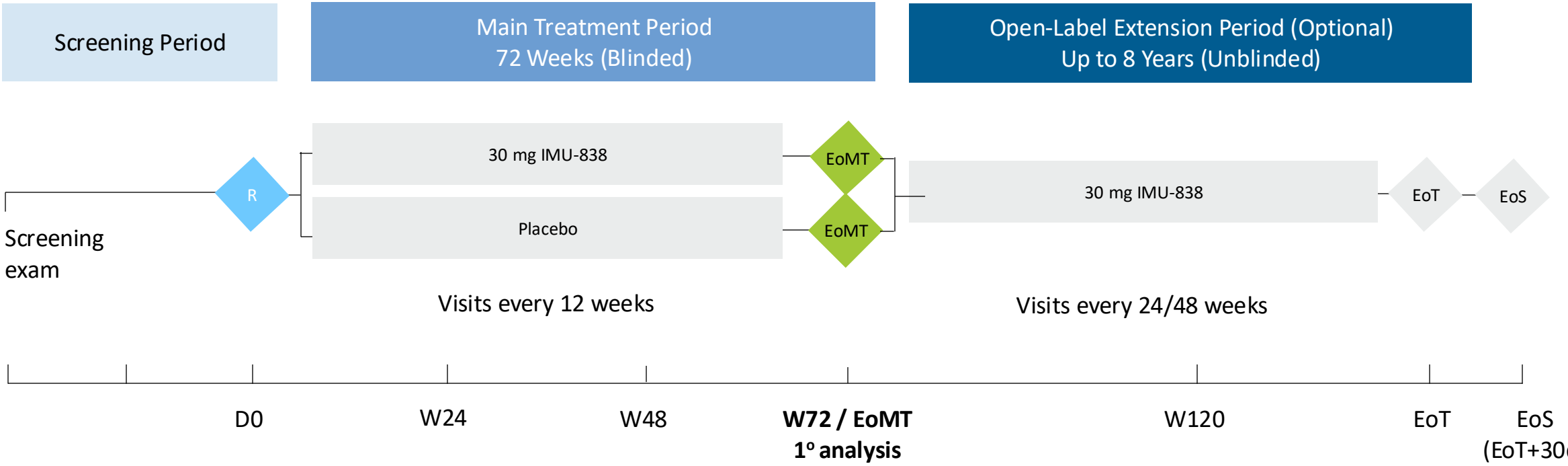
[1] Lublin FD, et al. Neurology. 2014;83(3):278-286
MS: multiple sclerosis; EDSS: Expanded Disability Status Scale; QD: quaque die = once-daily

Two Multicenter, Randomized, Double-Blind Phase 3 Trials

- Approximately 1,050 patients in each trial
- More than 100 sites in the United States, Latin America, Central and Eastern Europe, and India in each trial
- Randomization to 30 mg vidofludimus calcium or placebo QD
- Completion ENSURE-1 expected in Q2/2026, ENSURE-2 in H2/2026



ENSURE: General Phase 3 Study Design in RMS



- **Primary endpoint:** delaying the occurrences of relapses based on time to first relapse*
- **Key secondary endpoints:** time to confirmed disability worsening based on EDSS disability progression, volume of new T2-lesions, time to sustained clinically relevant changes in cognition, percentage of whole brain volume change

D: day; EoMT: end of main treatment period; EoS: end of study; EoT: end of treatment; R: randomization; W: week
* First relapse that after the start of treatment administration and before the end of the double-blind treatment period (censored at 72 weeks)

ENSURE: Key Study Assumptions and Interim Analysis Procedures

Key Study Assumptions

- Primary endpoint: comparison of time to first relapse between the 30 mg vidofludimus calcium and placebo treatment arms
- Time to event endpoint customarily visualized in Kaplan Meier curves
- Maximum duration of blinded study treatment: 72 weeks
- Key powering assumptions:
  - Event rate in placebo patients of 31% by 72 weeks
  - Powered to detect a hazard ratio difference of 0.67 between vidofludimus calcium and placebo
  - Resulting target number of first relapses: 262 per trial
- With these assumptions, each trial needs to have a sample size of 1,050 RMS patients

Interim Analysis Procedures

- Conditional power (CP) estimates the power of the study given the results observed so far and the original assumptions used to power the study. The calculation of CP is based on published methodologies.[1,2]
- The interim analysis will use CP to re-evaluate the calculation of the required sample size for each ENSURE trial separately and provide non-binding recommendations for potential adjustments.[3]

[1] Jennison, C., & Turnbull, B.W. (1999). Group Sequential Methods with Applications to Clinical Trials (1st ed.). 205 – 210. Chapman and Hall/CRC [2] Chen YH, DeMets DL, Lan KK. Stat Med. 2004 Apr 15;23(7):1023-38
[3] For the conditional power method to not have an impact on the final alpha level, it is not permissible to reduce the sample size.

ENSURE: Positive Outcome of Interim Analysis

Assumptions

- Based on a pre-specified assessment after approximately half of the planned first relapse events occurred in the double-blind treatment periods
- Based on a conditional power analysis by an unblinded Independent Data Monitoring Committee (IDMC):
  - Allowed for non-binding futility analysis to help prevent the final study readout from occurring before sufficient events have been achieved
  - Intended to inform potential sample size increase based on event rate and therapy effect size

Results

- Two decisions made by the unblinded IDMC:
  - **First question, whether the trials are futile, answered by the IDMC with "futility criteria have not been met"**
  - **Second question, whether the sample size in each trial should be increased, answered by the IDMC with "continue as planned"**
- Immunic has remained blinded during the interim analysis and has not seen any of the data available to the IDMC to make their recommendations.

Andreas Muehler, M.D., M.B.A.
Chief Medical Officer of Immunic

“The IDMC’s favorable recommendations in this interim analysis corroborate our initial assumptions for the design, powering and relapse rate of the twin phase 3 trials of vidofludimus calcium in RMS, and suggest that they are in line with the data observed so far. In particular, the planned sample size seems appropriate to address the primary endpoint of time to first relapse.”

Interim Futility Analysis of the Phase 3 ENSURE Program

Q&A Session

Interim Futility Analysis of the Phase 3 ENSURE Program

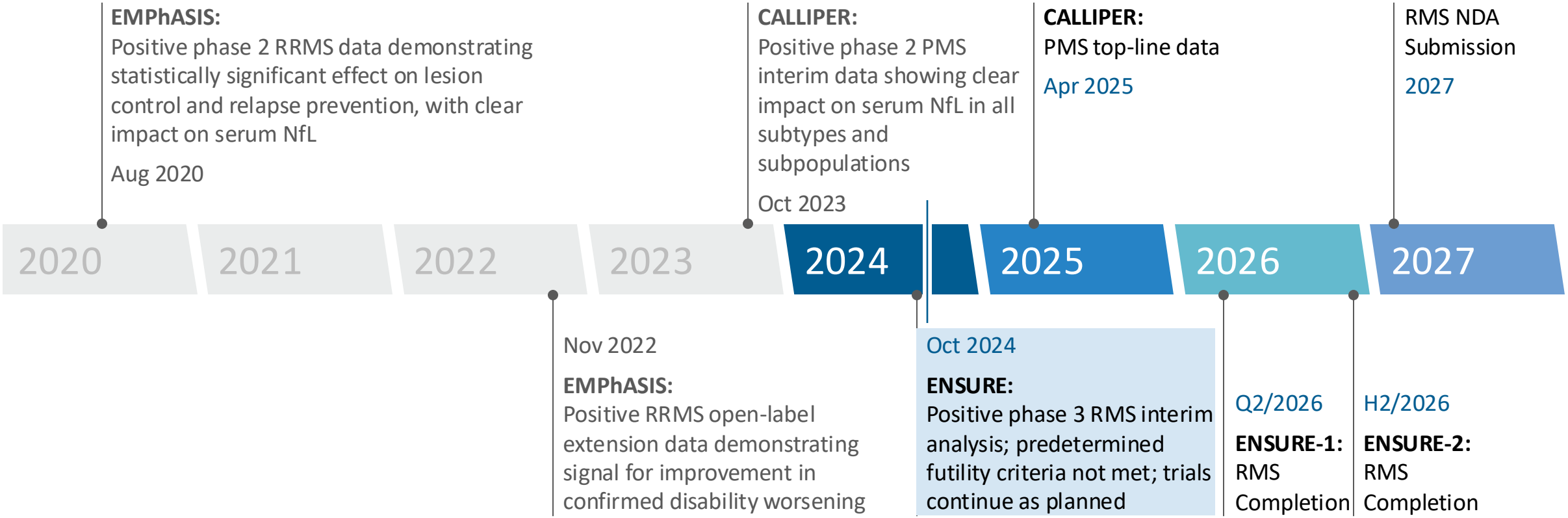
Summary

Daniel Vitt, Ph.D.
Chief Executive Officer of Immunic

“I am particularly excited about the positive outcome of the interim analysis of our phase 3 ENSURE trials, marking the successful achievement of a critical milestone for the program. We are confident in vidofludimus calcium’s potential to transform the oral MS market and continue to believe that the phase 3 program provides a clear and straightforward path towards seeking potential regulatory approval in RMS.”

Vidofludimus Calcium in Multiple Sclerosis

Consistent and Differentiated Results to Date Support Straightforward Path Towards Potential Regulatory Approvals



Although we currently believe that each of these goals is achievable, they are each dependent on numerous factors, most of which are not under our direct control and can be difficult to predict. We plan to periodically review this assessment and provide updates of material changes as appropriate. / MS: multiple sclerosis; RRMS: relapsing-remitting MS; RMS: relapsing MS; PMS: progressive MS; NfL: neurofilament light chain

Immunic THERAPEUTICS

Vidofludimus Calcium Aims to Redefine the Oral Multiple Sclerosis Treatment Landscape

1 Designed to combine the **best of two worlds**: **neuroprotection** and **relapse prevention**

- Positive phase 2 data in relapsing-remitting MS
- Hints to slowing down disability worsening
- Positive outcome of interim futility analysis of phase 3 program in relapsing MS, confirming trials are on track
- Positive biomarker data from phase 2 trial in progressive MS
- Unique dual mode of action addressing relapsing and progressive disease
- First-in-class Nurr1 activation going beyond inflammation

2 **Easy to use:** once-daily oral tablet

3 **Easy initiation:** No complex screening requirements for doctors

4 **Unique** safety and tolerability profile

- Preventing Epstein-Barr virus (EBV) reactivation
- No increased infection risks observed, so far – no PML case reported

MS: multiple sclerosis; Nurr1: nuclear receptor related 1; PML: progressive multifocal leukoencephalopathy

Immunic THERAPEUTICS

Thank You!

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