

A Phase 3 Study of Revumenib in Combination With Intensive Chemotherapy in Patients With Newly Diagnosed *NPM1*-Mutated Acute Myeloid Leukemia (REVEAL-ND *NPM1*): Trial in Progress

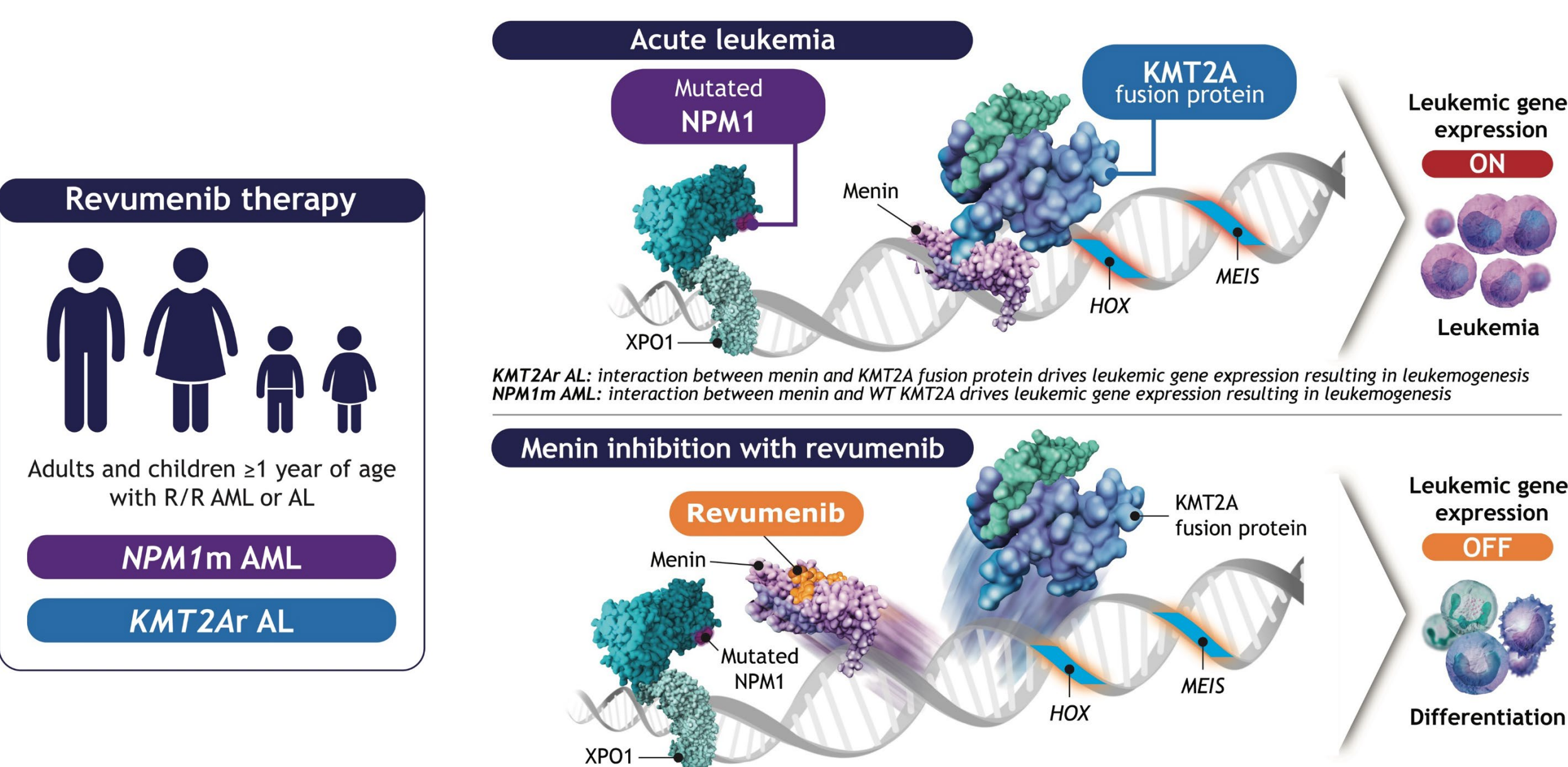
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INTRODUCTION

- Acute myeloid leukemia (AML) harboring a nucleophosmin-1 mutation (*NPM1*m) occurs in ~30% of newly diagnosed (ND) adult AML cases, for which there were no approved therapies until recently¹⁻³
- In *NPM1*m AML, the *NPM1*m/XPO1 protein complex binds to DNA to sustain the menin-KMT2A interaction that drives upregulation of homeobox (*HOX*)/Meis homeobox (*MEIS*) gene expression, resulting in hematopoietic differentiation arrest and leukemogenesis⁴⁻⁶ (Figure 1)
- Revumenib is a first-in-class, oral, potent, and selective inhibitor of the menin-KMT2A interaction⁷
- In the phase 2 AUGMENT-101 study (NCT04065399), revumenib monotherapy demonstrated clinically meaningful response rates and was generally well tolerated in patients with relapsed/refractory *NPM1*m AML, leading to US Food and Drug Administration approval for that patient population on October 24, 2025⁸
- Standard AML treatment for younger, nonfrail adults is based on intensive chemotherapy (IC) regimens and hematopoietic stem cell transplant (HSCT)^{2,9}
 - The addition of revumenib to standard IC may further improve treatment responses, specifically in the ND setting

Figure 1. Revumenib mechanism of action



OBJECTIVE

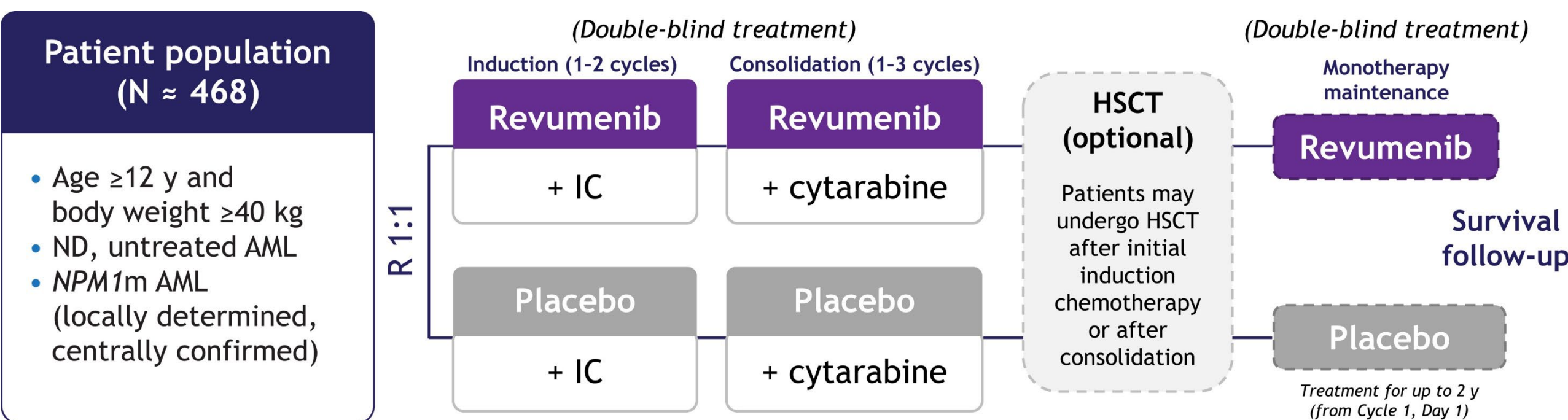
- The REVEAL-ND *NPM1* study will assess the safety and efficacy of revumenib in combination with IC in patients with ND *NPM1*m AML

METHODS

Study design

- REVEAL-ND *NPM1* (NCT07211958/EU-CT 2025-522279-27-00) is a multicenter, randomized, double-blind, placebo-controlled, phase 3 trial (Figure 2)
- Patients will be randomized 1:1 to receive either revumenib or placebo in combination with IC
- Overall, ~468 patients will be randomized

Figure 2. REVEAL-ND *NPM1* study design



Key inclusion criteria

- ≥12 years of age
- Body weight ≥40 kg
- Treatment-naïve, ND *NPM1*m AML according to the 2022 International Consensus Classification (ie, ≥10% blasts)¹⁰
- Locally determined, centrally confirmed *NPM1*m
- AML with *FLT3* mutation (tyrosine kinase domain) with any variant allele frequency, if use of *FLT3* inhibitor is not planned or standard of care

Treatment and follow-up

- Induction consists of 1-2 cycles of revumenib or placebo, dosed orally, with IC (cytarabine and daunorubicin or idarubicin, dosed intravenously)
- Consolidation consists of 1-3 cycles of revumenib or placebo plus cytarabine
- Treatment with revumenib or placebo monotherapy will continue for up to 2 years, with long-term follow-up until death, withdrawal of consent, or study closure
- Optional HSCT may be performed following initial induction or consolidation, with the ability to continue treatment with revumenib or placebo as post-transplant maintenance

Key exclusion criteria

- Prior treatment for AML (except for hydroxyurea and leukapheresis)
- Not eligible for standard IC, including anthracycline-based induction or cytarabine-based induction/consolidation
- AML with *FLT3* mutation (internal tandem duplication) with a variant allele frequency of ≥5%, or if *FLT3* inhibitor use is indicated
- Active acute promyelocytic leukemia
- Significant active cardiovascular disease ≤6 months prior to the start of study entry

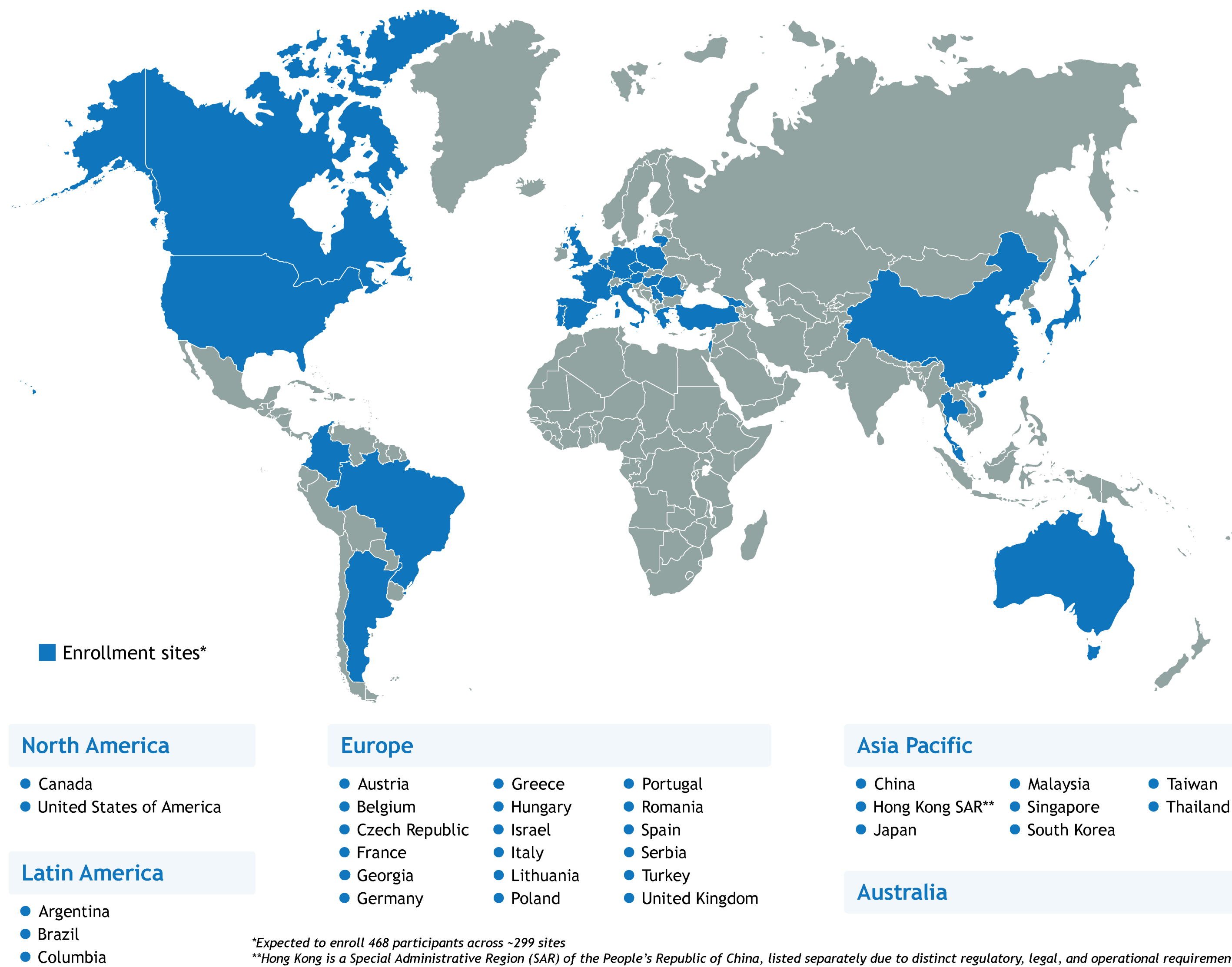
Study endpoints

- Dual primary endpoints:
 - Event-free survival
 - Measurable residual disease-negative complete remission (CR) rate
- Key secondary endpoint:
 - Overall survival
- Additional endpoints:
 - Rates of CR and composite CR (CRc)
 - Overall response rate
 - Durations of CR and CRc
 - Duration of response
 - Safety
 - Quality of life

CURRENT STATUS

- As of May 29, 2026, this study is open to enrollment globally (Figure 3)

Figure 3. Map of countries with clinical study sites



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ACKNOWLEDGMENTS

REVEAL-ND *NPM1* is sponsored by Syndax Pharmaceuticals, Inc. Medical writing and editorial support were provided by Alex Dimitri, PhD, of Humanity Communications Inc., and were funded by Syndax Pharmaceuticals, Inc.

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