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Phase III study of revumenib in combination with intensive chemotherapy in newly diagnosed NPM1-mutated AML

Submission date 24/10/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol
Registration date 06/02/2026	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 10/03/2026	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
This study aims to determine if adding a drug called revumenib to standard chemotherapy can improve outcomes for patients with newly diagnosed acute myeloid leukemia (AML) that has a specific genetic mutation called NPM1. AML is an aggressive blood cancer, and while current treatments can lead to remission, many patients still relapse. This research is important because it could potentially lead to a more effective first-line treatment for this type of AML.
The study will test revumenib, an oral medication that targets a specific protein interaction involved in AML development. The use of revumenib in this study is investigational, which means that revumenib is not approved by any regulatory authorities for this indication.

Who can participate?
Participants aged 12 years and older with newly diagnosed NPM1-mutated AML who are eligible for intensive chemotherapy

What does the study involve?
Participants will be randomly assigned to receive either revumenib or a placebo along with standard chemotherapy. Neither participants nor doctors will know who receives revumenib versus placebo. Patients will undergo regular blood tests, bone marrow biopsies, imaging scans and other assessments to monitor their response to treatment and any side effects.

What are the possible benefits and risks of participating?
There is no guarantee that taking part in this study will improve participants' health and it is possible that their condition may get worse. However, participants will contribute to important research that could improve treatment options for AML.
Due to the character count limit for this question it is not possible to add the full list of potential risks and burdens. Please see the following sections of the Main Participant Information Sheet and Informed Consent Form for a full list of potential risks and burdens: "What side effects or risks can I expect from being in the study?" and "Risks Associated with the Study Tests and Procedures".

Where is the study run from?
Syndax Pharmaceuticals, Inc. (USA)

When is the study starting and how long is it expected to run for?
October 2025 to January 2031

Who is funding the study?
Syndax Pharmaceuticals, Inc. (USA)

Who is the main contact?
clinicaltrials@syndax.com

Contact information

Type(s)
Scientific

Contact name
None Syndax Pharmaceuticals

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Type(s)
Principal investigator

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Additional identifiers

Central Portfolio Management System (CPMS)
68660

Integrated Research Application System (IRAS)
1012542

ClinicalTrials.gov (NCT)
NCT07211958

Protocol serial number
SNDX-5613-0710

Study information

Scientific Title
A Phase III, randomized, double-blind, placebo-controlled study of revumenib in combination with intensive chemotherapy in participants with newly diagnosed AML with an NPM1 mutation (REVEAL-ND NPM1)

Acronym
REVEAL-ND NPM1

Study objectives
Primary objectives:
1. To evaluate if revumenib + IC improves EFS compared to placebo + IC
2. To evaluate if revumenib + IC improves MRDBM (-) CR rate, compared to placebo + IC

Secondary objectives:
1. To evaluate if revumenib + IC improves OS compared to placebo + IC
2. To evaluate if revumenib + IC improves EFS compared to placebo + IC
3. To evaluate if revumenib + IC improves MRDBM (-) CR rate compared to placebo + IC
4. To evaluate the MRDPB (-) CR rate for revumenib + IC compared to placebo + IC
5. To evaluate the MRDBM (-) CR rate for revumenib + IC compared to placebo + IC
6. To evaluate if revumenib in combination with IC improves CR rate compared to placebo + IC
7. To evaluate CRc rate for revumenib + IC compared to placebo + IC
8. To evaluate ORR in revumenib + IC compared to placebo + IC
9. To evaluate duration of CR for revumenib + IC compared to placebo + IC
10. To evaluate duration of CRc for revumenib + IC compared to placebo + IC
11. To evaluate DOR for revumenib + IC compared to placebo + IC
12. To evaluate the safety and tolerability of revumenib + IC compared to placebo + IC
13. To evaluate patient-reported fatigue for revumenib + IC compared to placebo + IC

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 11/12/2025, London - Brighton & Sussex Research Ethics Committee (2 Redman Place, Stratford, London, E20 1QJ, United Kingdom; -; brightonandsussex.rec@hra.nhs.uk), ref: 25/LO/0831

Study design
Double-blind randomized placebo-controlled trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Newly diagnosed acute myeloid leukemia (AML) with an NPM1 mutation

Interventions
Experimental Arm: Revumenib + Intensive Chemotherapy (IC). Participants will receive revumenib orally plus an IC regimen of cytarabine and danorubicin by intravenous (IV) infusion.
Placebo Comparator: Placebo + IC. Participants will receive placebo (non-active agent) orally plus and IC regimen of cytarabine and danorubicin by IV.

Please note that the dose range, frequency and randomisation process are considered CCI and cannot be disclosed.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Revumenib, cytarabine, daunorubicin, idarubicin

Primary outcome(s)
1. Event-Free Survival (EFS): Defined as the time from the date of randomization to the date of induction treatment failure, relapse, or death due to any cause, whichever occurs first. Time frame up to 2 years.
2. Minimal Residual Disease in Bone Marrow Negative Complete Response Rate (MRDBM- CR rate): Defined as the percentage of participants with Complete Response (CR) (IRC-assessed). Time frame up to 2 years.

Key secondary outcome(s))
1. Overall Survival (OS): Defined as the time from the date of randomization to the date of death from any cause. Time frame up to 5 years.
2. Event-Free Survival (EFS, Investigator-assessed): Defined as the time from the date of randomization to the date of Induction treatment failure, relapse or death due to any cause, whichever occurs first. Time frame up to 2 years.
3. Minimal Residual Disease in Bone Marrow Negative Complete Response Rate (MRDBM- CR rate, molecular assay): Defined as the percentage of participants with CR (Investigator-assessed) who achieve MRDBM (-) status by molecular assay. Time frame up to 2 years.
4. Minimal Residual Disease in Peripheral Blood Negative Complete Response Rate (MRDPB- CR rate, molecular assay): Defined as the percent of participants with CR (Investigator-assessed) who achieve MRDPB (-) status by molecular assay. Time frame up to 2 years.
5. Minimal Residual Disease in Bone Marrow Negative Complete Response Rate (MRDBM- CR rate, flow cytometry): Defined as the percent of participants with CR who achieve MRDBM (-) status by flow cytometry after Induction and/or Consolidation. Time frame up to 2 years.
6. Complete Response Rate (CR rate, Investigator-assessed): Defined as the percentage of participants who achieve CR. Time frame up to 2 years.
7. Composite Complete Response Rate (CRc rate, Investigator-assessed): Defined as the rate of CR + CRh + CRi. Time frame up to 2 years.

8. Overall Response Rate (ORR, Investigator-assessed): Defined as the rate of CR + CRh + CRi + MLFS + PR. Time frame up to 2 years.
9. Duration of Complete Response (Duration of CR): Defined as time from first date of first CR to relapse or death. Time frame up to 2 years.
10. Duration of Composite Complete Response (Duration of CRc): Defined as time from date of first CRc to relapse or death. Time frame up to 2 years.
11. Duration of Response (DOR): Defined as time from date of first documented response (CR, CRh, CRi, PR, or MLFS) to the first documented relapse or death. Time frame up to 2 years.
12. Treatment-Emergent Adverse Events (TEAEs), Treatment-Related Adverse Events (TRAEs), and Serious Adverse Events (SAEs): Frequency, duration, and severity. Time frame up to 2 years.
13. Clinical Laboratory Abnormalities: Incidence and shifts from baseline of clinically significant clinical laboratory abnormalities. Time frame up to 2 years.
14. Other Safety Observations: Change from baseline in ECGs, vital signs, and performance status. Time frame up to 2 years.

Completion date
01/01/2031

Eligibility

Key inclusion criteria
1. Participants must have newly diagnosed and previously untreated AML and be candidates for intensive chemotherapy
2. Presence of an NPM1 mutation
3. Eastern Cooperative Oncology Group performance status ≤2 (≤1 if >65 years old); Karnofsky or Lansky ≥40
4. Have a life expectancy of ≥3 months as judged by the Investigator
5. Negative serum pregnancy test
6. Adequate liver, kidney, and cardiac function

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
12 years

Upper age limit
110 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Diagnosis of active acute promyelocytic leukemia
2. Active central nervous system disease
3. Fridericia's corrected QT interval (QTcF) >450 milliseconds at screening, diagnosis or suspicion of Long QT syndrome or family history of Long QT syndrome
4. Any gastrointestinal (GI) issue of the upper GI tract likely to affect oral drug absorption or ingestion
5. Any concurrent malignancy requiring active therapy (except breast or prostate cancer stable on or responding to endocrine therapy)
6. Inability to swallow oral medication
7. Pregnant or nursing females
8. Participant has known active or chronic hepatitis B or active hepatitis C (HCV) infection or human immunodeficiency virus (HIV)-positive with detectable viral load

Date of first enrolment
16/03/2026

Date of final enrolment
30/11/2027

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Study participating centre
The Royal Marsden NHS Foundation Trust
Fulham Road
London
England
SW3 6JJ

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
England
B15 2GW

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
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AB25 2ZN

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
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W2 1BL

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
Headington
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OX3 9DU

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
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SO16 6YD

Study participating centre
Belfast Health and Social Care Trust
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A Floor - Belfast City Hospital
Lisburn Road
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BT9 7AB

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Beatson West of Scotland Cancer Centre
1053 Great Western Road
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G12 0YN

Study participating centre
University Hospitals of Derby and Burton NHS Foundation Trust
Royal Derby Hospital
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DE22 3NE

Sponsor information

Organisation
Syndax Pharmaceuticals, Inc.

Funder(s)

Funder type
Industry

Funder Name
Syndax Pharmaceuticals

Alternative Name(s)
Syndax Pharmaceuticals Inc., Syndax Pharmaceuticals Inc, Syndax

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date