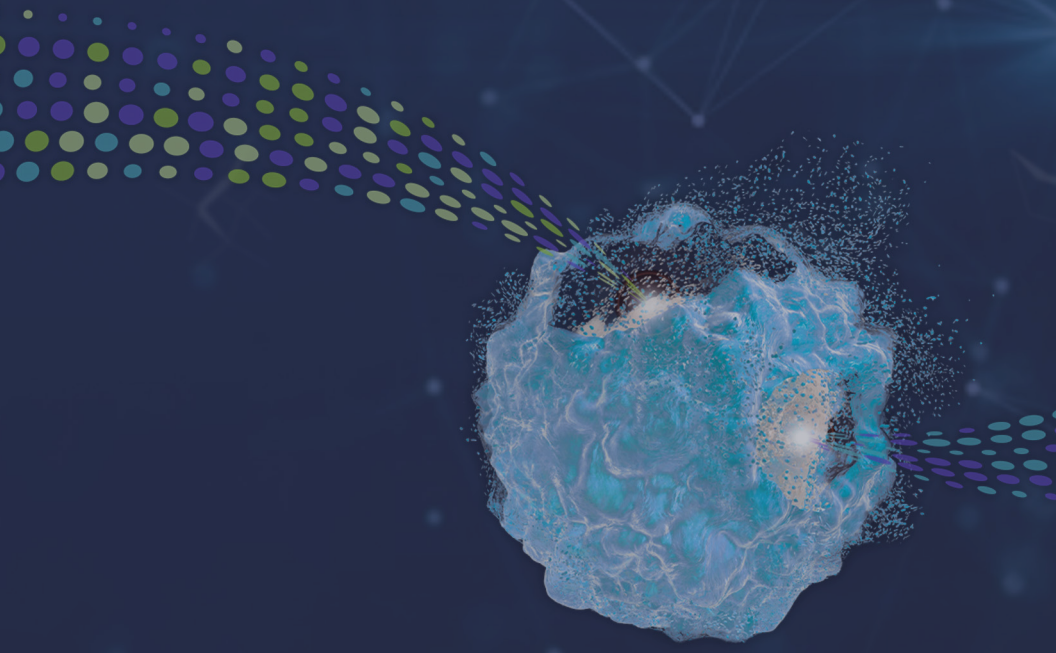
PRELUDE THERAPEUTICS CLINICAL PROGRAM



Now enrolling patients with hematologic malignancies

Do you have eligible patients who have exhausted current standards of care?

Prelude Therapeutics is currently recruiting patients with advanced hematologic malignancies and myeloproliferative disorders for our phase 1 clinical trials. Continue reading to find out more about our target platforms, drug candidates, clinical trial enrollment, and patient eligibility.

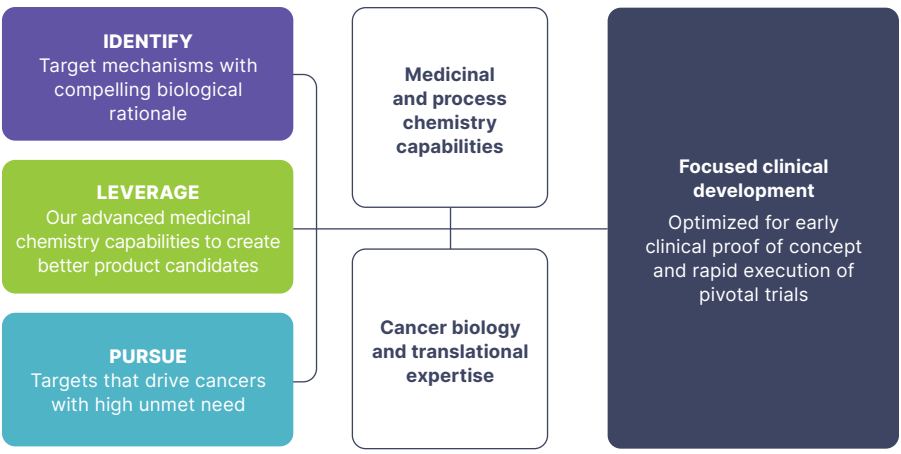
Prelude THERAPEUTICS

Advancing innovation for patients with hematologic malignancies

Prelude Therapeutics is a clinical-stage precision oncology company focused on discovering and developing small molecule therapies that target key drivers of cancer cell growth, resistance, and survival. By developing therapies that target broad oncogenic mechanisms, Prelude Therapeutics strives to serve patients with high unmet medical needs, including those with hematologic malignancies.

We apply deep expertise in cancer biology and medicinal chemistry to identify targets in cancer signaling pathways amenable to small molecule-based therapies

Our discovery and developmental approach



Targeting key drivers in hematologic malignancies

Our current pipeline includes investigational agents that target PRMT5 and MCL1, both of which are important oncogenic drivers in multiple types of cancer.

PRMT5

- Protein arginine methyltransferase 5 (PRMT5) is an enzyme that catalyzes the formation of symmetric dimethylarginine residues on proteins that regulate biological processes that drive oncogenesis[1]
- Overexpression and increased activity of PRMT5 are associated with poor outcomes and decreased survival in patients with solid tumors and hematologic malignancies, including certain leukemias and lymphomas, myelodysplastic syndrome (MDS), and myelofibrosis (MF)[1-3]
- PRT543 is an investigational, oral, potent, and selective PRMT5 inhibitor currently in clinical development as a potential therapy for these malignancies*

MCL1

- Myeloid cell leukemia-1 (MCL1) is a member of the B-cell lymphoma 2 (BCL2) family of anti-apoptotic proteins and plays a key role in cancer cell survival[4]
- MCL1 is frequently overexpressed in many tumor types including hematologic malignancies and is often a driver of resistance to BCL2 inhibitors[5]
- PRT1419 is an investigational, potent, and selective MCL1 inhibitor that can be administered orally or by intravenous (IV) infusion. PRT1419 is currently in clinical development for patients with advanced solid tumors and relapsed/refractory hematological malignancies*

*PRT543 and PRT1419 are investigational agents. Safety and efficacy have not been established by any agency.

NCT03886831

Now recruiting

eligible patients with hematologic malignancies who have exhausted current standards of care

A phase 1, multicenter, open-label, sequential-cohort, dose-escalation, dose-expansion study of PRT543, an oral, selective PRMT5 inhibitor, in patients with advanced solid tumors and hematologic malignancies[6]

The recommended expansion dose has now been established[7,8]

Recruiting eligible patients with advanced solid tumors and the following hematologic malignancies:

Diffuse large B-cell lymphoma (DLBCL)

Mantle cell lymphoma (MCL)

Myelodysplastic syndrome (MDS)

Acute myeloid leukemia (AML)

Chronic myelomonocytic leukemia (CMML)

Myelofibrosis (MF)

NCT03886831

1

Primary outcome measures

- Dose-limiting toxicities
- Maximum tolerated dose/recommended dose for further study

2

Secondary outcome measures

- Safety
- Pharmacokinetics

Select key eligibility criteria*

- Advanced DLBCL
- Advanced MCL
- Relapsed MDS
- Relapsed AML or CMML
- Relapsed MF
- All malignancies must be refractory to established therapies
- Eastern Cooperative Oncology Group (ECOG) Performance Score of 0 or 1
- Adequate organ function (bone marrow, hepatic, renal, cardiovascular)
- No primary central nervous system (CNS) malignancies or uncontrolled CNS metastases
- No requirement of pharmacologic doses of glucocorticoids
- No prior treatment with chimeric antigen receptor T (CAR-T) cells
- No prior allogeneic bone marrow transplant or autologous hematopoietic transplantation less than 100 days since transplantation

*Visit clinicaltrials.gov for full criteria details.

To see if your patients qualify and for additional study details, visit **clinicaltrials.gov** or contact us directly at **PreludeClinOps@preludetx.com**

NCT04543305

Now recruiting

eligible patients with relapsed/ refractory hematologic malignancies

A phase 1, multicenter, open-label, dose-escalation study of PRT1419, an oral, selective MCL1 inhibitor, in patients with relapsed/refractory hematologic malignancies[9]

Recruiting eligible patients with:

Acute myeloid leukemia (AML)

Chronic myelomonocytic leukemia (CMML)

Myelodysplastic syndrome (MDS)

Myelodysplastic syndrome/myeloproliferative neoplasm (MDS/MPN) overlap syndrome

Non-Hodgkin lymphoma (NHL)

Multiple myeloma (MM)

NCT04543305

1

Primary outcome measures

- Dose-limiting toxicities
- Maximum tolerated dose/recommended dose for further study

2

Secondary outcome measures

- Safety
- Pharmacokinetics
- Objective response

Select key eligibility criteria*

- Pathologically confirmed AML
- Intermediate-2 or high risk CMML per CMML-specific prognostic scoring system (CPSS) or clinical/molecular (CPSS-mol) criteria
- Intermediate, high, or very high risk MDS per International Prognostic Scoring System-Revised (IPSS-R) criteria that is relapsed or refractory to approved therapies
- MDS/MPN overlap syndrome displaying fibrosis and dysplastic features
- Histologically or cytologically confirmed NHL, with one measurable lesion
- MM defined as ≥1 of the following: serum M-protein ≥0.5 g/dL, urine M-protein ≥200 mg/24 hours, serum free light chain (sFLC) >10 mg/dL with normal sFLC ratio, with presence of soft tissue plasmacytoma confirmed by imaging
- NHL and MM patients must have absolute neutrophil count (ANC) ≥1.0 x 10^3 µL and platelet count ≥50,000 µL within 14 days prior to Day 1 of study
- Eastern Cooperative Oncology Group (ECOG) performance status ≤2
- Adequate organ function (bone marrow, hepatic, renal, cardiovascular)
- Left ventricular ejection fraction ≥50%
- No prior exposure to an MCL1 inhibitor

*Visit clinicaltrials.gov for full criteria details.

To see if your patients qualify and for additional study details, visit **clinicaltrials.gov** or contact us directly at **PreludeClinOps@preludetx.com**

NCT05107856

Now recruiting

eligible patients with relapsed/ refractory hematologic malignancies

A phase 1, multicenter, open-label, dose-escalation study of PRT1419, a selective MCL1 inhibitor, administered via intravenous (IV) infusion in patients with relapsed/refractory hematologic malignancies[10]

Recruiting eligible patients with:

Acute myeloid leukemia (AML)

Chronic myelomonocytic leukemia (CMML)

Myelodysplastic syndrome (MDS)

Myelodysplastic syndrome/myeloproliferative neoplasm (MDS/MPN) overlap syndrome

NCT05107856

1

Primary outcome measures

- Dose-limiting toxicities
- Minimum safe and biologically effective dose/recommended dose for further study

2

Secondary outcome measures

- Safety
- Pharmacokinetics
- Objective response

Select key eligibility criteria*

- Pathologically confirmed AML
- Intermediate-2 or high risk CMML per CMML-specific prognostic scoring system (CPSS) or clinical/molecular (CPSS-mol) criteria
- Intermediate, high, or very high risk MDS per International Prognostic Scoring System-Revised (IPSS-R) criteria that is relapsed or refractory to approved therapies
- MDS/MPN overlap syndrome displaying fibrosis and dysplastic features
- Eastern Cooperative Oncology Group (ECOG) performance status ≤2
- Adequate organ function (bone marrow, hepatic, renal, cardiovascular)
- Left ventricular ejection fraction ≥50%
- No prior exposure to an MCL1 inhibitor

*Visit clinicaltrials.gov for full criteria details.

To see if your patients qualify and for additional study details, visit **clinicaltrials.gov** or contact us directly at **PreludeClinOps@preludetx.com**

Partner with us

in our commitment to advancing novel treatments for patients with hematologic malignancies

At Prelude Therapeutics, we focus on advancing novel therapeutics through clinical trials for patients with cancers that have high unmet needs.

Clinical studies of our investigational PRMT5 inhibitor, PRT543 (**NCT03886831**), and MCL1 inhibitor, PRT1419 (**NCT04543305**, **NCT05107856**), are currently enrolling.

If you want more information on clinical trial opportunities for your patients with hematologic malignancies, visit **clinicaltrials.gov** using the links below for each investigational therapy, or contact us directly at **PreludeClinOps@preludetx.com.**

Visit **NCT03886831** for more information about our **PRT543** clinical trial.

Visit **NCT04543305** and **NCT05107856** for more information about our **PRT1419** clinical trials.

References: 1. Xiao W, Chen X, Liu L, Shu Y, Zhang M, Zhong Y. Role of protein arginine methyltransferase 5 in human cancers. *Biomed Pharmacother.* 2019;114:108790. doi:10.1016/j.biopha.2019.108790. **2.** Shailesh H, Zakaria ZZ, Baiocchi R, Sif S. Protein arginine methyltransferase 5 (PRMT5) dysregulation in cancer. *Oncotarget*. 2018;9(94):36705-36718. doi:10.18632/oncotarget.26404. **3.** Pastore F, Bhagwat N, Pastore A, *et al.* PRMT5 inhibition modulates E2F1 methylation and gene-regulatory networks leading to therapeutic efficacy in JAK2 V617F-mutant MPN. *Cancer Discov.* 2020;10(11):1742-1757. doi:10.1158/2159-8290.CD-20-0026. **4.** Xiang W, Yang CY, Bai L. MCL-1 inhibition in cancer treatment. *Onco Targets Ther.* 2018;11:7301-7314. Published 2018 Oct 23. doi:10.2147/OTT.S146228. **5.** Hird AW, Tron AE. Recent advances in the development of Mcl-1 inhibitors for cancer therapy. *Pharmacol Ther.* 2019;198:59-67. doi:10.1016/j.pharmthera.2019.02.007. **6.** A study of PRT543 in participants with advanced solid tumors and hematologic malignancies. ClinicalTrials.gov identifier: NCT03886831. Updated July 30, 2021. Accessed October 17, 2021. https://clinicaltrials.gov/ct2/show/NCT03886831. **7.** Patel MR, Monga V, Jauhari S, et al. A phase 1 dose escalation study of protein arginine methyltransferase 5 (PRMT5) inhibitor PRT543 in patients with myeloid malignancies. Poster presented at: The 63rd ASH Annual Meeting and Exposition; December 11-14, 2021; Atlanta, GA. **8.** McKean M, Patel MR, Wesolowski R, et al. A phase 1 dose-escalation study of protein arginine methyltransferase 5 (PRMT5) inhibitor PRT543 in patients with advanced solid tumors and lymphoma. Poster presented at: The AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer; October 7-10, 2021. **9.** A study of PRT1419 in patients with relapsed/refractory hematologic malignancies. ClinicalTrials.gov identifier: NCT04543305. Updated April 5, 2021. Accessed October 17, 2021. https://clinicaltrials.gov/ct2/show/NCT04543305. **10.** A study of PRT1419 injection in patients with relapsed/refractory hematologic malignancies. ClinicalTrials.gov identifier: NCT05107856. Updated November 4, 2021. Accessed November 5, 2021. https://clinicaltrials.gov/ct2/show/NCT05107856.

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