UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): March 15, 2023

Prelude Therapeutics Incorporated

(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-39527**	**81-1384762**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

200 Powder Mill Road **Wilmington, Delaware**	**19803**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (302) 467-1280

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	PRLD	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition

On March 15, 2023, Prelude Therapeutics Incorporated (the "Company") issued a press release announcing its financial results for the year ended December 31, 2022. A copy of the press release is attached as Exhibit 99.1 to this report.

Item 7.01 Regulation FD Disclosure

The Company has prepared investor presentation materials with information about the Company, which it intends to use as part of investor presentations. A copy of the investor presentation materials to be used by management for presentations is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 8.01 Other Events

The Company announced a clinical trial collaboration with BeiGene, for future evaluation of the Company's CDK9 inhibitor, PRT2527, in combination with BeiGene's BTK inhibitor, zanubrutinib, in hematologic malignancies. A copy of the press release is attached as Exhibit 99.3 to this report.

The information in this Current Report on Form 8-K and in Exhibits 99.1, 99.2, and 99.3 attached hereto is being furnished, but shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended ("Exchange Act"), and is not incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press release issued by Prelude Therapeutics Incorporated regarding its financial results for the year ended December 31, 2022, dated March 15, 2023
99.2	Presentation
99.3	Press release issued by Prelude Therapeutics Incorporated regarding clinical trial collaboration
104	Cover Page Interactive Data File (embedded within the Inline XBRL Document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PRELUDE THERAPEUTICS INCORPORATED

Date: March 15, 2023

By: /s/ Laurent Chardonnet
Laurent Chardonnet
Chief Financial Officer

Exhibit 99.1

Prelude Therapeutics Reports Full Year 2022 Financial Results and Provides Corporate Update

Four differentiated clinical compounds progressing through Phase 1 towards key data milestones

Eight abstracts accepted for presentation at the 2023 American Association for Cancer Research (AACR) Annual Meeting

Cash balance of $201.7 million as of December 31, 2022; runway remains unchanged through Q4 2024

Wilmington, DE – March 15, 2023 – Prelude Therapeutics Incorporated (Nasdaq: PRLD), a clinical-stage precision oncology company, today reported its financial results for the fiscal year ended December 31, 2022, and provided a corporate update.

"We made considerable progress in 2022, including the filing and acceptance of two new INDs for our next generation CDK4/6 inhibitor and our first-in-class, highly selective SMARCA2 degrader. Our current clinical pipeline consists of four differentiated and internally discovered molecules that effectively target and block key oncogenic pathways in both hematological malignancies and solid tumors. Prelude's highly productive internal discovery engine continues to deliver novel molecules across multiple therapeutic classes, including significant advances in our research efforts focused on identifying an orally available SMARCA2 degrader," **stated Kris Vaddi, Ph.D., Chief Executive Officer of Prelude**.

Jane Huang, M.D., President and Chief Medical Officer of Prelude stated, "Prelude's six preclinical and two clinical abstracts accepted for presentation at the upcoming AACR Annual Meeting reflect the productivity and success of our research and development efforts. Initial data from PRT2527 and PRT1419 demonstrate encouraging safety, favorable pharmacokinetic and pharmacodynamic profiles in solid tumors, and support continued advancement in hematological cancers. Looking ahead, our top priority for 2023 is to efficiently advance these compounds forward into proof-of-concept clinical studies and determine appropriate next steps for each program."

"Our recently announced collaboration with BeiGene reflects our commitment to maximize the therapeutic value of combining our highly selective and potent CDK9 inhibitor, PRT2527, with BTK inhibitors in hematologic malignancies," added Dr. Huang.

Program Updates and Upcoming Milestones

PRT2527- CDK9 Inhibitor Program
PRT2527 is a potent and selective small molecule that has the potential to avoid off target toxicity and achieve higher clinical activity than other CDK9 programs currently in development. The Company is currently advancing PRT2527 as monotherapy in both solid and hematological indications. The Company also intends to pursue the clinically validated approach of combining PRT2527 with approved BTK inhibitors, beginning with its recently announced clinical collaboration with BeiGene.

Key 2023 objectives for this program include:

- *Present solid tumor safety dose escalation data at AACR 2023*
- *Determine RP2D in hematological malignancies in 2H 2023*
- *Present initial clinical results for hematological malignancies at a medical conference in 2H 2023*

PRT1419- MCL1 Inhibitor Program

Based on the Phase 1 dose escalation study in solid tumors, and safety measured by troponin levels and changes in ejection fraction, the Company is now advancing PRT1419 in hematologic malignancies as monotherapy. The Company also plans to study PRT1419 in combination with venetoclax and in combination with azacytidine.

Key 2023 objectives for this program include:

- *Solid tumor safety data to be presented at AACR 2023*
- *RP2D expected in hematological malignancies in 2H 2023*
- *Hematological malignancy data expected to be presented in 2H 2023*

PRT3645-Next Generation CDK4/6 Inhibitor Program

PRT3645 is a highly selective and differentiated CDK4/6 inhibitor. PRT3645 is a CDK4 biased compound with tissue and brain penetration qualities, and has potential in multiple indications including gliomas, head and neck cancers and non-small cell lung cancer, in addition to HR+/HER2- and HR+/HER2+ breast cancers.

Key 2023 objective includes:

- *Present initial Phase 1 clinical results at a medical conference in 2H 2023*

SMARCA2 Targeted Protein Degrader Program

PRT3789 is an IV administered, potent and highly selective SMARCA2 degrader. It is designed to achieve the requisite high selectivity for SMARCA2 over the isoform, SMARCA4, through a targeted protein degrader approach. PRT3789 is a first-in-class SMARCA2 candidate and is currently in Phase 1 clinical development in biomarker selected SMARCA4 mutant patients.

Prelude's discovery team has also identified orally bioavailable SMARCA2 degraders.

Key objectives include:

- *Provide Clinical update on PRT3789 2H 2023*
- *Advance an oral SMARCA2 degrader for investigational new drug (IND) submission in 1H 2024*

Upcoming presentations

The following clinical abstracts will be presented at AACR 2023:

1. **Title: A phase 1, open-label, dose-escalation study of PRT1419, a selective induced myeloid leukemia cell differentiation protein (MCL-1) inhibitor, in patients (pts) with advanced/metastatic solid tumors**.

Presenter: Gerald Falchook

- Session Title: First-in-Human Phase I Clinical Trials 2
- Session Date and Time: Tuesday Apr 18, 2023, 9:00 AM - 12:30 PM
- Location: Poster Section 45
- Poster Board Number: 4
- Abstract Presentation Number: CT172

2. **Title: A phase 1, open-label, multicenter, dose-escalation study of PRT2527, a cyclin-dependent kinase 9 (CDK9) inhibitor, in adult patients (pts) with advanced solid tumors**.

Presenter: Jason Henry

- Session Title: First-in-Human Phase I Clinical Trials 2

- Session Date and Time: Tuesday Apr 18, 2023 9:00 AM - 12:30 PM
- Location: Poster Section 45
- Poster Board Number: 5
- Abstract Presentation Number: CT173

The following preclinical abstracts will be presented at AACR 2023:

1. **Title: SMARCA2 (BRM) degraders promote differentiation and inhibit proliferation in AML models**
Presenter: Anjana Agarwal
- Session Category: Experimental and Molecular Therapeutics
- Session Title: New Therapeutic Targeted Agents
- Session Date and Time: Monday Apr 17, 2023 9:00 AM - 12:30 PM
- Location: Section 16
- Poster Board Number: 17
- Abstract Presentation Number: 1594

2. **Title: Development of pharmacodynamic assays for quantifying SMARCA2 protein degradation and target gene expression in response to a SMARCA2 degrader (PRT3789)**
Presenter: Andrew Moore
- Session Category: Experimental and Molecular Therapeutics
- Session Title: Pharmacokinetics, Pharmacodynamics, and Molecular Pharmacology
- Session Date and Time: Monday Apr 17, 2023 1:30 PM - 5:00 PM
- Location: Section 18
- Poster Board Number: 15
- Abstract Presentation Number: 2792

3. **Title: Combination therapy with selective SMARCA2 (BRM) degraders for treatment of SMARCA4 (BRG1)-deficient cancers**
Presenter: Michael Hulse
- Session Category: Experimental and Molecular Therapeutics
- Session Title: Epigenetics
- Session Date and Time: Wednesday Apr 19, 2023 9:00 AM - 12:30 PM
- Location: Section 20
- Poster Board Number: 8
- Abstract Presentation Number: 6270

4. **Title: The brain penetrant CDK4/6 Inhibitor, PRT3645, is highly effective in combination with other targeted therapies in preclinical models of NSCLC and HER2-positive breast cancer**
Presenter: Yue Zou
- Session Category: Molecular/Cellular Biology and Genetics
- Session Title: Cyclin-dependent Kinases and Cyclin-dependent Kinase Inhibitors
- Session Date and Time: Wednesday Apr 19, 2023 9:00 AM - 12:30 PM
- Location: Section 9
- Poster Board Number: 2
- Abstract Presentation Number: 5973

5. **Title: MCL1 inhibitor PRT1419 demonstrates anti-tumor activity in PBRM1-altered clear cell renal cancer and synergizes with standard of care agents**

Presenter: Norman Fultang

- Session Category: Experimental and Molecular Therapeutics
- Session Title: Cell Death Pathways and Treatment / Molecular Classification of Tumors for Diagnostics, Prognostics, and Therapeutic Outcomes
- Session Date and Time: Wednesday Apr 19, 2023 9:00 AM - 12:30 PM
- Location: Section 16
- Poster Board Number: 9
- Abstract Presentation Number: 6147

6. **Title: Selective and orally bioavailable SMARCA2 targeted degraders induce synthetic lethality in SMARCA4- deficient solid tumor**
Presenter: Koichi Ito

- Session Category**:** Experimental and Molecular Therapeutics
- Session Title: Epigenetics
- Session Date and Time: Wednesday Apr 19, 2023 9:00 AM - 12:30 PM
- Location: Section 20
- Poster Board Number: 15
- Abstract Presentation Number: 6277

Corporate Update

On February 20, 2023, Bryant D. Lim, Esq., joined Prelude Therapeutics as Chief Legal Officer and Corporate Secretary. He has more than 20 years of experience in pharma and biotech, with expertise in business development, regulatory matters, fundraising and SEC reporting. Kris Vaddi, Ph.D. commented, "We are excited to welcome Bryant to Prelude and expand our leadership team to include his relevant expertise. Bryant is an excellent addition, helping us to move forward in our growth as a Company."

Full Year 2022 Financial Results

- **Cash and Cash Equivalents:** Cash and cash equivalents as of December 31, 2022 were $201.7 million. Following Prelude's recently announced program prioritization initiatives, the Company has extended its cash guidance and anticipates that its existing cash, cash equivalents and marketable securities will fund Prelude's operations through the fourth quarter of 2024.

- **Research and Development (R&D) Expenses**: R&D expenses for the year ended December 31, 2022 increased $6.1 million to $92.9 million compared to $86.8 million for the year ended December 31, 2021. Included in research and development expenses for the year ended December 31, 2022, was $11.5 million of non-cash expense related to stock-based compensation expense, including employee stock options, compared to $9.5 million for the year ended December 31, 2021. The increase in research and development expense was primarily due to an increase in discovery-stage program expenses and from the growth and advancement of our clinical pipeline and an increase in non-cash stock-based compensation expense.

- **General and Administrative (G&A) Expenses**: G&A expenses for the year ended December 31, 2022 increased by $3.7 million to $30.7 million compared to $27.0 million for the year ended December 31, 2021. Included in the general and administrative expenses for the year ended December 31, 2022, was $13.6 million of non-cash expense related to stock-based compensation expense, including employee stock options, as compared to $11.5 million for the

same period in 2021. The increase in general and administrative expense was primarily due to an increase in non-cash stock-based compensation expense.

- **Net Loss:** Net loss for the year ended December 31, 2022 was $115.4 million or $2.44 per share, compared with a net loss of $111.7 million, or $2.43 per share for the year ended December 31, 2021.

About Prelude Therapeutics

Prelude Therapeutics is a clinical-stage precision oncology company developing innovative drug candidates targeting critical cancer cell pathways. The Company's diverse pipeline is comprised of highly differentiated, potentially best-in-class proprietary small molecule compounds aimed at addressing clinically validated pathways for cancers with selectable underserved patients. Prelude's pipeline includes four candidates currently in clinical development: PRT1419, a potent, selective inhibitor of MCL1, PRT2527, a potent and highly selective CDK9 inhibitor, PRT3645 a next generation CDK4/6 inhibitor**,** and PRT3789 an IV administered, potent and highly selective SMARCA2 degrader.

For more information, visit our website and follow us on LinkedIn and Twitter.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, anticipated discovery, preclinical and clinical development activities, timing of availability and announcements of clinical results for PRT2527 and PRT1419, the timing of reporting expected findings related to PRT1419, PRT2527, PRT3645 and PRT3789, the potential benefits of Prelude's product candidates and platform, and the sufficiency of cash and cash equivalents to fund operating expenses and capital expenditures through the fourth quarter of 2024. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Although Prelude believes that the expectations reflected in such forward-looking statements are reasonable, Prelude cannot guarantee future events, results, actions, levels of activity, performance or achievements, and the timing and results of biotechnology development and potential regulatory approval is inherently uncertain. Forward-looking statements are subject to risks and uncertainties that may cause Prelude's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to Prelude's ability to advance its product candidates, the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, the impact of the COVID-19 pandemic on Prelude's business, clinical trial sites, supply chain and manufacturing facilities, Prelude's ability to maintain and recognize the benefits of certain designations received by product candidates, the timing and results of preclinical and clinical trials, Prelude's ability to fund development activities and achieve development goals, Prelude's ability to protect intellectual property, and other risks and uncertainties described under the heading "Risk Factors" in documents Prelude files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and Prelude undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

PRELUDE THERAPEUTICS INCORPORATED
STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except share and per share data)	Year ended December 31, 2022	2021
Operating expenses:		
Research and development	$ 92,889	$ 86,778
General and administrative	30,651	26,957
Total operating expenses	123,540	113,735
Loss from operations	(123,540)	(113,735)
Other income, net	8,102	2,041
Net loss	$ (115,438)	$ (111,694)
Per share information:		
Net loss per share of common stock, basic and diluted	$ (2.44)	$ (2.43)
Weighted average common shares outstanding, basic and diluted	47,371,589	46,049,763
Comprehensive loss		
Net loss	$ (115,438)	$ (111,694)
Unrealized gain (loss) on marketable securities, net of tax	(981)	(711)
Comprehensive loss	$ (116,419)	$ (112,405)

PRELUDE THERAPEUTICS INCORPORATED
BALANCE SHEETS

(in thousands, except share and per share data)	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 30,605	$ 31,828
Marketable securities	171,123	259,405
Prepaid expenses and other current assets	2,652	3,882
Total current assets	204,380	295,115
Restricted cash	4,044	4,044
Property and equipment, net	4,908	3,929
Right-of-use asset	1,792	1,707
Other assets	5,376	303
Total assets	$ 220,500	$ 305,098
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,777	$ 7,840
Accrued expenses and other current liabilities	13,093	9,621
Operating lease liability	1,832	1,740
Total current liabilities	21,702	19,201
Other liabilities	3,361	-
Total liabilities	25,063	19,201
Commitments		
Stockholders' equity:		
Voting common stock, $0.0001 par value: 487,149,741 shares authorized; 36,496,994 and 36,200,299 shares issued and outstanding at December 31, 2022 and 2021, respectively	4	4
Non-voting common stock, $0.0001 par value: 12,850,259 shares authorized; 11,402,037 and 11,402,037 shares issued and outstanding at December 31, 2022 and 2021, respectively	1	1
Additional paid-in capital	531,682	505,723
Accumulated other comprehensive income (loss)	(1,692)	(711)
Accumulated deficit	(334,558)	(219,120)
Total stockholders' equity	195,437	285,897
Total liabilities and stockholders' equity	$ 220,500	$ 305,098

Investor Contact:
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Vice President, Investor Relations
240.543.7970
ltrickett@preludetx.com

Media Contact:
Helen Shik
Shik Communications
617.510.4373
Helen@ShikCommunications.com

Prelude THERAPEUTICS

Exhibit 99.2

Corporate Presentation

March 2023

Patient focused.
Science driven.
Precision oncology.

Forward Looking Statements

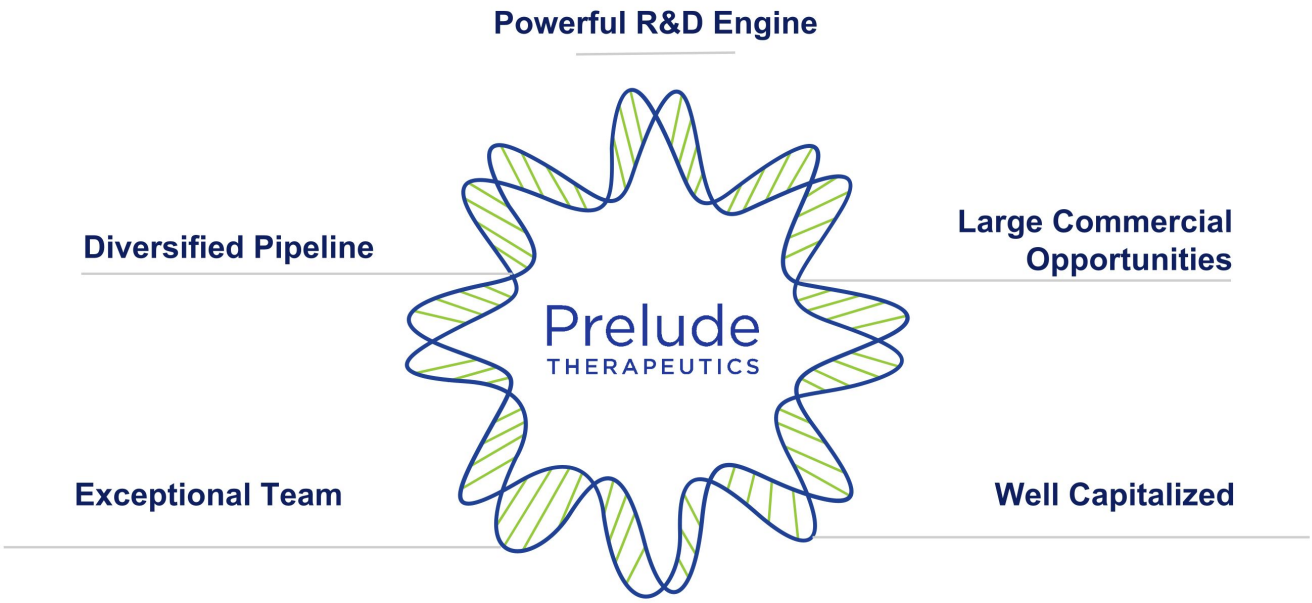
This presentation contains “forward-looking” statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: our plans to develop and commercialize small molecule therapies, our expectations about timing and ability to commence, enroll or complete clinical studies, present data and clinical results or updates, and to obtain regulatory approvals for PRT1419, PRT2527, PRT3645, PRT3789, our oral SMARCA2 candidate and other candidates in development, the ability of our product candidates to treat various cancers, the ability to discover additional suitable candidates for regulatory approval, the potential impact of the COVID-19 pandemic, and the sufficiency of our cash and cash equivalents to fund our operations.

Any statements contained herein or provided orally that are not statements of historical fact may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by such terminology as ‘‘believe,’’ ‘‘may,’’ ‘‘will,’’ ‘‘potentially,’’ ‘‘estimate,’’ ‘‘continue,’’ ‘‘anticipate,’’ ‘‘intend,’’ ‘‘could,’’ ‘‘would,’’ ‘‘project,’’ ‘‘plan,’’ ‘‘expect’’ and similar expressions that convey uncertainty of future events or outcomes, although not all forward-looking statements contain these words. Statements, including forward-looking statements, speak only to the date they are provided (unless an earlier date is indicated).

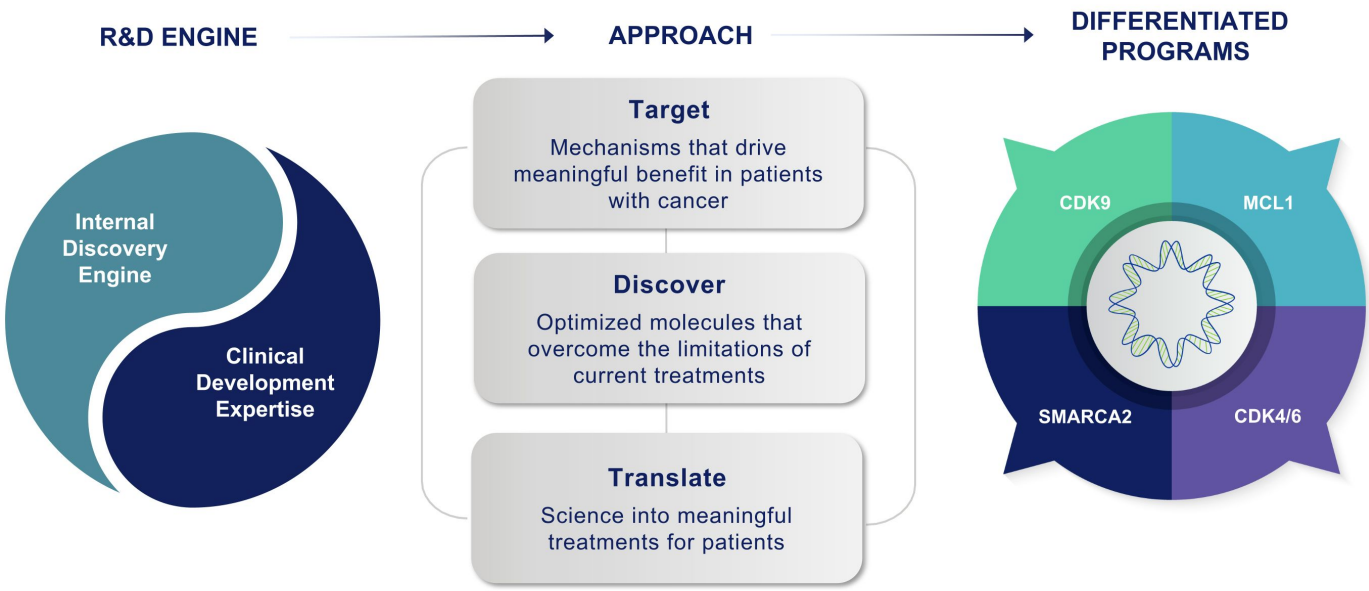
Certain data in this presentation are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities or differences. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction.

These forward-looking statements are based on the beliefs of our management as well as assumptions made by and information currently available to us. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. If such assumptions do not fully materialize or prove incorrect, the events or circumstances referred to in the forward-looking statements may not occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations, except as required by law. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. Additional risks and uncertainties that could affect our business are included under the caption “Risk Factors” in our filings with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2022.

Prelude Therapeutics: Delivering Precision Medicines to Patients with Cancer



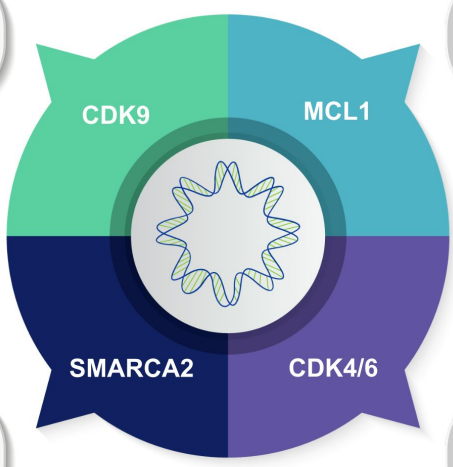
Prelude Discovery and Development Engine: Positioned to Succeed



Differentiated Programs with Transformative Potential for Patients with Cancer

Potentially Best-in-Class Selectivity
Potential to avoid off-target toxicity and higher clinical activity

Optimized PK Profile
Potential for maximal target engagement and improved cardiac safety



Potent and Selective Degrader
Potential to address major unmet need in biomarker-selected patients

Highly Selective CDK4 Bias
Potential for high tissue and brain penetration and better combinability

Powerful Discovery Engine generating new INDs every 12-18 months

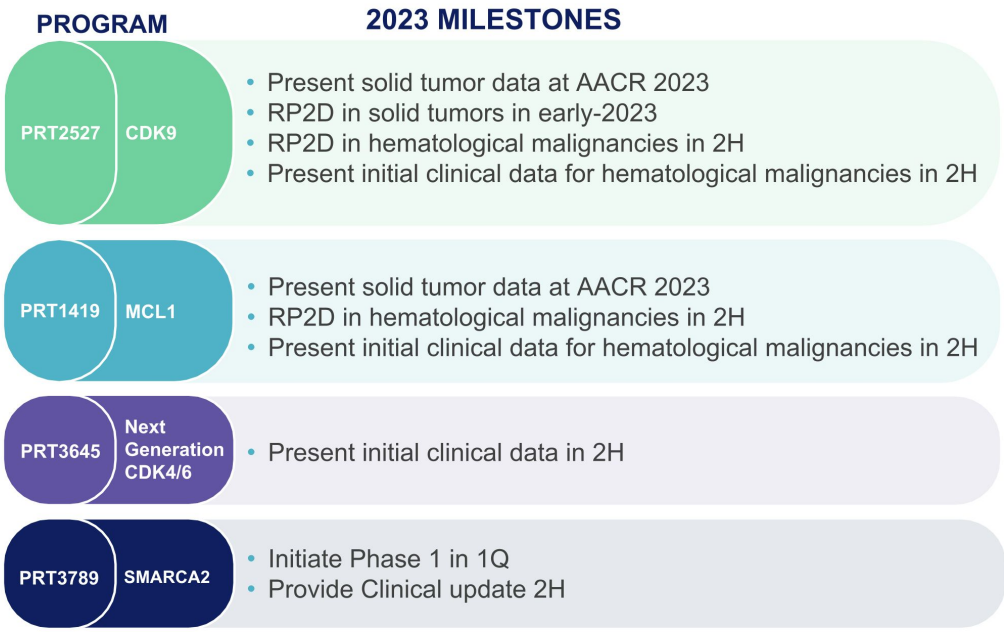
Prelude THERAPEUTICS

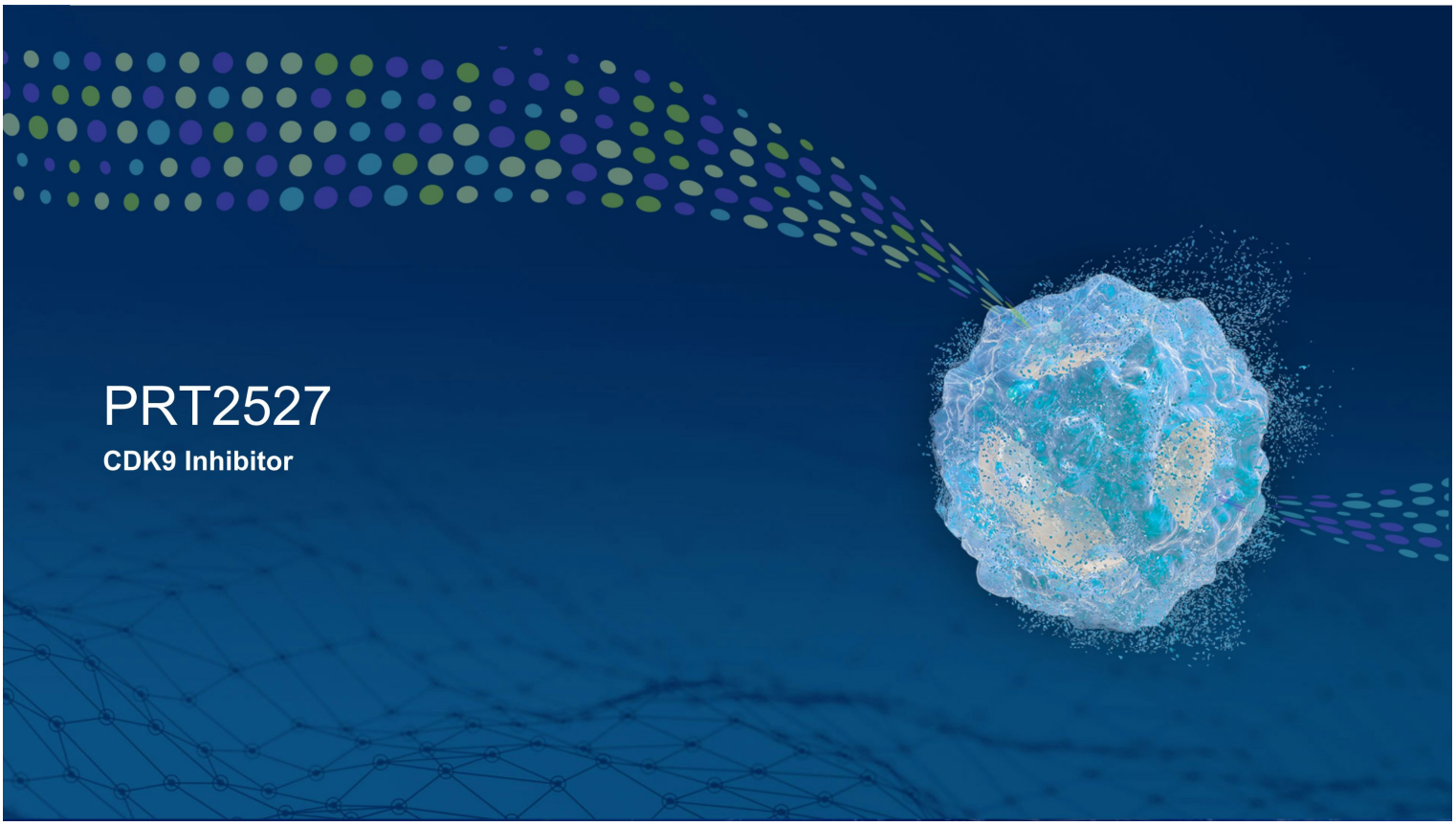
Prelude Precision Oncology Pipeline: Diversified and Differentiated

PROGRAM	CANCER INDICATIONS	DISCOVERY	PHASE 1	PHASE 2/3	AREAS OF CLINICAL FOCUS
CDK9 PRT2527	Selected solid and hematologic malignancies				R/R MCL, CLL, Aggressive Lymphomas as Monotherapy or in Combination with BTKi
MCL1 PRT1419	Selected hematologic malignancies and solid tumors				CLL Post Ven/BTKi, AML in combo with Azacitidine/Venetoclax
CDK4/6 PRT3645	Selected solid tumors				HR+/HER2-, HR+/HER2+ Breast cancer treatment through multiple lines, GBM, H&N, NSCLC in combination with KRAS inhibitors
SMARCA2 PRT3789 (IV)	Multiple genomically-selected cancers				SMARCA4 deleted NSCLC and Other cancers
SMARCA2 (Oral)	Multiple genomically-selected cancers				SMARCA4 deleted NSCLC and Other cancers
New Programs (Multiple targets)	Selected solid and hematologic malignancies				Solid Tumors Heme Malignancies

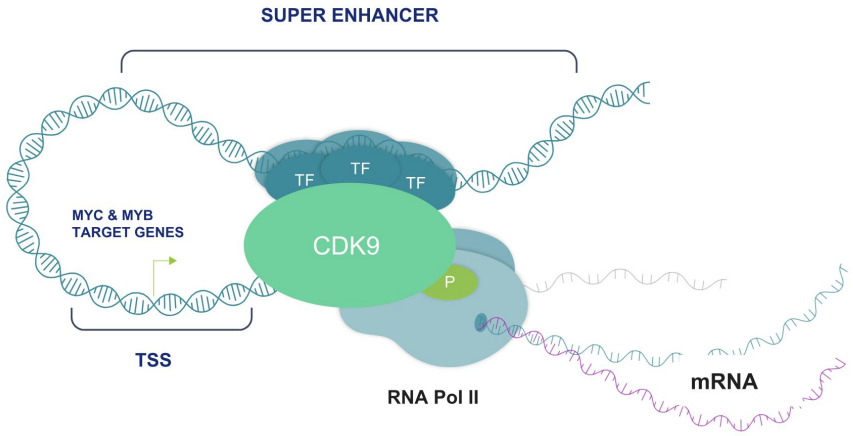
Prelude THERAPEUTICS

Driving The Programs to Key Milestones and Value Creation




PRT2527
CDK9 Inhibitor

CDK9 Inhibition: Targeting Cancer by Regulating Oncogene Expression

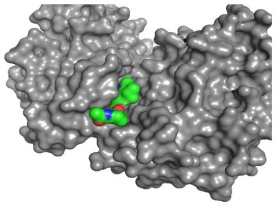


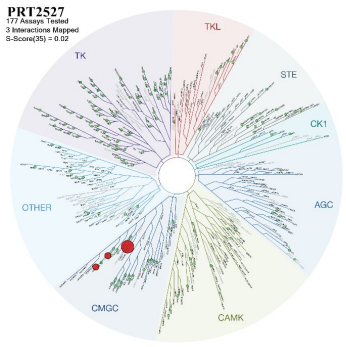
- CDK9 regulates expression of several **oncogenes that drive cancer cell growth and resistance** (i.e. MYC, MYB, MCL1)
- Non-selective CDK9 inhibitors have demonstrated clinical activity in multiple tumor types but poor tolerability
- **Improving the selectivity** of CDK9 inhibitors may translate to **better activity and safety**

Prelude THERAPEUTICS

PRT2527: Potent and Highly Selective CDK9 Inhibitor

Highly Selective, ATP Competitive CDK9 Inhibitor





Compound		AZD4573	KB0742	VIP152**	PRT2527
Biochemical* IC_{50} (nM)	**CDK9**	1.9	483	16	0.95
Proliferation* IC_{50} (nM)		11	915	84	18
Plasma* IC_{50} (nM)		192	1056	923	196
Fold Selectivity CDK9 *vs* Other Isoforms	**CDK1**	23x	>20x	371x	73x
	CDK2	35x	>20x	147x	340x
	CDK3	2x	>20x	37x	35x
	CDK4	53x	>20x	38x	250x
	CDK5	37x	>20x	>600x	>1000x
	CDK6	79x	>20x	296x	>1000x
	CDK7	150x	>20x	>600x	>1000x

>100x 100-10x <10x

*Internal data; biochemical assay at 1 mM ATP, H929 CTG proliferation assay; **VIP151 was formerly BAY151 and licensed to Vincerx by Bayer

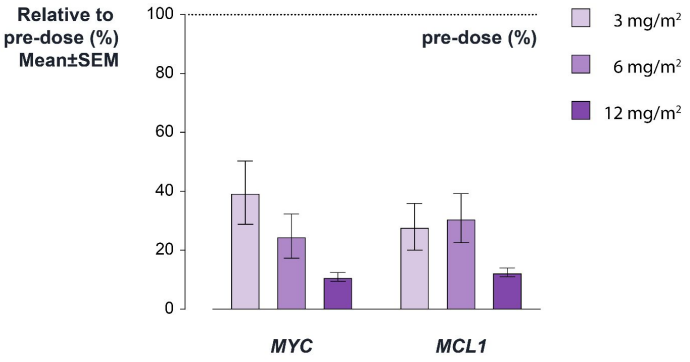
Prelude THERAPEUTICS

CDK9 inhibitor: PRT2527

Phase 1 Dose-Escalation Study in Advanced Solid Tumors

- Phase 1 dose escalation study of PRT2527 is ongoing and enrolling following tumor types
  - Selected sarcomas displaying a gene fusion
  - Castrate resistant prostate cancer
  - HR+ HER2- breast cancer
  - Non-small cell lung cancer
  - Solid tumors with MYC amplification
- Nine patients have been treated in the first three dose levels (3, 6 and 12 mg/m^2 I.V. weekly), with no dose-limiting toxicities and acceptable tolerability to date

- Dose-dependent inhibition of CDK9 transcription targets observed in PBMCs

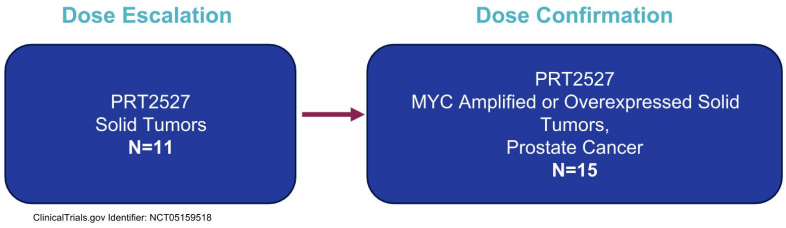


ASH Annual Meeting 2022 Abstract No. 210

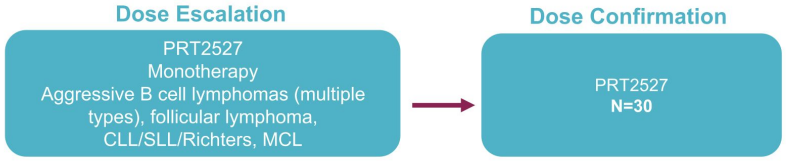
HR+ Hormone receptor positive; HER2- Human epidermal growth factor negative
ClinicalTrials.gov Identifier: NCT05159518

CDK9 Inhibitor: PRT2527

Phase 1 Studies in Solid Tumors and Hematologic Malignancies



Solid Tumor data at AACR 2023



RP2D in hematological malignancies 2H 2023
Initial clinical data in 2H 2023

ClinicalTrials.gov Identifier: NCT05665530

Solid Tumors

- Dose dependent increases in exposure and target engagement observed in Phase 1
- Clinical MYC and MCL1 depletion to levels consistent with tumor regression in preclinical models
- Generally well tolerated

Hematologic Malignancies

- ASH 2022 preclinical oral presentation
- CDK9 as a target externally validated in aggressive lymphoma and other heme malignancies

CDK9 Inhibitor Differentiation and Market Opportunity

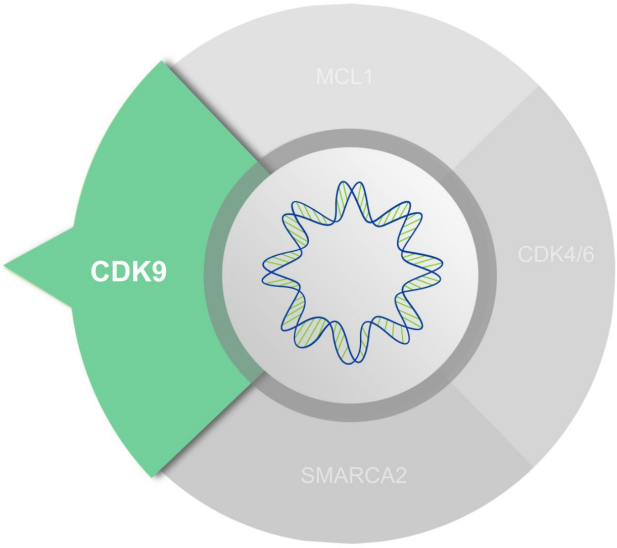
Potential for Improved Safety Based on Best-in-Class Kinome Selectivity

PRT2527 is a highly potent CDK9 inhibitor with **best-in-class kinome selectivity** compared to competitor compounds

- **Optimized PK profile** to maximize therapeutic window
- **Well-tolerated in GLP preclinical studies** at doses exceeding those required for efficacy
- **High levels of inhibition** of CDK9 dependent genes in Phase 1

Market Opportunity

- CDK9 inhibitors in CLL, Mantle cell lymphoma, and DLBCL may address areas of high unmet need

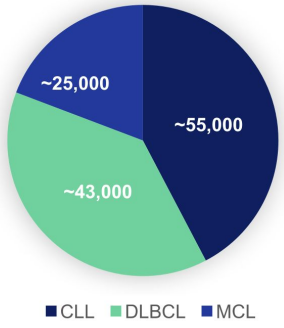


Prelude THERAPEUTICS

PRT2527: Broad Potential Addressing areas of High Unmet Need

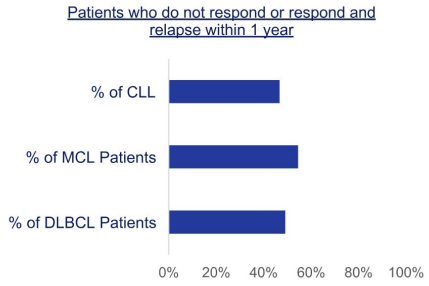
Broad Opportunity:

~125K patients treated annually(US): CLL, MCL and DLBCL[1,2,3,4,5]



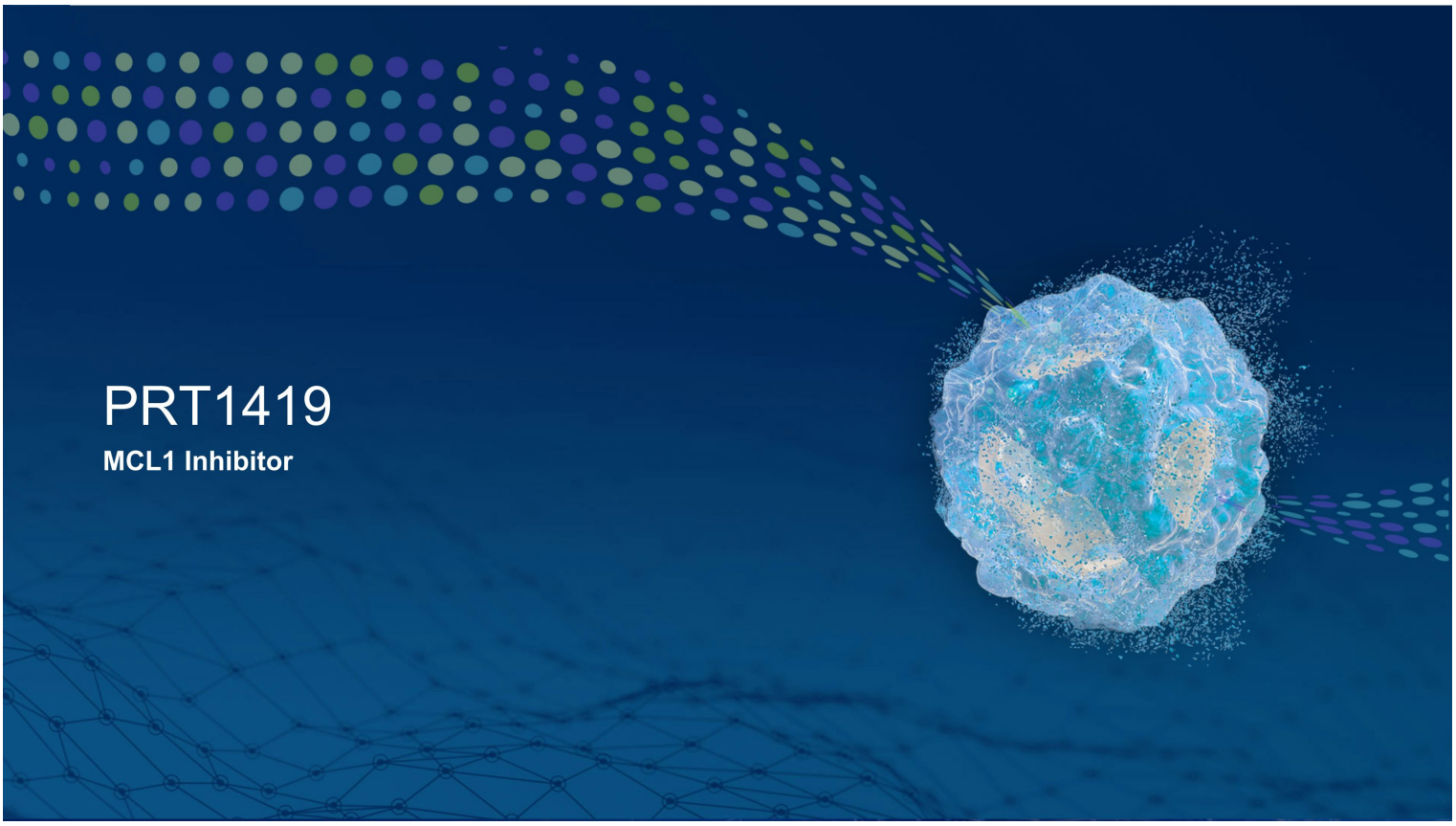
Limited Treatment Options:

***>50%** of High Risk CLL, MCL and DLBCL patients are refractory/relapsed within 1 year after 2L Treatment* [2,3]



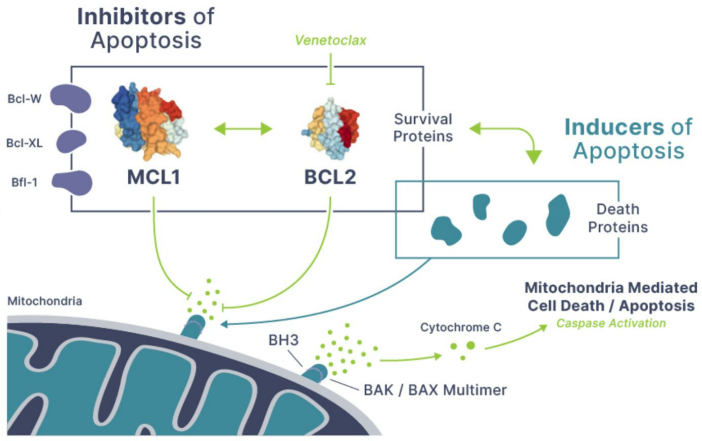
1. SEER Cancer Stat Facts: https://seer.cancer.gov/statfacts/html/clyl.html; 2. Gena Kanas, et. al. Epidemiology of diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) in the United States and Western Europe 3. CancerMPact® Treatment Architecture, Non-Hodgkin US, 4. CancerMPact® Treatment Architecture, Chronic Lymphocytic Leukeimia, US, 5. CLL Patient Based Forecast, Datamonitor Healthcare

Prelude THERAPEUTICS


PRT1419
MCL1 Inhibitor

MCL1 inhibition: Targeting Cancer Cell Survival

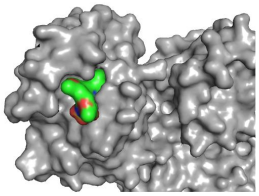
Mechanism



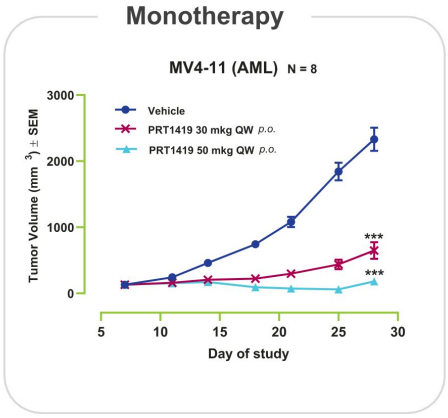
- MCL1 is a member of the **BCL2 family of inhibitors** of apoptosis
- **Established resistance** mechanism to the BCL2 inhibitor Venetoclax
- Prolonged depletion of MCL1 is undesirable and may be associated with cardiac toxicity
- Optimizing the PK profile of an MCL1 inhibitor may **maximize the therapeutic window**

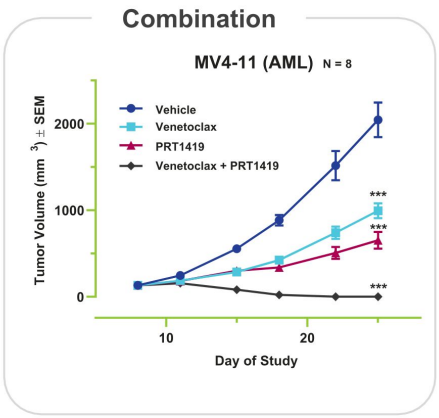
PRT1419 is Potent MCL1 Inhibitor with Demonstrated Preclinical Activity as Monotherapy and in Combination

Prelude compounds are competitive inhibitors of BIM binding



	Proliferation IC_{50} (nM)	Whole Blood IC_{50} (nM)
AMG176	150	1800
AZD5991	31	320
MIK665	4.5	430
PRT1419	80	210

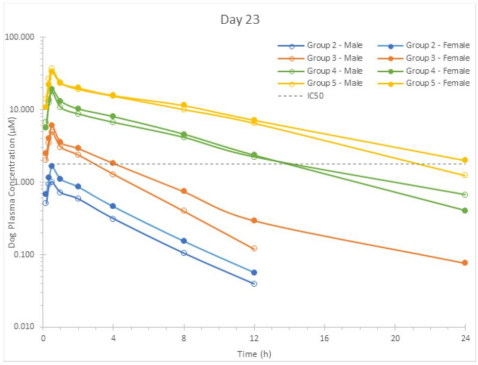




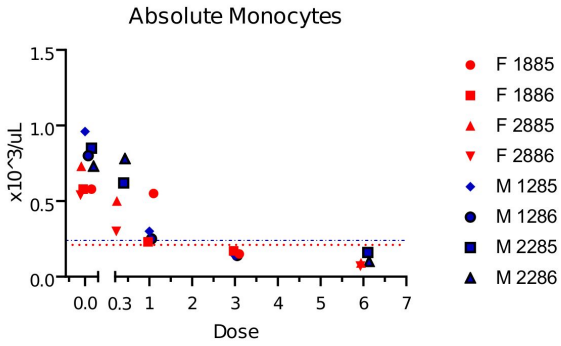
Robust monotherapy activity also seen in models of DLBCL & MM

PRT1419 Does Not Cause Cardiac Injury in Preclinical Toxicology Studies

Pharmacokinetics



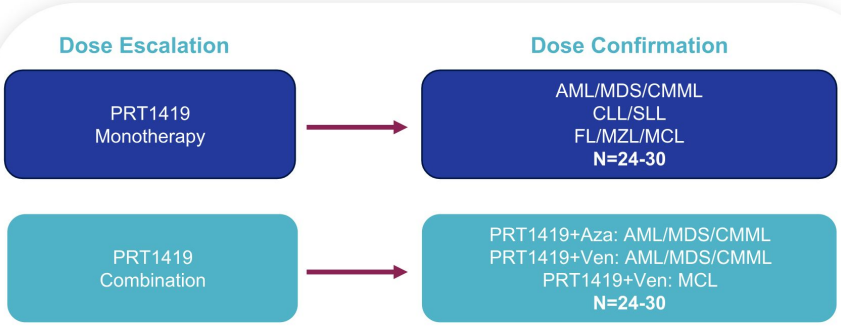
Pharmacodynamics



- Doses: 0.3, 1, 3 and 6 mg/m2; once weekly
- Linear increases in exposure
- No troponin elevations observed at any doses, even high dose which covered EC90 for 24h
- No histopathological evidence of cardiac injury

MCL1 inhibitor: PRT1419

Phase 1 Study in Hematologic Malignancies



RP2D in heme monotherapy expected 2H 2023
Initial clinical data in 2H 2023

- In the solid tumor PRT1419 dose escalation Phase 1, 26 patients have been treated and 15 patients @ RP2D
- No cardiac toxicity seen @ RP2D as measured by ejection fraction decline/troponin elevation
- Solid tumor data to be presented 1H 2023
- Upregulation of MCL1 is a mechanism of resistance to BCL2 inhibition, particularly in CLL and AML; Strong preclinical hypothesis in heme[1]

ClinicalTrials.gov Identifier: NCT05107856

[1] Ong et al. Cancer Drug Resist 2022;5:380-400

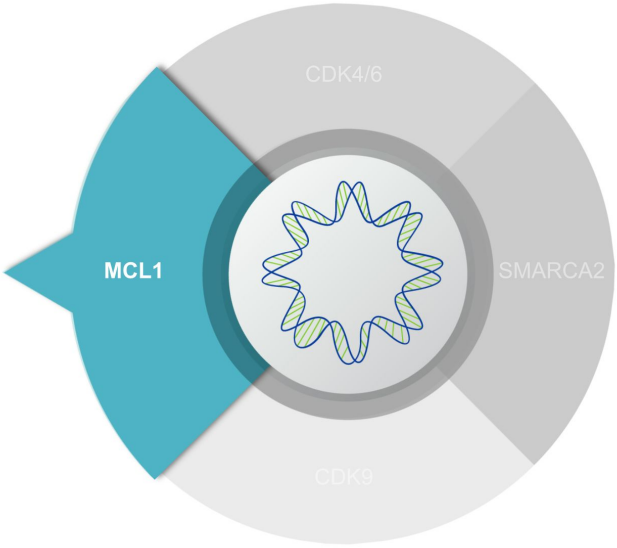
MCL1 Inhibitor Differentiation and Market Opportunity

Optimized PK Profile to Achieve Desired Target Engagement

- PRT1419 is a **highly potent and selective** MCL1 inhibitor
- Designed to have a PK profile with **high clearance** to provide desired target engagement with **improved safety**
- **No cardiotoxicity or troponin changes** in GLP preclinical studies at doses exceeding those required for efficacy
- **No evidence of cardiotoxicity** in the solid tumor Phase 1 at the recommended Phase 2 dose

Market Opportunity

- AML, MDS, CLL, MCL patients need additional treatment options



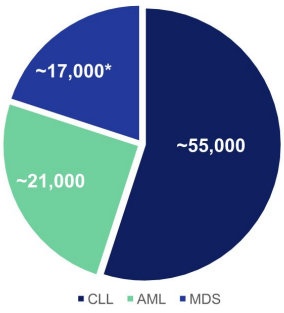
Prelude THERAPEUTICS

PRT1419: MCL1 Inhibitor Offers Potential Benefit for Patients with Poor Outcomes

Broad Opportunity:

~95K patients treated annually(US): CLL, AML, MDS [1,2,3,4]

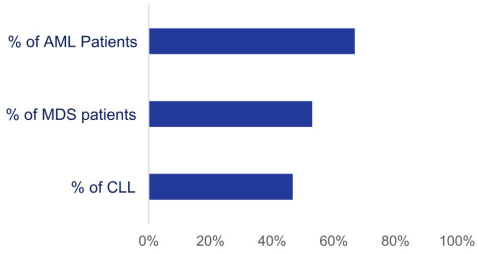
Annual Treated Patients (US Only)



Outcomes for relapsed / refractory patients are poor:

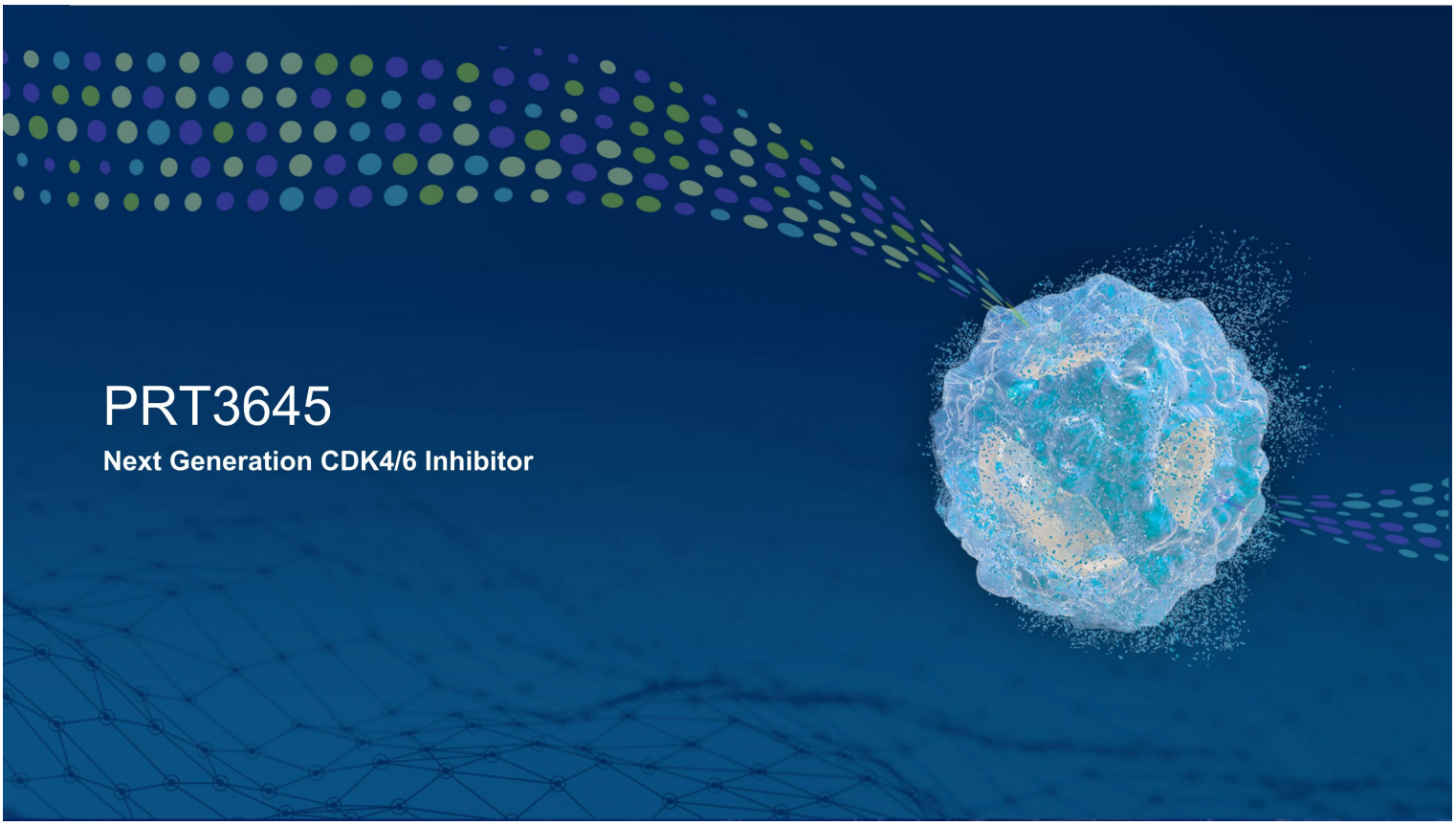
>50% *of CLL, High Risk MDS and Unfit AML patients are refractory/relapsed within 1 year after second relapse*[2,3,4]

Patients who do not respond or respond and relapse within 1 year



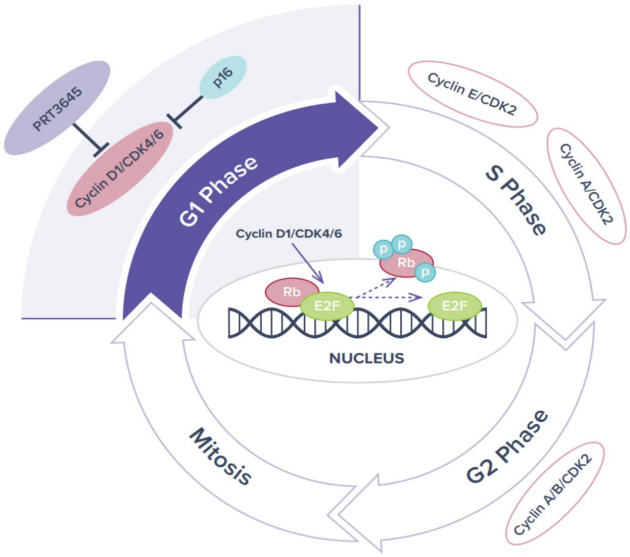
1. SEER, https://seer.cancer.gov/statfacts/html/clyl.html; 2,3,4, CancerMPact® Treatment Architecture, * MDS number represents annual incident patients, treated patient number may be higher.

Prelude THERAPEUTICS


PRT3645
Next Generation CDK4/6 Inhibitor

Next Generation CDK4/6 Inhibition: Targeting Cancer Through Cell Cycle Regulation

Mechanism



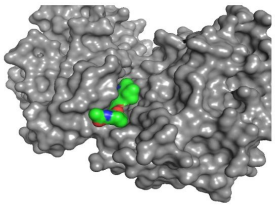
- **Validated mechanism** with approval of Next Generation CDK4/6 inhibitors in HR+ breast cancer
- **Resistance mechanism** to other targeted therapies including KRAS G12C inhibitors
- Current CDK4/6 inhibitors limited by poor tolerability and lack broad tissue penetration
- Next generation CDK4/6 inhibitor with **improved tolerability and tissue penetrance** could translate into **activity in areas of unmet need** beyond HR+ breast cancer
- Sequential use of Next Generation CDK4/6 inhibitors in breast cancer may also improve outcomes

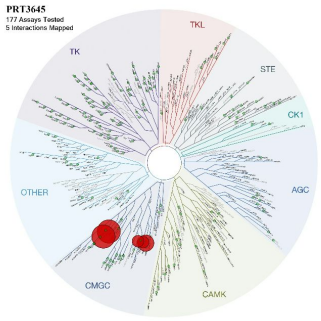
Prelude THERAPEUTICS

PRT3645 – Highly Selective Next Generation CDK4/6 Inhibitor

Bias towards CDK4 over CDK6

Highly Selective, ATP Competitive





Compound		Palbociclib	Abemaciclib	PRT3645
Biochemical* IC_{50} (nM)	CDK4	25	5	3
Proliferation* IC_{50} (nM)		52	70	47
Phospho-Rb* IC_{50} (nM)		28	30	16
Fold Selectivity CDK4 *vs* Other Isoforms	CDK6	1x	6x	5x
	CDK1	>500x	>500x	>500x
	CDK2	>500x	173x	>500x
	CDK3	>500x	212x	>500x
	CDK5	>500x	>500x	>500x
	CDK7	>500x	>500x	>500x
	CDK9	209x	59x	>500x

>500x 500-50x 50-5x <2x

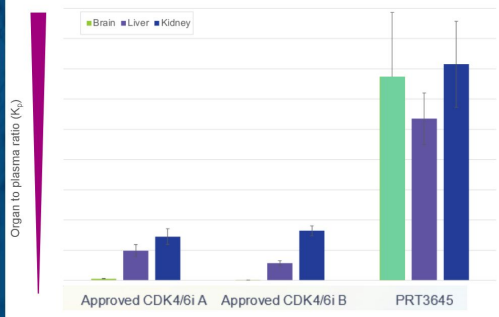
*Internal data; biochemical assay at 1 mM ATP, MCF7 CTG proliferation assay; MCF7 pRB

Prelude THERAPEUTICS

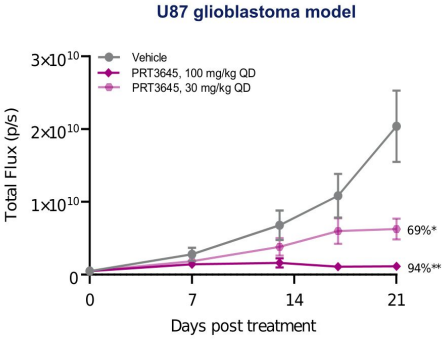
Next Generation CDK4/6 inhibitor PRT3645

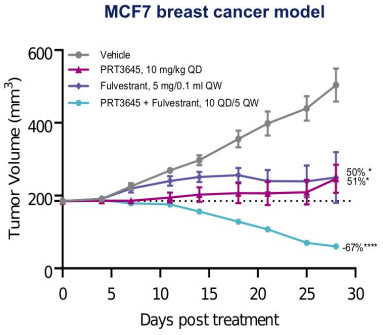
Improved Tissue Penetration and Robust Activity in Preclinical Models

PRT3645 demonstrates higher brain penetration than approved CDK4/6 inhibitors



PRT3645 shows robust activity in vivo as monotherapy and in combination

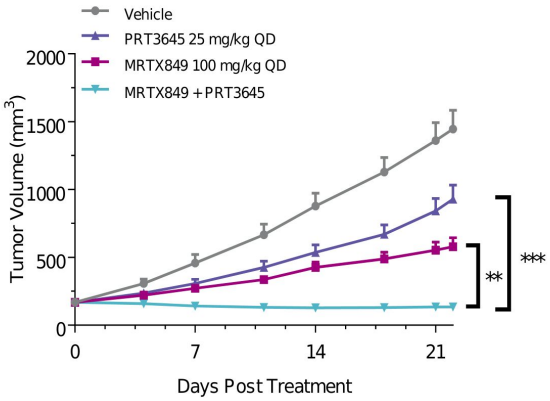




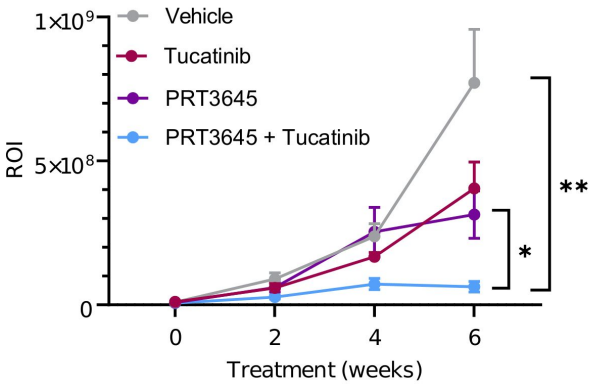
Prelude THERAPEUTICS

Novel Combinations to Extend the Potential of CDK4/6 Inhibition Beyond ER+ Breast Cancer

H2122 NSCLC Model



DFBM-355 PDX model of ER+/HER2+ Breast Cancer



PRT3645 significantly enhances the activity of KRAS G12C inhibitor in NSCLC models and with HER2 kinase inhibitor in ER+/HER2+ BC models

Next Generation CDK4/6 Inhibitor: PRT3645

Phase 1 Study in Solid Tumors

Dose Escalation and Confirmation

PRT3645
Biomarker enriched patients with select tumor types including sarcomas, mesothelioma, gliomas, head and neck cancers and non-small cell lung cancer, in addition to breast cancer with or without brain metastases

Initial clinical data in 2H 2023
RP2D in solid tumors in 2H 2024

ClinicalTrials.gov Identifier: NCT05538572

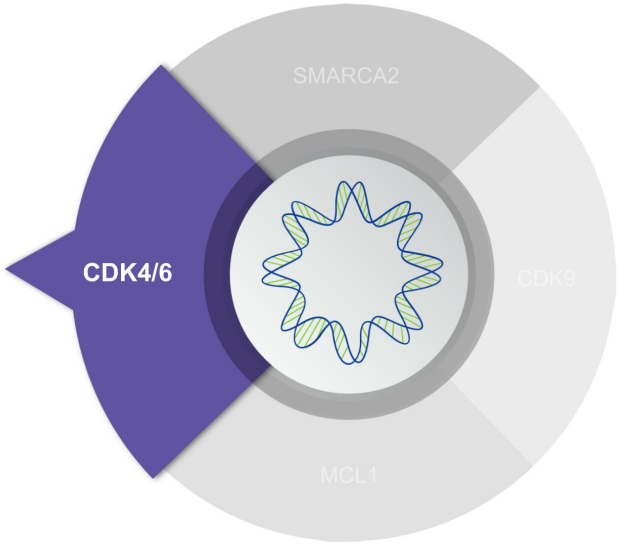
- A differentiated and highly brain penetrant Next Generation CDK4/6 inhibitor
- Potential to extend the reach of CDK4/6 inhibition beyond HR+ breast cancers, for which the first generation CDK4/6 inhibitors were approved

Prelude THERAPEUTICS

Next Generation CDK4/6 Inhibitor Differentiation and Market Opportunity

Deep Tissue Penetration with Potential for Activity in Areas of Unmet Need

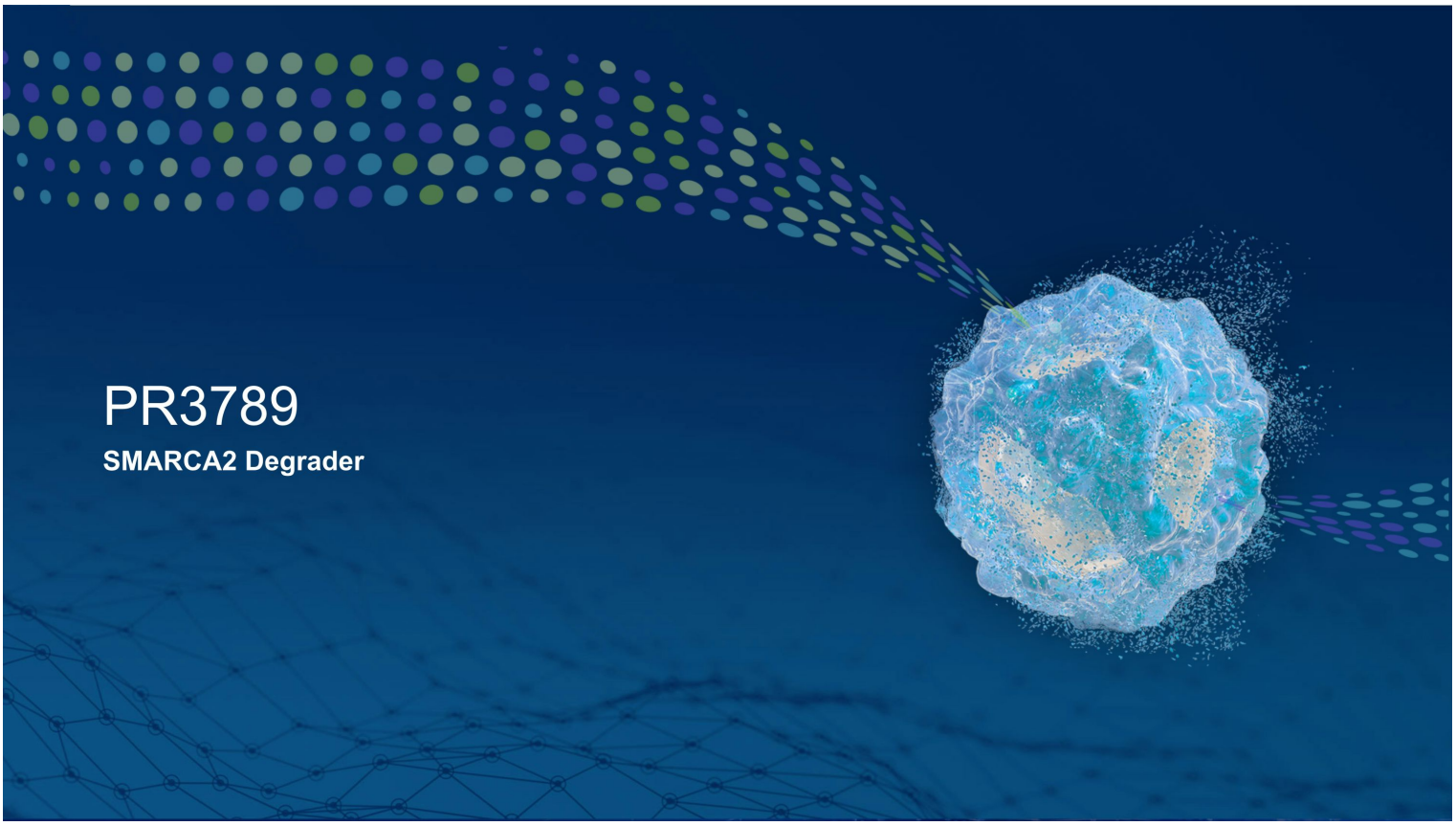
- PRT3645 is a **highly potent and selective** Next Generation CDK4/6 inhibitor
- Optimized to demonstrate **deep tissue penetration including brain penetrance**
- **Improved metabolic profile** to allow for combination treatment in diseases beyond breast cancer
- **Reduced toxicity** in preclinical GLP studies with **potential for improved tolerability** in the clinic



Market Opportunity:

- Breast cancer patients may benefit from sequential CDK4/6 inhibitors treatment
- There are estimated to be 65,000 breast cancer patients treated with CDK4/6 inhibitors in 2023 in the U.S.
- Other solid tumors (lung cancer, glioma, HER2+ breast cancer) may demonstrate activity in combination

Prelude THERAPEUTICS

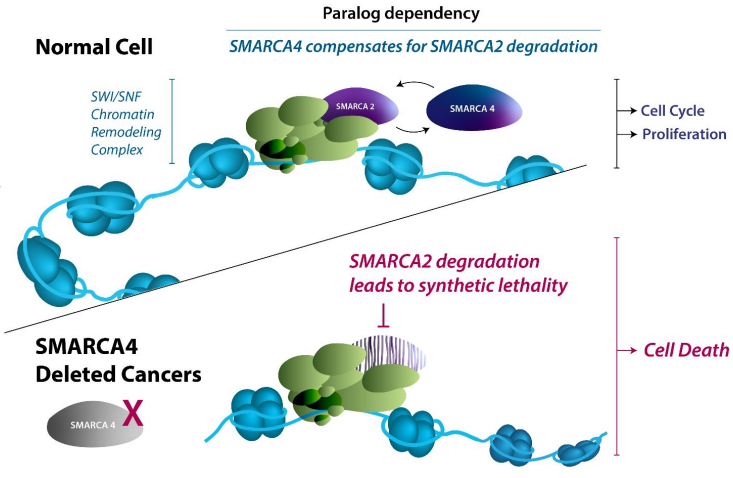


PR3789

SMARCA2 Degrader

Targeting SMARCA2 (BRM): Leveraging Synthetic Lethality

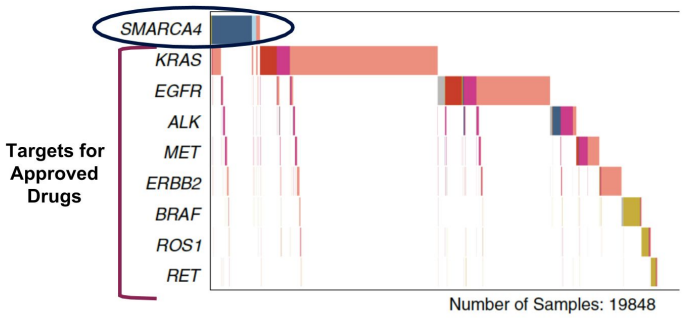
Mechanism



- The chromatin remodeling (SWI/SNF) complex is frequently mutated in cancer making it a **potential therapeutic target**
  - Activity of the SWI/SNF complex requires either SMARCA4 (BRG1) or SMARCA2 (BRM)
  - Loss of SMARCA4 (BRG1) through mutation leads to dependency on SMARCA2 (BRM)
  - Subsets of solid tumors express SMARCA4 (BRG1) mutations
  - Selectively inhibiting SMARCA2 (BRM) offers an attractive approach to target SMARCA4 (BRG1) mutant tumors

SMARCA4 Mutations in NSCLC: An Opportunity with No Approved Therapies

SMARCA4 Deletion – A Novel Biomarker for NSCLC



Fernando et al. Nature Communications 2020

SMARCA4 Prevalence across selected Solid Tumors

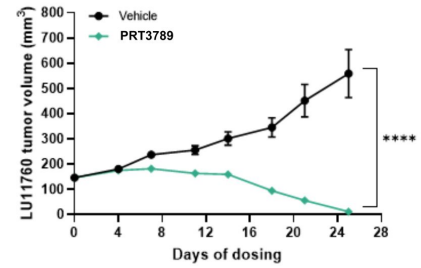
Indication	Any SMARCA4 Mutation[1]
NSCLC	10.0%
Esophageal	8.0%
Gastric (stomach adeno)	8.3%
Skin (invasive and in situ melanoma)*	21.0%
Endometrial (uterine corpus)	13.3%
Squamous cell lung	7.7%
Urinary (bladder)	9.0%
Colorectal	6.0%
Pancreatic	2.9%
Melanoma (invasive)	8.7%

1.cBioPortal; FoundationCore; 2.SMARCA4 LOF mutations included homozygous missense, hotspot mutations with LOF, and damaging mutations; 3.SEER 2022; Globocan; * Source: American Cancer Society – Cancer Facts & Figures 2022

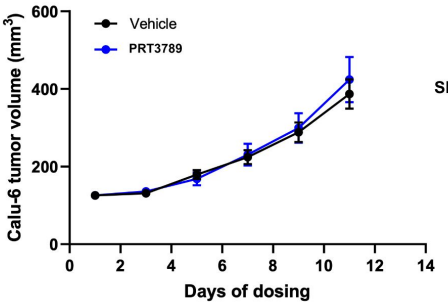
Prelude THERAPEUTICS

PRT3789: Potent and Selective SMARCA2 Degrader with *In Vivo* Activity

Robust Tumor Growth Inhibition of SMARCA4 mutated but not WT Xenograft

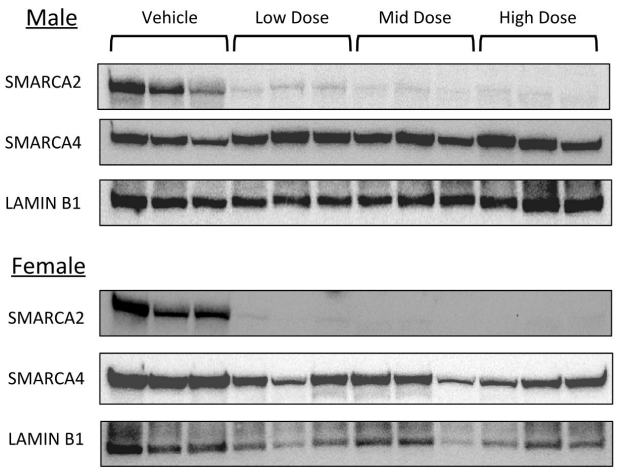


SMARCA4 mutant



SMARCA4 WT

Significant Degradation of SMARCA2 Protein but not SMARCA4 in Preclinical Models



Prelude THERAPEUTICS

SMARCA2 Degrader: PRT3789

Phase 1 Study in Solid Tumors

Dose Escalation and Confirmation

PRT3789
Solid Tumors with loss of SMARCA4
Backfill: up to 10 participants with a minimum of 6 NSCLC participants with loss of SMARCA4

IND cleared Q4 2022
Clinical update expected 2H 2023

- SMARCA2 inhibition has the greatest potential in patients with SMARCA4 deficient cancers, including approximately 10-20% of all non-small cell lung cancers
- SMARCA2 degradation to be evaluated in Phase 1
- Study population: advanced, recurrent, or metastatic disease, with loss of SMARCA4 due to truncating mutation and/or deletion
- Biomarker selected by local NGS or IHC in tumor tissue or blood

ClinicalTrials.gov Identifier: NCT05639751

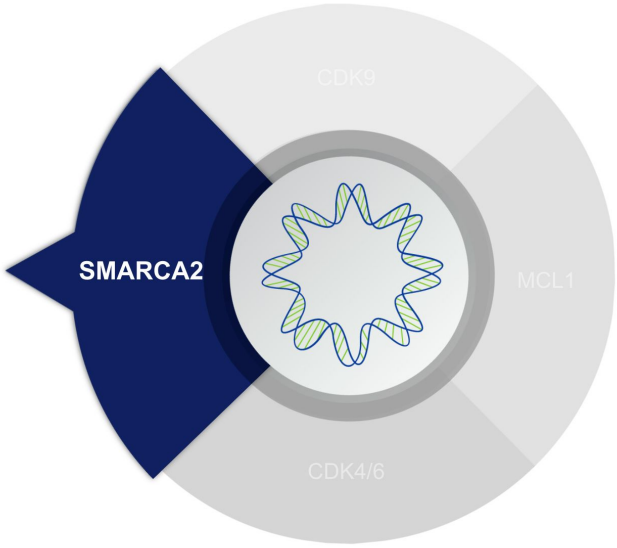
SMARCA2 Differentiation and Market Opportunity

Potential First-in-Class SMARCA2 (BRM) Targeted Protein Degrader

- PRT3789 is **a first-in-class** SMARCA2 Degrader
- **Potent and selective** over the related isoform, SMARCA4, through a targeted protein degrader approach
- **Improved tolerability** compared to non-selective SMARCA2 inhibition
- **Robust efficacy** in SMARCA4 mutant preclinical models, providing **clear patient selection strategy** in the clinic

Market Opportunity:

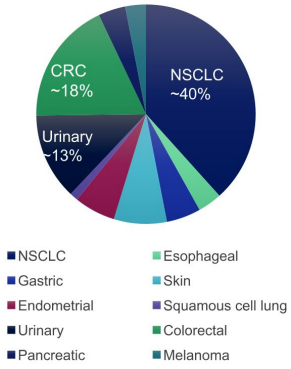
- 70,000 patients with SMARCA4 mutation in the US/EU5



PRT3789: Large Pan-Tumor Unmet Need in Patients with SMARCA4 Mutation

Broad Opportunity:

Distribution of Patients with SMARCA4 mutation by Tumor, based on study of ~130k patients[1,2,3]



Improvement vs SoC:

Most common 2L mNSCLC regimen offers minimal benefit and significant toxicity [4]

mPFS ~ 4.5 months

docetaxel + ramucirumab

SMARCA 4 Degrader offers:

First in Class Treatment Option in patients with no approved drugs

1. Fernando, T.M., Piskol, R., Bainer, R. *et al.* Functional characterization of *SMARCA4* variants identified by targeted exome-sequencing of 131,668 cancer patients..https://doi.org/10.1038/s41467-020-19402-8; 2. https://www.mycancergenome.org/content/gene/smarca4/ 3. US SEER Database 4. CancerMPact® Treatment Architecture, NSCLC – Non Driver Mutation.

Prelude THERAPEUTICS

Prelude Therapeutics: Key Takeaways and Reasons to Invest

- Deep clinical pipeline with unique and potentially **best-in-class or first-in-class molecules**
- Opportunity to drive programs to key inflection points in the next **12 – 24 months**
- Emerging clinical data on CDK9 and MCL-1 programs demonstrate the potential for **class-leading opportunities**
- Potentially **first-in-class SMARCA2 degrader program** with a significant lead over competitors and offers transformational potential for the company
- Current cash runway expected through **Q4 2024**

Prelude THERAPEUTICS

Experienced Management Team: Proven Track Records

Kris Vaddi, PhD

Founder & Chief Executive Officer

Jakafi (ruxolitinib tablets)
olumiant (baricitinib tablets) 2mg
TABRECTA (capmatinib) tablets
VELCADE (bortezomib)

Jane Huang M.D.

President and Chief Medical Officer

Brukinsa (zanubrutinib) 80mg capsules
CALQUENCE (acalabrutinib) 100 mg capsules
VENCLEXTA venetoclax tablets 10mg, 50mg, 100mg
GAZYVA obinutuzumab injection 1,000mg/40mL
Kadcyla ado-trastuzumab emtansine
AVASTIN bevacizumab

Peggy Scherle, PhD

Chief Scientific Officer

Jakafi (ruxolitinib tablets)
olumiant (baricitinib tablets) 2mg
Pemazyre (pemigatinib tablets)
TABRECTA (capmatinib) tablets

Andrew Combs, PhD

Executive Vice President and Head of Chemistry

Jakafi (ruxolitinib tablets)
olumiant (baricitinib tablets) 2mg

Laurent Chardonnet, MBA

Chief Financial Officer

Incyte
axcella
sanofi

Bryant Lim, J.D.

Chief Legal Officer and Corporate Secretary

MERCK
ViroPharma Incorporated
Incyte
idera

Exhibit 99.3

Prelude Therapeutics Announces Clinical Trial Collaboration with BeiGene to Evaluate PRT2527 in Combination with Zanubrutinib in Hematologic Cancers

WILMINGTON, Del. – March 15, 2023 – Prelude Therapeutics Incorporated (Prelude) (Nasdaq: PRLD), a clinical-stage precision oncology company, today announced a clinical trial collaboration with BeiGene, for future evaluation of its investigational CDK9 inhibitor, PRT2527, in combination with BeiGene's BTK inhibitor, zanubrutinib, in hematologic malignancies.

Inhibition of BTK is an active therapeutic approach in several B cell malignancies and the combination of CDK9 inhibition with BTK inhibition has demonstrated, in recent data publications, synergistic clinical efficacy over BTK inhibition alone; hence, there is a strong rationale for studying the combination in patients with certain hematologic malignancies.

"The opportunity to combine Prelude's potent, selective and potentially best-in-class CDK9 inhibitor with BeiGene's next-generation highly efficacious and tolerable BTK inhibitor, zanubrutinib, reflects our commitment to bringing the most promising options to patients," said Jane Huang, MD, President and Chief Medical Officer, Prelude Therapeutics.

Under terms of the clinical trial collaboration agreement, BeiGene will provide zanubrutinib to Prelude, and Prelude will retain all global operational, development and commercialization rights and responsibilities for PRT2527.

About PRT2527

PRT2527 was designed to be a potent and selective Cyclin-dependent kinase 9, or CDK9, inhibitor. In preclinical studies, PRT2527 was shown to reduce MCL1 and MYC protein levels and was highly active in preclinical models at well-tolerated doses. PRT2527 has demonstrated high potency and kinase selectivity which may offer improved efficacy and safety compared to less selective CDK9 inhibitors, allowing for rapid development in combinations. PRT2527 is currently being studied as monotherapy in a Phase 1 dose-escalation study in advanced solid tumors, as well as in relapsed/refractory hematologic malignancies.

About Prelude Therapeutics

Prelude Therapeutics is a clinical-stage precision oncology company developing innovative drug candidates targeting critical cancer cell pathways. Prelude's diverse pipeline is comprised of highly differentiated, potentially best-in-class and first-in-class proprietary small molecule compounds aimed at addressing clinically validated pathways for cancers with selectable underserved patients. Prelude's pipeline includes four candidates currently in clinical development: PRT1419, a potent, selective inhibitor of MCL1, PRT2527, a potent and highly selective CDK9 inhibitor, PRT3645, a next-generation CDK4/6 inhibitor, and PRT3789 a first-in-class SMARCA2/BRM protein degrader.

For more information, visit our website and follow us on LinkedIn and Twitter.

About zanubrutinib

Zanubrutinib is a small-molecule inhibitor of Bruton's tyrosine kinase (BTK) discovered by BeiGene scientists that is currently being evaluated globally in a broad clinical program as a monotherapy and in combination with other therapies to treat various B-cell malignancies. Zanubrutinib was specifically designed to deliver targeted and sustained inhibition of the BTK protein by optimizing bioavailability, half-life, and selectivity. With differentiated pharmacokinetics compared

to other approved BTK inhibitors, zanubrutinib has been demonstrated to inhibit the proliferation of malignant B cells within a number of disease-relevant tissues.

Zanubrutinib is supported by a broad clinical program which includes more than 4,700 subjects in 35 trials in more than 30 geographies. To date, zanubrutinib (BRUKINSA®) is approved in over 60 markets, including the United States, China, the European Union, Great Britain, Canada, Australia, South Korea, Iceland, Norway and Switzerland.

About BeiGene

BeiGene is a global biotechnology company that is developing and commercializing innovative and affordable oncology medicines to improve treatment outcomes and access for far more patients worldwide. With a broad portfolio, we are expediting development of our diverse pipeline of novel therapeutics through our internal capabilities and collaborations. We are committed to radically improving access to medicines for far more patients who need them. Our growing global team of more than 9,000 colleagues spans five continents, with administrative offices in Beijing, China; Cambridge, U.S.; and Basel, Switzerland. To learn more about BeiGene, please visit www.beigene.com and follow us on Twitter at @BeiGeneGlobal.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, anticipated discovery, preclinical and clinical development activities, timing of availability and announcements of clinical results for PRT2527, the timing of reporting expected findings related to PRT2527, the potential benefits of Prelude's product candidates, alone or in combination, and the sufficiency of cash and cash equivalents to fund operating expenses and capital expenditures into the fourth quarter of 2024. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Although Prelude believes that the expectations reflected in such forward-looking statements are reasonable, Prelude cannot guarantee future events, results, actions, levels of activity, performance or achievements, and the timing and results of biotechnology development and potential regulatory approval is inherently uncertain. Forward-looking statements are subject to risks and uncertainties that may cause Prelude's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to Prelude's ability to advance its product candidates, the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, the impact of the COVID-19 pandemic on Prelude's business, clinical trial sites, supply chain and manufacturing facilities, Prelude's ability to maintain and recognize the benefits of certain designations received by product candidates, the timing and results of preclinical and clinical trials, Prelude's ability to fund development activities and achieve development goals, Prelude's ability to protect intellectual property, and other risks and uncertainties described under the heading "Risk Factors" in documents Prelude files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and Prelude undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

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