



Rain Oncology Inc.

CORPORATE PRESENTATION – Mar 2023



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This presentation contains “forward-looking statements” within the meaning of the federal securities laws, which statements are subject to substantial risks and uncertainties and are based on estimates and assumptions. Other than statements of historical facts, all statements included in this presentation are forward-looking statements, including statements concerning the ability of our clinical trials to demonstrate safety and efficacy of our product candidates and other positive results, the timing and focus of our ongoing and future preclinical studies and clinical trials, the design of those studies and trials, and the reporting of data from those studies and trials, the timing for enrollment of trials, our plans relating to commercializing our product candidates, if approved, including the geographic areas of focus and sales strategy, the size of the market opportunity for our product candidates, including our estimates of the number of patients who suffer from the diseases we are targeting, our expectations regarding the approval and use of our product candidates as first, second or subsequent lines of therapy or in combination with other drugs, the success of competing therapies that are or may become available, our estimates of the number of patients that we will enroll in our clinical trials, the beneficial characteristics, safety, efficacy and therapeutic effects of our product candidates, the timing or likelihood of regulatory filings and approvals, including our expectation to seek an accelerated approval pathway and special designations, such as orphan drug designation, for our product candidates for various diseases, our ability to obtain and maintain regulatory approval of our product candidates, and our plans relating to the further development of our product candidates, including collaborations with research partners and additional indications we may pursue. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “design,” “estimate,” “predict,” “potential,” “plan” or the negative of these terms, and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the forward-looking statements expressed or implied in this presentation including our limited operating history, the significant losses that we have incurred since inception, the substantial additional capital that we will require to finance our operations in the future, our ability to identify and acquire or in-license products, our dependence on our lead candidates, our ability to enroll patients in our clinical trials, the fact that interim results of our clinical trials may not be indicative of future results and those risks described in “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K for the year ended December 31, 2022 and subsequent filings with the Securities and Exchange Commission.

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We obtained the industry, market and competitive position data used throughout this presentation from our own internal estimates and research, as well as from industry and general publications, and research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of the industry and market, which we believe to be reasonable. In addition, while we believe the industry, market and competitive position data included in this presentation are reliable and based on reasonable assumptions, we have not independently verified any third-party information, and all such data involve risks and uncertainties and are subject to change based on various factors. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

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Executive Officer



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Cofounder, President & Chief
Scientific Officer



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Executive VP &
Chief Medical Officer



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Senior VP,
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Mehdi Paborji, PhD
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Compliance Officer



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Rain Oncology Overview

Milademetan (RAIN-32), an oral inhibitor of the MDM2-p53 complex, represents a “pipeline in a program”



PRECISION ONCOLOGY STRATEGY

Milademetan offers an opportunity to treat a significant number of cancers across multiple tumor types with an oral, small molecule inhibitor of the MDM2-p53 complex



ATTRACTIVENESS OF REGULATING MDM2-p53 COMPLEX

Loss of the transcription factor p53 can facilitate tumor growth, with elevated levels of MDM2 facilitating wildtype p53 loss

Up to 50% of cancers may be addressable by impeding the MDM2-p53 interaction and restoring p53 and its protective properties



MILADEMETAN ADDRESSES HISTORICAL PITFALLS OF THE CLASS

Perturbances of the MDM2-p53 complex in blood cells leads to on-target cell death and cytopenias, predominately thrombocytopenia

Milademetan represents the first potential NDA filing for an inhibitor of the MDM2-p53 complex in the US, with a novel dose schedule devised to address historical on-target limitations



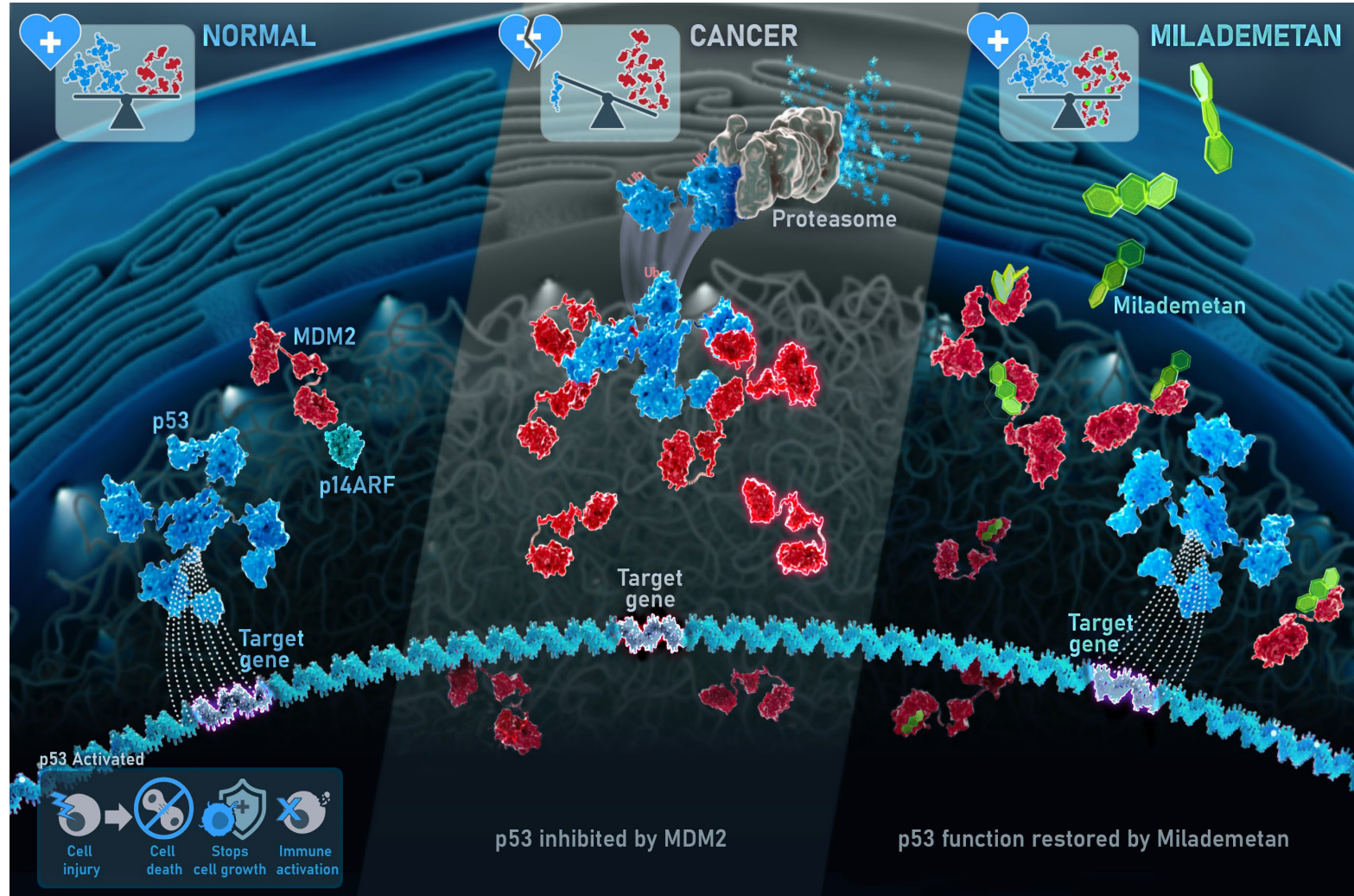
STRONG CASH POSITION TO ADVANCE ONGOING & PLANNED TRIALS

With a year-end cash balance of over \$130 million, Rain is well-financed to complete several trials for milademetan, including the phase 3 registrational study in liposarcoma

Rain has no exposure to any liquidity concern at Silicon Valley Bank



MDM2-p53 Axis & Milademetan MoA



Source: Rain Oncology

Wildtype p53 responds to normal cellular injury to protect against cancer via induction of cellular apoptosis or senescence

- Mutated p53 incapable of target gene binding and function

Dysregulated MDM2 can facilitate or support oncogenicity

- *MDM2* gene amp
- MDM2 over-expression
- MDM2 regulator loss (*CDKN2A/p14ARF*)

As an inhibitor of the MDM2-p53 interaction, milademetan restores wildtype p53



Rain Oncology: Overview

With a year-end cash balance of over **\$130 million**, Rain is well-financed to complete several trials for milademetan, including the phase 3 registrational study in liposarcoma

Milademetan (RAIN-32)								
INDICATION	MANTRA	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER	PLANNED DATA	2022 ELIGIBLE ANNUAL US POP
DD Liposarcoma	--	Mila monotherapy	Enrollment Completed			-	2Q 2023	~1,400
MDM2-amp Basket	2	Mila monotherapy	Enrolling			-	-	~8,000
CDKN2A loss, p53 WT Adv Solid Tumors	4	Mila + atezolizumab	Planned: Mid 2023				-	~45,000

Rain anticipated clinical studies

Milademetan

Phase 3 MANTRA

(Dedifferentiated Liposarcoma)



Liposarcoma Overview

PFS is the primary outcome measured in most sarcomas

TOTAL ADDRESSABLE MARKET

Liposarcoma is 20% of all sarcomas²

Liposarcoma US annual incidence ~3,500¹

WD/DD is 65% of LPS and p53 WT & MDM2 amplified in nearly 100% of WDLS/DDLS cases³⁻⁶

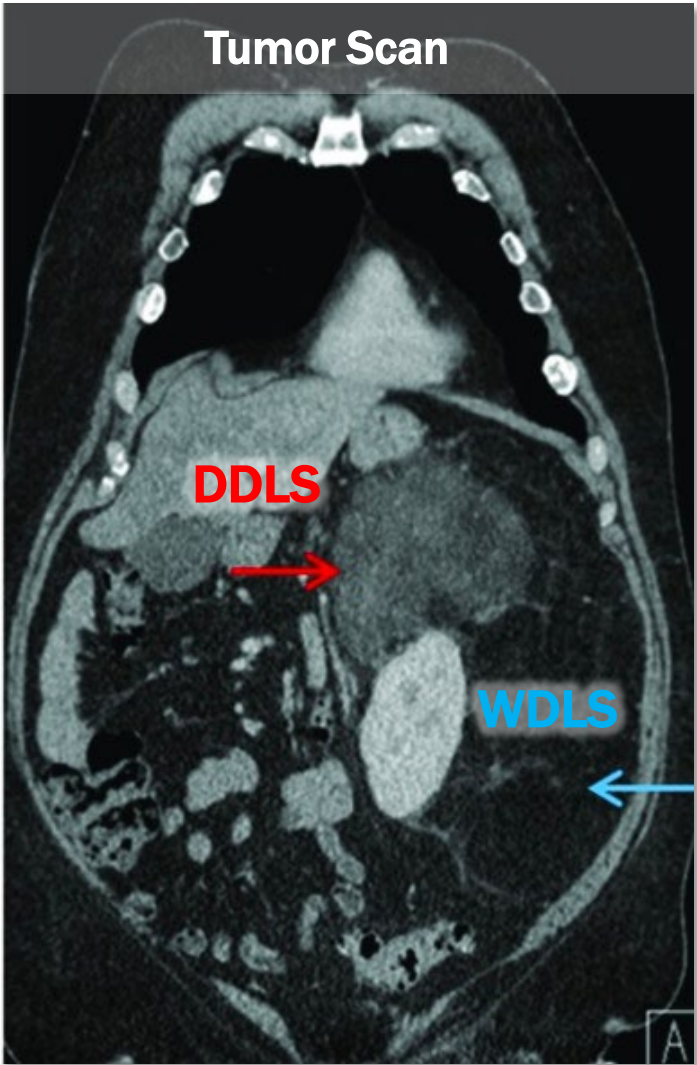
DD LPS incidence ~2,300

Annual US Addressable Market⁷

TAM in DD LPS ~1,400

APPROVED THERAPIES IN LPS

Drug	Company	Approved	Mechanism	Efficacy in DD LPS (mPFS)
 Yondelis (trabectedin)		2015	DNA binding / alkylator	2.2 mo ⁸
 Halaven (irinotecan mesylate injection)		2016	Microtubule targeting	2.0 mo ⁹



¹ TM Mack. Cancer, 1995 Jan 1;75(1 Suppl):211-44.

² Bock et al., Int. J. Environ. Res. Public Health 2020, 17, 2710.

³ Pedetour et al., Genes Chromosomes Cancer 24:30-41, 1999.

⁴ Italiano et al., Int. J. Cancer: 122, 2233-2241 (2008).

⁵ Kashima et al., Modern Pathology volume 25, pages 1384-1396(2012)

⁶ The Cancer Genome Atlas Research Network, Cell 171, 950-965, November 2, 2017

⁷ Newly diagnosed adv DD LPS, unresectable early DD LPS, resectable disease progressing to adv DD LPS, and WD LPS progressing to DD LPS

⁸ Demetri et al., J Clin Oncol 34:786-793, 2015

⁹ Demetri et al., J Clin Oncol 35:3433-3439, 2017

Phase 3 Registrational Trial

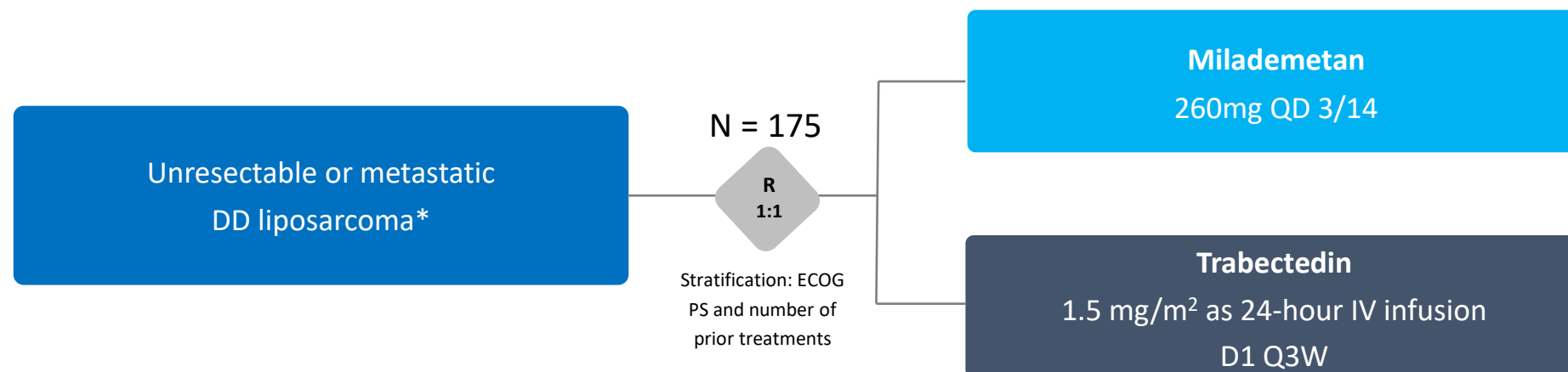
- 72 sites
- US, Europe, Asia

Patient Enrollment

- Commenced July 2021
- Closed July 2022
- N = 175

MANTRA (Phase 3): Unresectable / Metastatic DD Liposarcoma

Safety and Efficacy of Milademetan vs. Yondelis® (trabectedin)



Overview

- Patients with de-differentiated (DD) LPS with or without well-differentiated LPS component
- ≥ 1 prior systemic treatment, including at least 1 prior anthracycline
- Treatment until PD or intolerability

* Includes with or without a well differentiated (WD) component

DCR, disease control rate; DOR, duration of response; ECG, electrocardiogram; HRQoL, health-related quality of life; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression free survival; PK, pharmacokinetics; PO, by mouth; QD, once per day; Q3W, every three weeks

Endpoints

- PFS (Primary): Approximately 105 events by blinded central review to trigger primary analysis
- OS, ORR, DCR, DOR,
- HR QoL, Safety

Statistical Assumptions

- HR = 0.5; 94% powered
- mPFS: trabectedin (3.0 mo) / milademetan: (6.0 mo)

Dosing Schedule for 4 Cohorts

Schedule A: QD 21/28

Schedule B: QD 28/28

Schedule C: QD 7/28

Schedule D: QD 3/14

Milademetan Phase 1 (U101) Trial

Select Treatment Emergent Adverse Events

Organ Class n (%)	Schedule A, B, and C Cohorts (n=78)		Schedule D All doses (n=29)		Schedule D 260mg (n=20)	
	All Grades	Grade ≥ 3	All Grades	Grade ≥ 3	All Grades	Grade ≥ 3
All drug-related TEAEs	74 (95)	43 (55)	25 (86)	5 (17)	18 (90)	4 (20)
Blood and lymphatic disorders						
Thrombocytopenia	52 (67)	27 (35)	13 (45)	4 (14)	9 (45)	3 (15)
Anemia	33 (42)	14 (18)	5 (17)	0	4 (20)	0
Neutropenia	10 (13)	8 (10)	2 (7)	1 (3)	1 (5)	1 (5)
Gastrointestinal disorders						
Nausea	57 (73)	2 (3)	20 (69)	0	16 (80)	0
Vomiting	22 (28)	2 (3)	13 (45)	1 (3)	10 (50)	1 (5)
Diarrhea	26 (33)	0	9 (31)	0	5 (25)	0
General disorders						
Fatigue	36 (46)	3 (4)	12 (41)	0	8 (40)	0

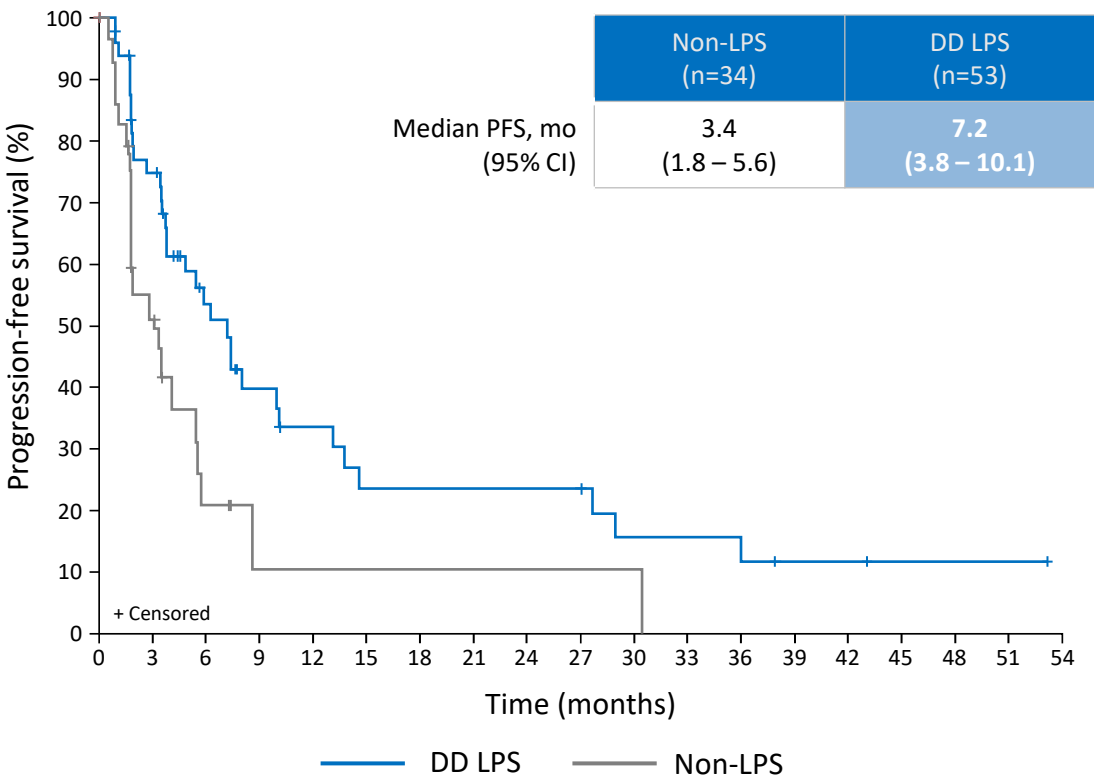


Milademetan Phase 1 (U101) Study

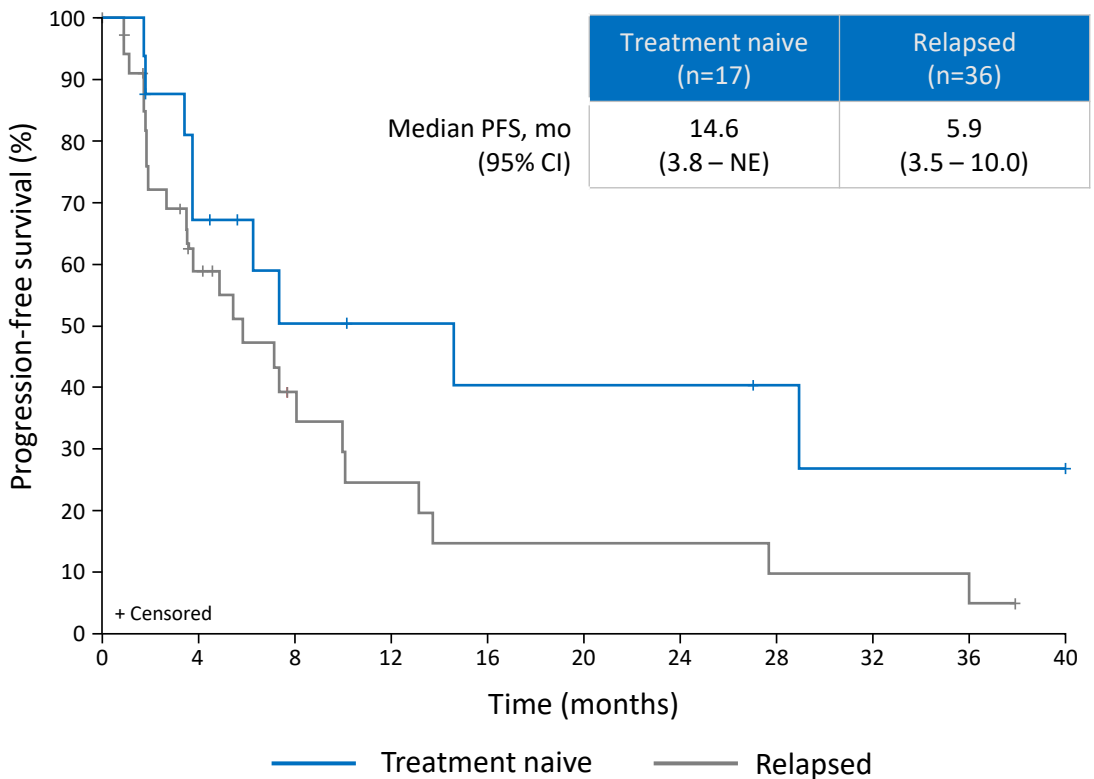
Observed Progression-Free Survival

All Doses & Treatment Schedules

All Patients (n=107)



DD LPS Patients (n=53)

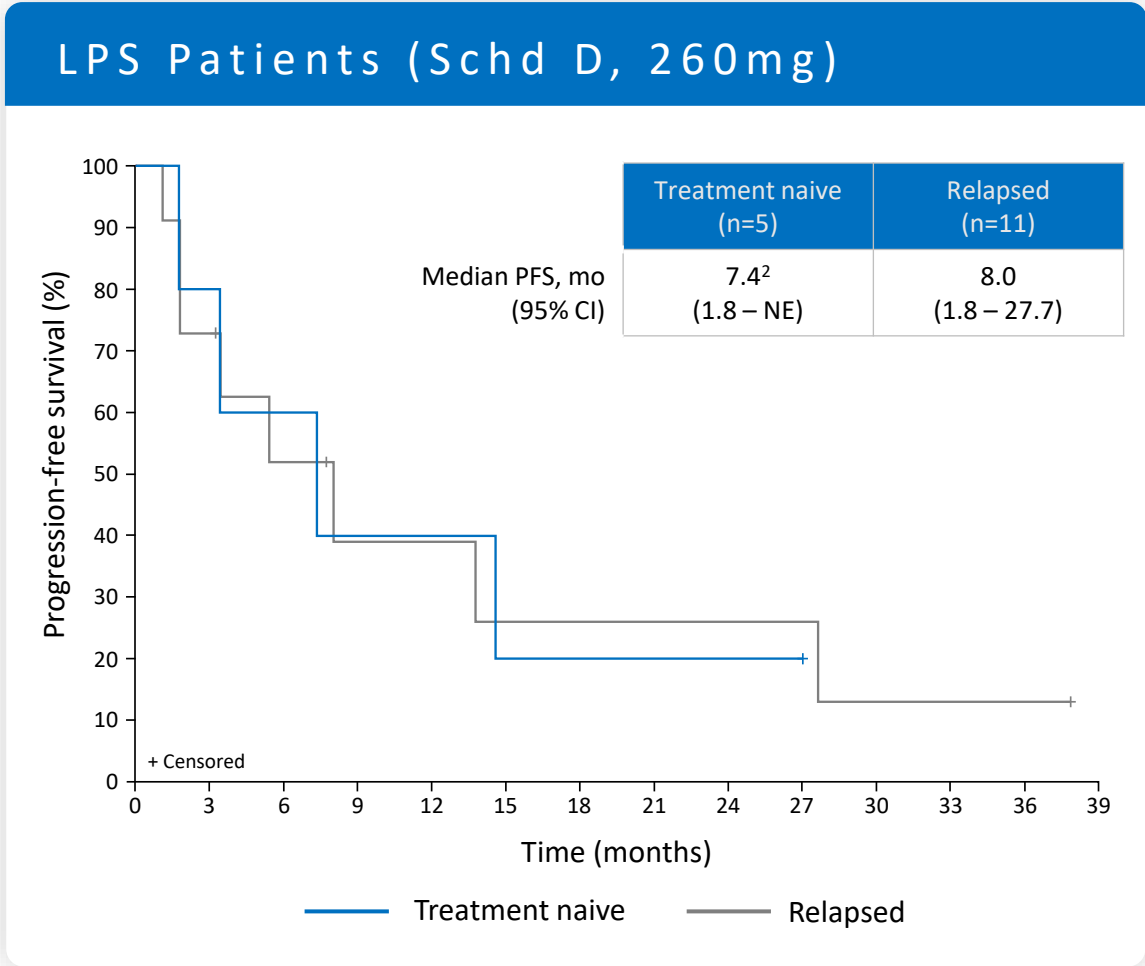
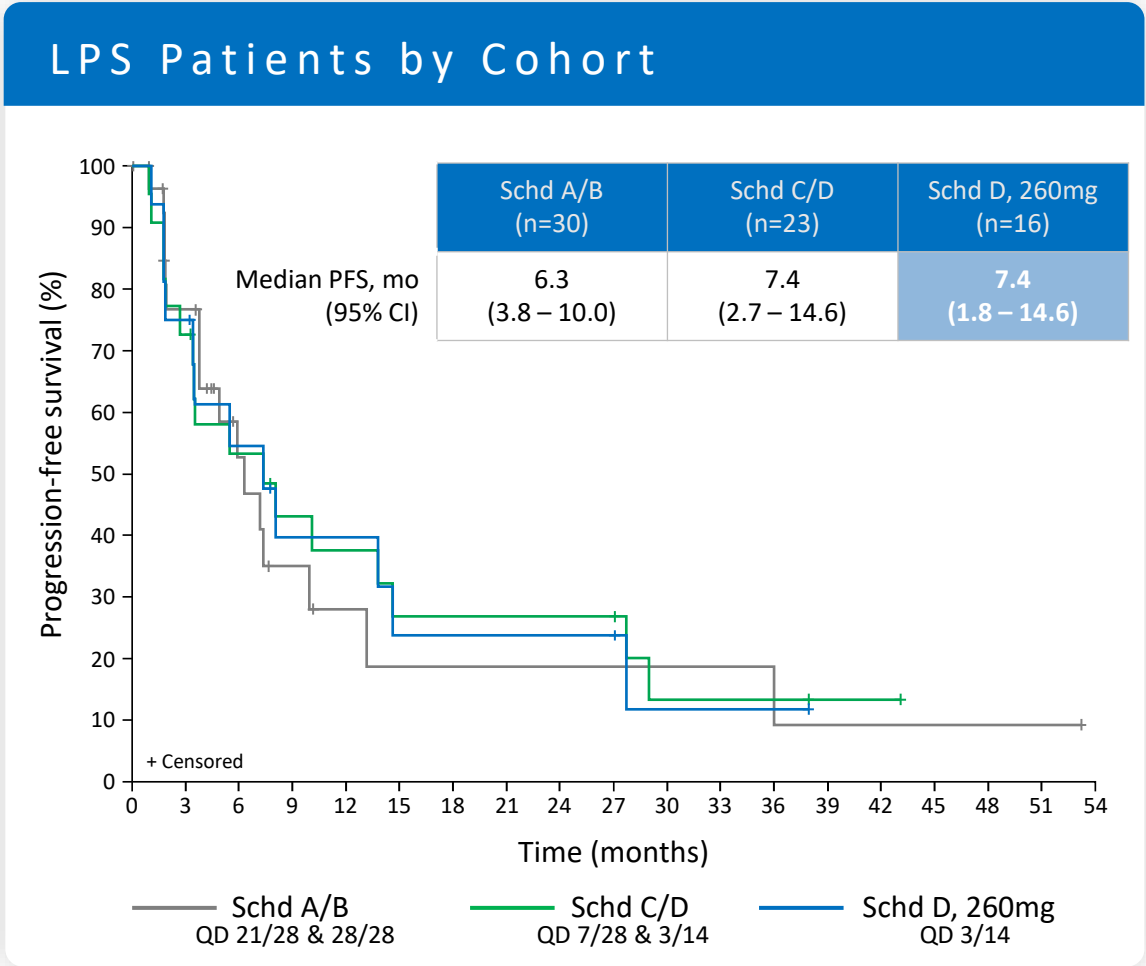


Source: Gounder et al., 2023 JCO



Milademetan Phase 1 (U101) Study

Of the four (4) dose schedules evaluated, **Schedule D (QD 3/14), 260mg** was identified to have the most favorable efficacy / safety profile, and to serve as the basis of milademetan dosing in subsequent studies



Source: Gounder et al., 2023 JCO

¹One or more prior therapies

²Rain data on file



Milademetan

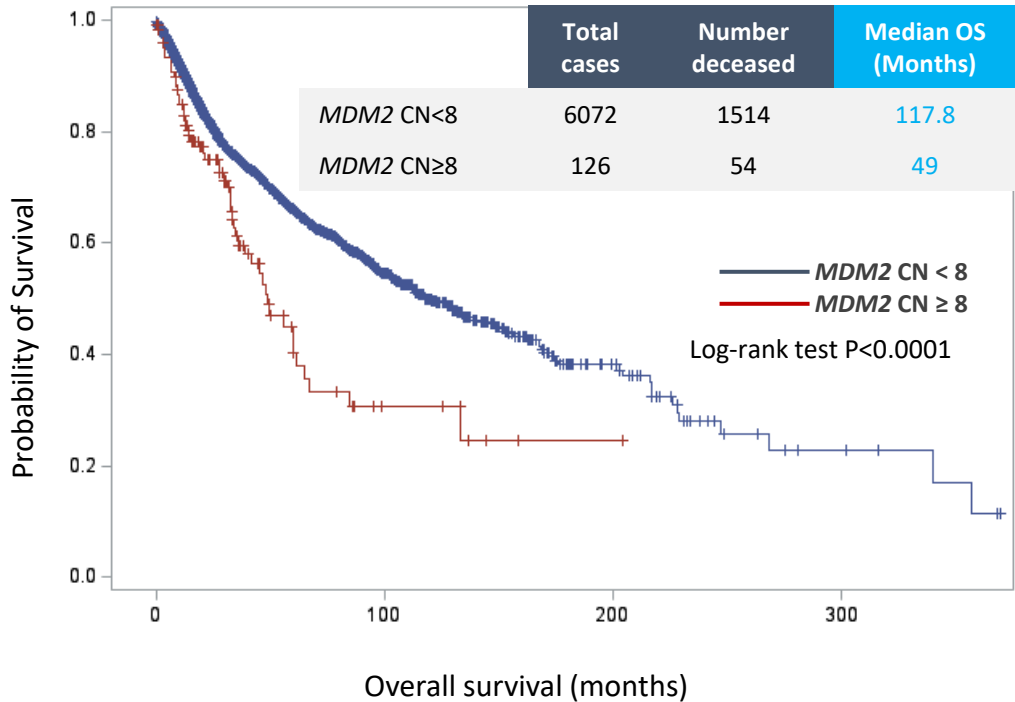
Phase 2 MANTRA-2
(MDM2 Amp Basket)



MDM2 Amplified Solid Tumors: Rationale

Approximately 8,000 patients per year exhibit MDM2 CN ≥ 8

MDM2 AMP CONFERS POOR PROGNOSIS



TCGA v23 data from GDC data portal

ELIGIBLE MDM2 AMP PATIENTS (CN ≥ 8)

Tumor Type	% Frequency ¹	Total Eligible Patients ²
Breast	1.6%	2413
NSCLC	1.5%	2249
Bladder (Urothelial)	6.2%	1874
Stomach	2.6%	433
Esophageal	2.6%	413
Melanoma	1.1%	367
Prostate	0.2%	125
Cholangiocarc.	2.0%	110
Pancreatic	0.2%	107
CRC	0.1%	100
Salivary Gland	1.3%	23
Cervical	0.2%	16
Total		8,230

¹ Caris Real World Analysis (01 Sep 2021 – 30 Sept 2022)

² Rain internal analysis based on NCI SEER, Oct 2022

Phase 2 Solid Tumor Basket

- Targeting n = 65 patients
- 10 active sites

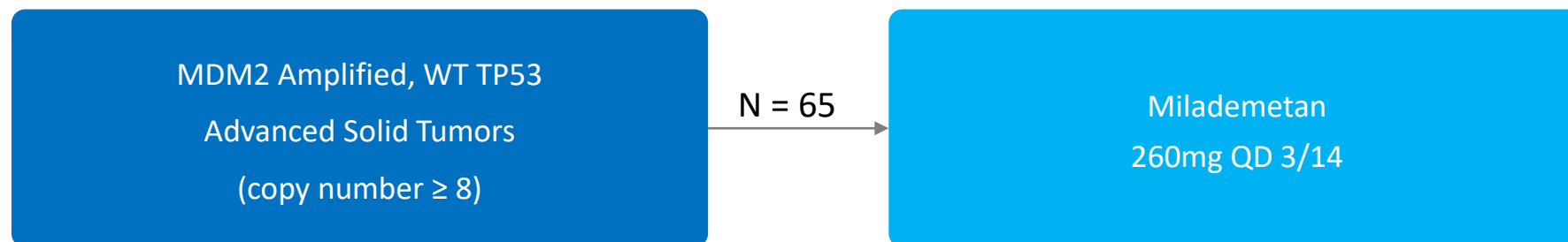
Patient Enrollment

- Commenced: Nov 2021

MANTRA-2 (Phase 2): MDM2 Amp Advanced Solid Tumor Basket

Determine Safety and Efficacy Of Milademetan In Patients With Relapsed / Refractory Advanced / Metastatic MDM2 Amplified Solid Tumors With Wildtype TP53

Overview



- Selecting patients with MDM2 gene copy number (CN) of ≥ 8
- Of 17 patients enrolled, 15 have received first dose of milademetan¹
 - Of 15 patients receiving at least one dose of milademetan, **10** patients evaluable for efficacy²
- Patients enrolled based on local NGS for CN, centrally confirmed by Rain's diagnostic partner, Tempus
- Evaluable tumor types included: lung, breast, biliary, pancreatic and other solid tumors

¹ As of Oct 26, 2022

² Of patients unevaluable for efficacy, one (1) patient not yet received first scan, two (2) withdrew consent for reasons unrelated to study drug and two (2) did not have central CN confirmation (CN <8)
Note: Data shown reflects interim analysis, and is preliminary, subject to change

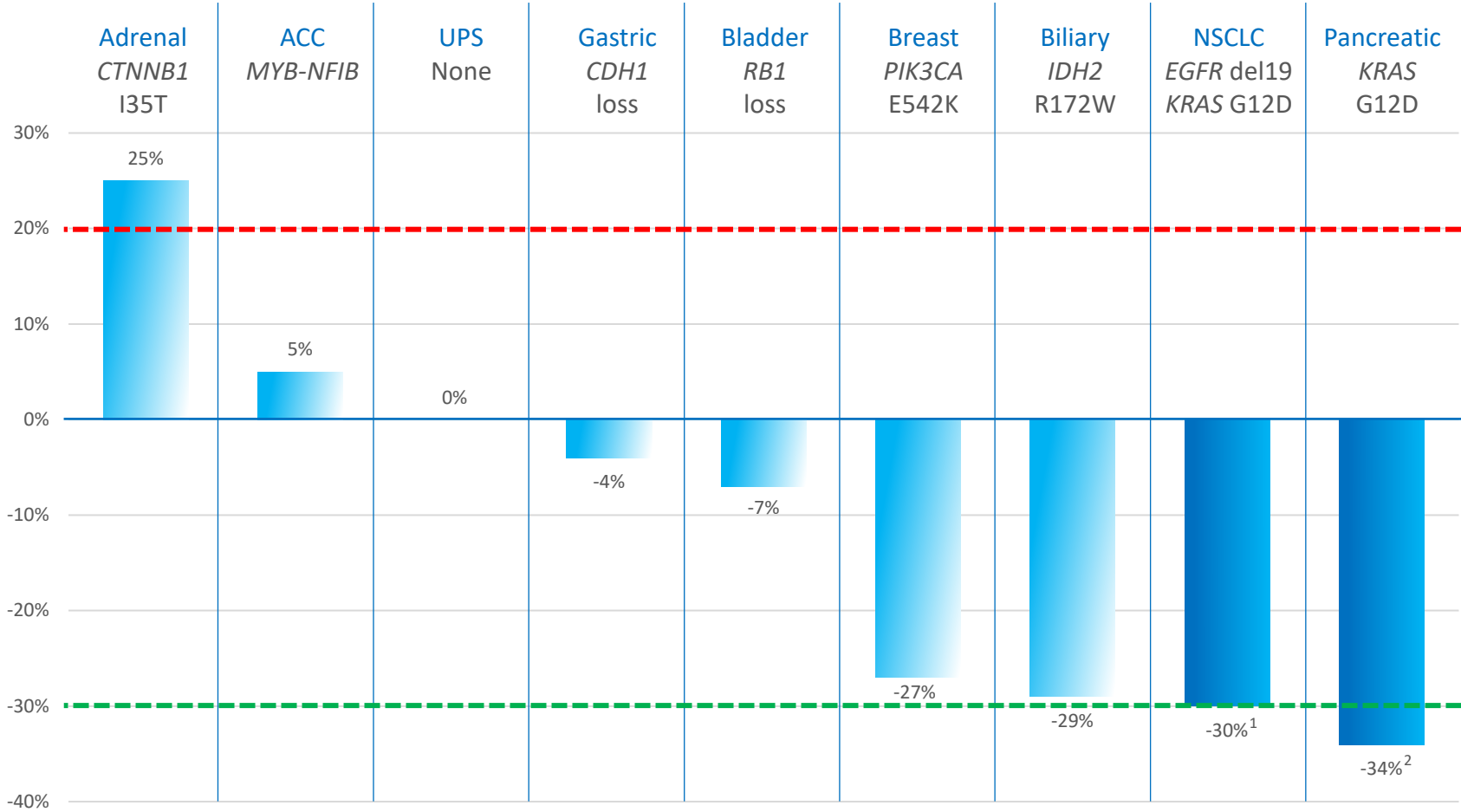


▼
At interim assessment,
9/10 efficacy evaluable
patients had post-baseline
tumor assessment

Interim MANTRA-2 Analysis: Patient Outcomes

Two (2) Partial Responses and two (2) near-PRs observed of 10 evaluable patients

Patient Tumor Diameter Change



Note: Data cutoff as of 26 Oct 2022, and reflects interim analysis subject to change
¹ Patient died post first scan due to COVID; response will not be confirmed
² Response pending confirmation and treatment ongoing

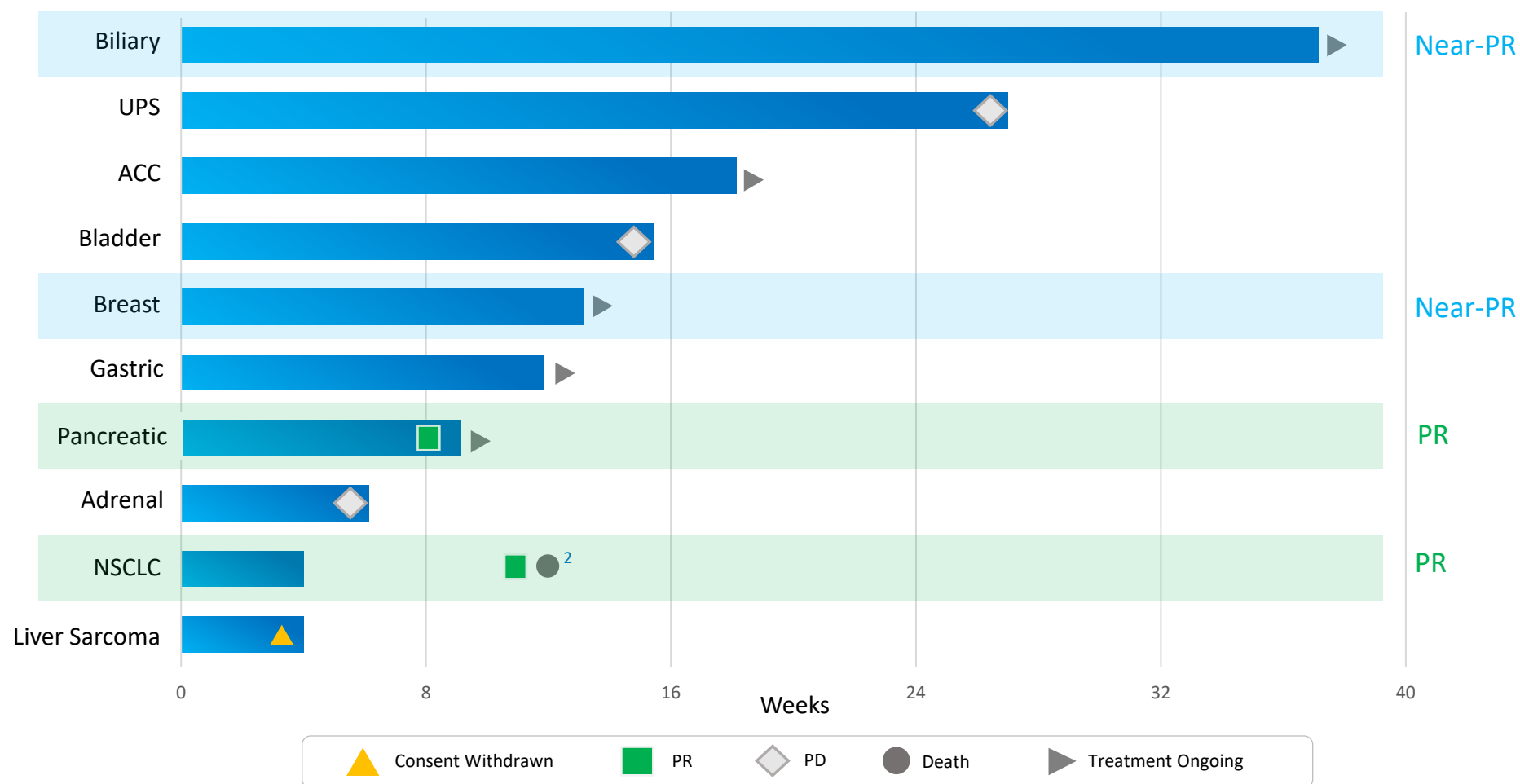
A total of eight (8) patients are actively enrolled in MANTRA-2¹

Safety in-line with prior milademetan clinical studies suggestive of potential best-in-class tolerability

Interim MANTRA-2 Analysis: Duration on Therapy

Two (2) Partial Responses and two (2) near-PRs observed of 10 evaluable patients

Patient Treatment Duration



Note: Data cutoff as of 26 Oct 2022, and reflects interim analysis subject to change

¹ Includes five (5) efficacy evaluable patients, one (1) patient dosed but not at first scan, and two (2) patients recently enrolled as of the data cutoff

² Patient died post first scan due to COVID; response will not be confirmed

Milademetan

Phase 1/2 MANTRA-4

(CDKN2A Loss / WT p53 Basket)

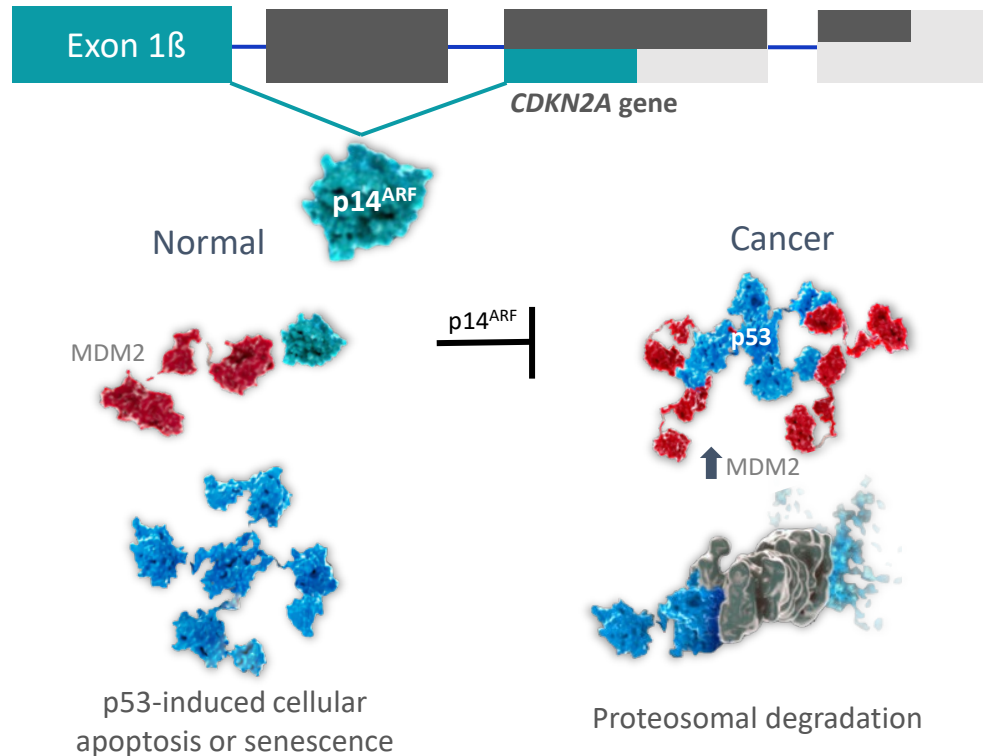




MANTRA-4: IO Combo in *CDKN2A* Loss, p53 WT Adv Solid Tumors

In the US, there are an estimated 45,000 patients¹ annually with advanced cancers exhibiting p53 WT and *CDKN2A* loss

Mechanism: *CDKN2A* Loss Increases MDM2 Activity

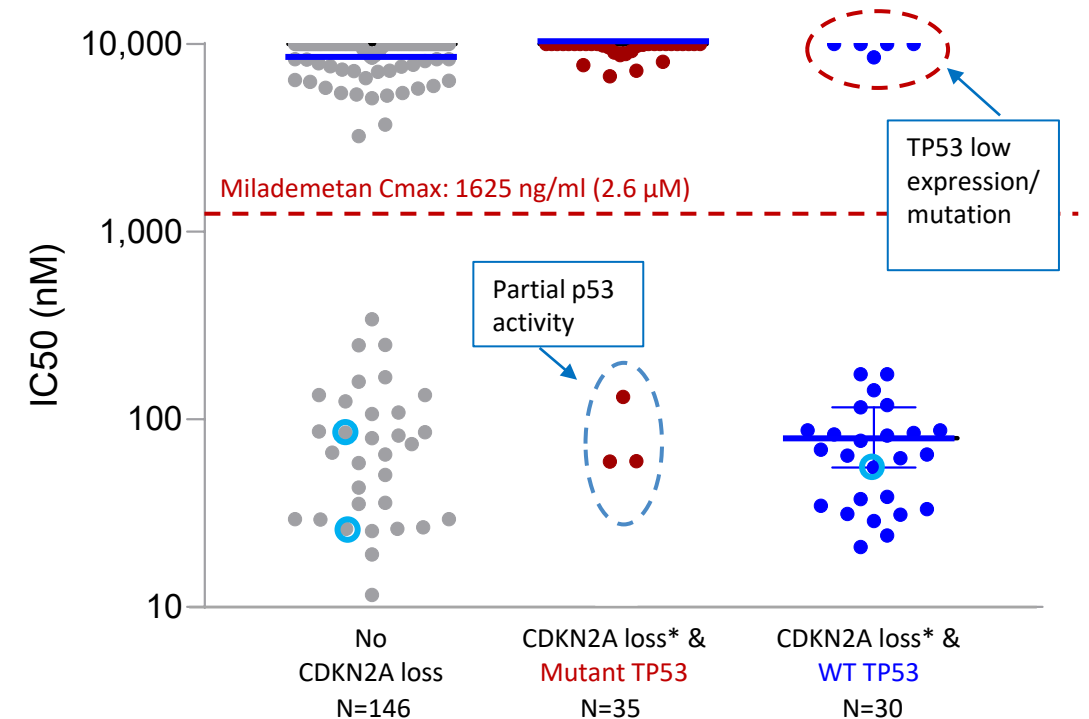


Source: Rain Oncology

¹ NCI SEER, Globocan, TCGA based on loss of 2 copies of *CDKN2A*

² Ishizawa et al., Cancer Res. 2018 May 15;78(10):2721-2731; Mutation/CN: CCLE database

Milademetan Antiproliferative Potency²



Error bars represent Median with 95% CI

○ MDM2 CN >12

* Homozygous *CDKN2A* loss

Combo Rationale:

- *CDKN2A* loss leads to MDM2 dependency¹
- *CDKN2A* loss is associated with poor outcomes on ICI²
- p53 reactivation induces immune surveillance via increased antigen presentation, IFN γ signaling and other mechanisms³

Phase 2

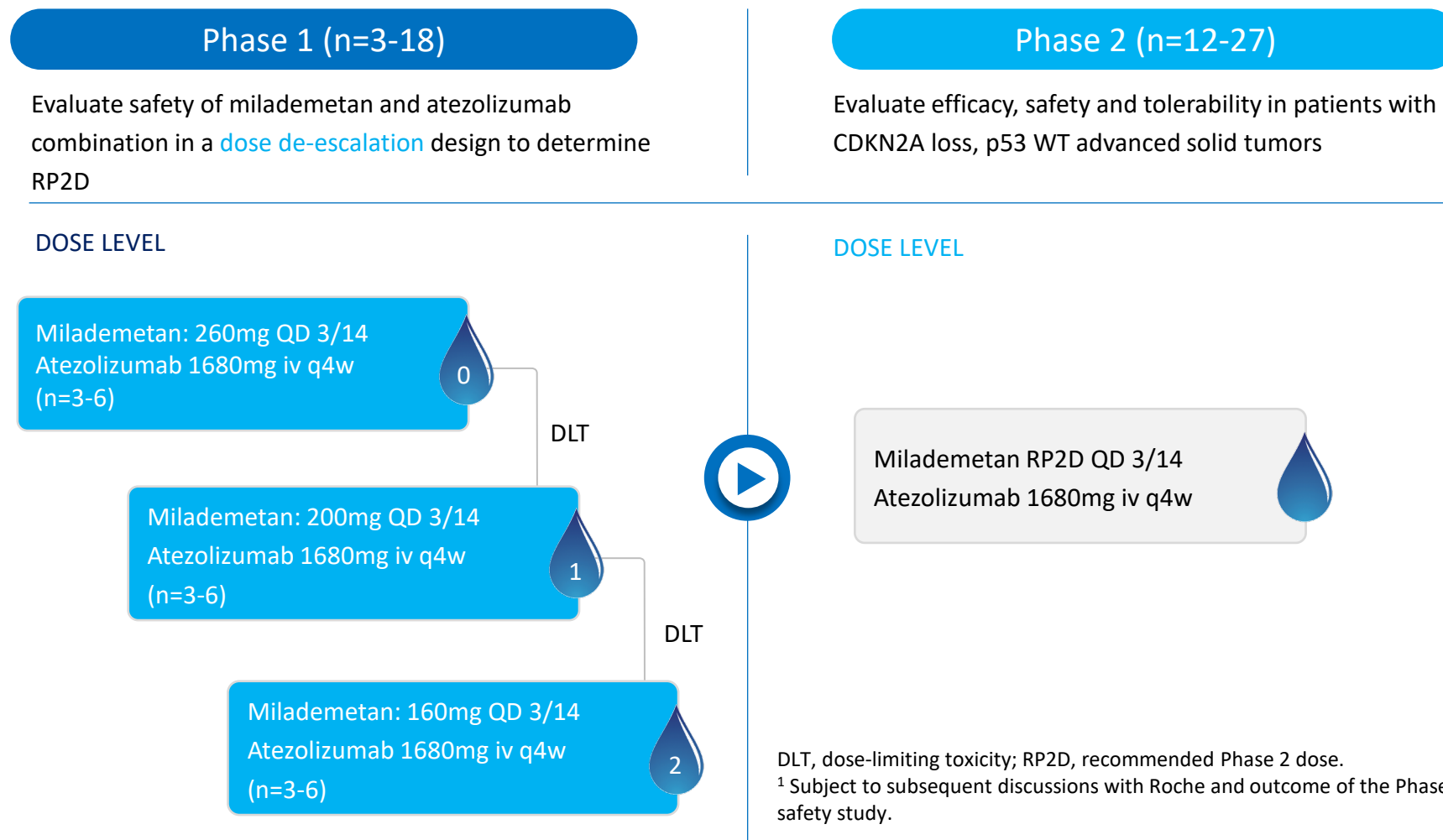
Opportunities:

If safety is deemed acceptable, the milademetan / checkpoint inhibition combination may be evaluated in additional tumors¹ including:

- MDM2 gene-amplified cancers,
- Other checkpoint inhibitor sensitive, WT p53 cancers

MANTRA-4: Milademetan + TECENTRIQ® (Phase 1/2)

Rain and Roche will evaluate the safety of MDM2-p53 complex inhibition with milademetan and PD-L1 inhibition with TECENTRIQ® (atezolizumab) in patients with *CDKN2A* loss and WT p53



DLT, dose-limiting toxicity; RP2D, recommended Phase 2 dose.

¹ Subject to subsequent discussions with Roche and outcome of the Phase 1 safety study.

¹ Tirunagaru et al., ASCO 2022

² Adib et al., Clin Can Research 2021; Gutiontov et al., Scientific Reports 2021; Brenner et al., Nat Communications 2020

³ Zhou et al., Can Discovery 2021; Braun and Iwakuma, Transl Cancer Res 2016;5(6):692-697; Wang et al., Can Res 2021 Tirunagaru et al., ASCO 2022



Key Takeaways and Anticipated Milestones

MANTRA: DD Liposarcoma

Median PFS of 7.2 months (n=53) and 7.4 months in optimized cohort (n=16) compares favorably to 2.2 months median PFS for standard of care (trabectedin)

May enable first NDA filing of a MDM2-p53 complex inhibitor

MANTRA Phase 3 Topline Results: 2Q 2023

01

Pipeline in a Program

Up to 50% of cancers with WT p53 targetable either via monotherapy or combination strategies

02

Tumor Agnostic Basket Trials: MANTRA-2 / MANTRA-4

MDM2 amp (MANTRA-2): Enrolling
CDKN2A loss (MANTRA-4):
Commencing in mid 2023

Exploring activity of milademetan in adv solid tumors with WT TP53

MANTRA-4 Trial Start: Mid 2023

03

Dose Scheduling: Addressing Historical Challenges

Prior clinical study identified 260mg QD 3/14 as an optimized dose and schedule

Optimized schedule suggests potential best-in-class safety for milademetan

Milademetan is most advanced inhibitor of the MDM2-p53 complex in development

04

Appendix





Rain's Corporate Governance

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