NASDAQ: MRTX

MIRATI THERAPEUTICS

Targeting the genetic and immunological drivers of cancer

Corporate Overview Presentation
September 2021

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Developing Novel Oncology Therapies, Including Two Registration-Enabling Programs in Large NSCLC Patient Populations

IO Resistance

Sitravatinib
Inhibitor of TAM and VEGFR2

Compelling P2 data in combination with a PD-1 support and inform SAPPHIRE P3 approach in NSCLC

KRAS Selective Inhibition

Adagrasib (MRTX849)
G12C selective inhibitor

Compelling efficacy and favorable tolerability with broad development in both monotherapy and combinations

G12D selective (MRTX1133) and pan-KRAS selective inhibitors

Potential first-in-class G12D inhibitor advancing in IND-enabling studies

Synthetic Lethality

MRTX1719
MTA Cooperative PRMT5 Inhibitor

Internally discovered synthetic lethal PRMT5/MTA cooperative program for MTAP-deleted cancers with IND submission by year end

Operational and commercial synergies across portfolio, particularly in NSCLC

Advancing **targeted novel oncology research platform:** ***KRAS mutant inhibition and KRAS signaling modifiers (e.g., SOS1)***

$1.2 billion in cash, cash equivalents and short-term investments as of 6/30/21

NSCLC: non-small cell lung cancer; CRC: colorectal cancer; IO: immuno-oncology; IND: investigational new drug; P = phase; MTA: methylthioadenosine; MTAP: methylthioadenosine phosphorylase

Mirati's Pipeline Spans Multiple Novel Oncology Programs and Tumor Types

Compound	Indication	Development Approach	Lead Optimization	IND-enabling	Phase 1/1b	Phase 2	Phase 3	Status / Near-Term Catalysts
Adagrasib *KRAS G12C Inhibitor*	2L NSCLC	Monotherapy	*K-1: P2 registration-enabling*					• NDA filing in Q4:2021 • P2 NSCLC data at medical meeting in early 2022
			K-12: P3 confirmatory trial, randomized vs. docetaxel					
		POC Combos: SHP2, SOS1, CDK4/6, Pan-EGFR, EGFR	*Multiple: POC combination trials*					• POC combos ongoing; pan-EGFR planned • Data from select combos expected in 1H:2022
	1L NSCLC	Monotherapy: STK11 co-mutations and TPS <1%	*K-1: STK11 co-mutations*					• STK11 cohort initiated Q1:2021 • TPS <1% to initiate Q4 2021
			K-7 (1 Arm): <1% TPS					
		Combo: Pembrolizumab (PD-1)	*K-7 (2 Arms): <1% TPS and ≥1% TPS*					• P2 enrollment on-going • Initial K-1 tolerability update in Q4:2021
	2L CRC	Combo: Cetuximab (EGFR)	*K-10: combination with cetuximab vs. FOLFIRI or FOLFOX*					• P3 initiated in 1H:2021
	3L+ CRC and Pancreatic	Monotherapy Combo: Cetuximab (EGFR)	*K-1: P1b and P2 monotherapy*					• CRC; Additional P2 EGFR combo cohort to initiate Q4:2021 • Pancreatic: POC P2 mono data in Q4:2021
			K-1: P1b and P2 combination					
MRTX1133 *KRAS G12D Inhibitor*	Pancreatic, CRC, NSCLC	Monotherapy and combination						• IND in 2022
Sitravatinib *Multi Kinase Inhibitor*	2/3L NS-NSCLC	PD-1	SAPPHIRE – Combination with *Nivolumab vs. docetaxel*					• P3 interim analysis of OS in 2H:2022
	2/3L S + NS-NSCLC	PD-1	*Tislelizumab Combinations (BeiGene)*[1]					• P3 initiated Q3:2021 by BeiGene
MRTX1719 *MTA cooperative PRMT5 Inhibitor*	MTAP-deleted Cancers	Monotherapy						• IND by YE 2021
Additional KRAS pathway preclinical programs	Solid Tumors	SOS1 Inhibitor						
	Solid Tumors	Other KRAS mutations						

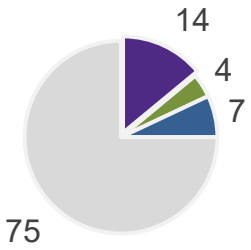
K: KRYSTAL (adagrasib trials); POC: Proof of Concept; NSCLC: non-small cell lung cancer; CRC: colorectal cancer; OS = Overall Survival; IND = investigational new drug; NDA = new drug application; MTAP: methylthioadenosine phosphorylase. 1. BeiGene is currently conducting certain combination studies of sitravatinib + tislelizumab for solid tumor indications in their Territory in Asia (ex-Japan). These trials include a P3 trial in non-squamous and squamous NSCLC randomized vs. docetaxel, as well as proof-of-concept trials in hepatocellular carcinoma, renal cell carcinoma, ovarian cancer and gastric cancers.

Mirati: Deep Commitment to Addressing Cancers With High Unmet Needs

KRAS: Drugging the Undruggable

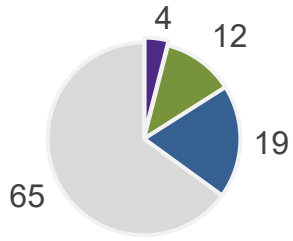
KRAS Prevalence in Tumors With High Unmet Needs[1-3]

NSCLC
Adenocarcinoma



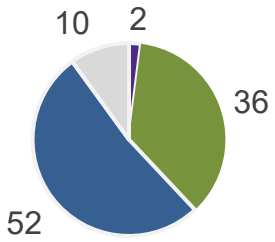
KRAS^{mt} Total	KRAS^{G12C}	KRAS^{G12D}
~25%	~14%	~4%

CRC



KRAS^{mt} Total	KRAS^{G12C}	KRAS^{G12D}
~35%	3-4%	~12%

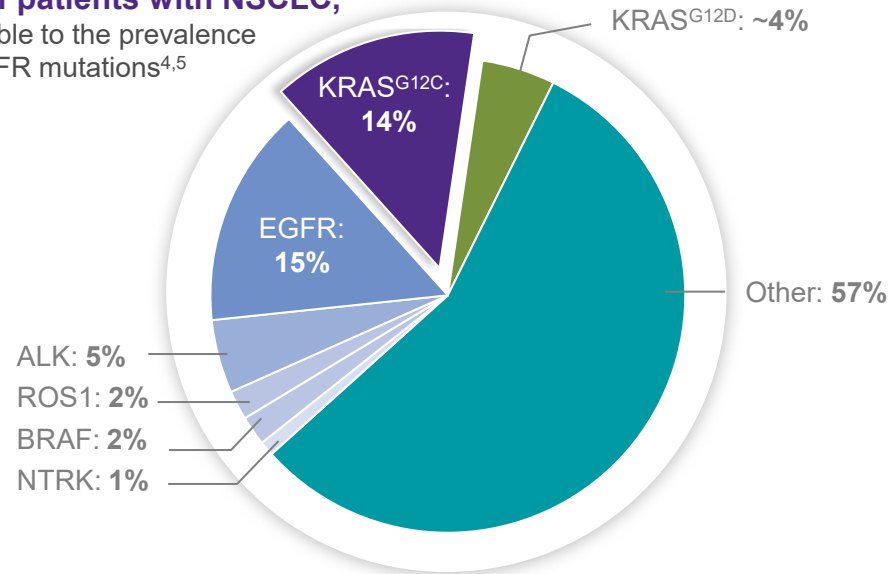
Pancreatic Cancer



KRAS^{mt} Total	KRAS^{G12C}	KRAS^{G12D}
~90%	~2%	~36%

Prevalence of Oncogenic Mutations in Lung Adenocarcinoma[4]

KRAS^{G12C} occurs in **~14% of patients with NSCLC,** comparable to the prevalence of all EGFR mutations[4,5]



Key: KRAS^{G12C} | KRAS^{G12D} | Other KRAS^{mut} | WT KRAS

- KRAS mutations are generally associated with poor prognosis
- The absence of known binding pockets made KRAS historically undruggable; discovery of the switch II binding pocket by Shokat et al has changed this

1. Zehir A, et al. *Nat Med*. 2017;23(6)703-713. 2. Krakstad C, et al. *PLoS One*. 2012;7(12):e52795. 3. NIH TCGA: *The Cancer Genome Atlas*. February 11, 2021. https://www.cbioportal.org. 4. Biernacka A, et al. *Cancer Genet*. 2016;209(5):195-198. 5. Pakkala S, Ramalingam SS. *JCI Insight*. 2018;3(15):e120858.

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Adagrasib (MRTX849):
$KRAS^{G12C}$ Selective Inhibitor

Adagrasib: Potentially Differentiated Therapy in NSCLC and CRC for Patients with KRAS^{G12C} Mutations

- Molecular profile, including CNS penetration
  - Encouraging preclinical and early clinical evidence of activity in the brain
- NSCLC: potentially best-in-class
  - 2L+ NSCLC: differentiated response rate and initial durability in heavily pretreated patients
- CRC: potentially first-in-class and best-in-class
  - 3L+: Response rate and initial durability in heavily pretreated patients
    - Both in monotherapy and in combination with cetuximab
  - 2L: P3 randomized trial in combination with cetuximab is ongoing

Adagrasib: Multiple Paths to Potential Commercialization

Tumor Type	KRAS^{G12C} Patient Population	Development Approach	Development Status
NSCLC	2nd line and beyond	Monotherapy	➢ NDA filing Q4:2021 (accelerated approval) ➢ P3 confirmatory study in 2L (randomized to docetaxel) initiated Q1:2021
	1st line with STK11 co-mutation	Monotherapy	➢ P2 initiated Q1:2021
	1st line with TPS < 1%	Monotherapy	➢ P2 TPS <1% planned for Q4 2021
	1st line stratified by TPS score of <1% and ≥*1%*	Combo: PD-1	➢ P2 pembrolizumab combination: enrollment ongoing
	2nd line and beyond	Combo: other	➢ Multiple POC trials ongoing or to be initiated with SHP2, SOS1, pan-EGFR and CDK4/6
CRC	≥ 3rd line	Monotherapy and Combination (EGFR)	➢ Monotherapy.: P2 initiated Q2:2021; Combination: P2 planned for Q4:2021
	2nd line	Combo: EGFR	➢ P3 cetuximab combination in 2nd line (randomized to chemotherapy) initiated in 1H:2021

*Mirati and Zai Lab have a collaboration and license agreement under which Zai obtains the right to research, develop, manufacture and exclusively commercialize adagrasib in Greater China (mainland China, Hong Kong, Macau and Taiwan). Zai also has obligations to support enrollment in Mirati's adagrasib global registrational studies. Mirati has an option to co-commercialize in Greater China and retains full and exclusive rights to adagrasib in all countries outside of Greater China.

Adagrasib: Desired Properties Include Complete Inhibition of KRAS^{G12C} for Full Dosing Interval, Long Half-Life, CNS Penetrance and Dose-Dependent PK

Long Half Life

Human Half Life ~24 hours[1]

Long half-life ensures pathway maximally inhibited throughout entire dosing interval

Comprehensive target coverage combats new KRAS protein synthesis (half-life ~ 24h) and reactivation of signaling[2]

CNS Penetrant

Encouraging CSF/CNS penetration

Encouraging and clinically meaningful adagrasib exposure in patients

Clinical POC: heavily pre-treated NSCLC patient had 63% reduction of primary tumor and disappearance of active brain metastases

Extensive Tissue Distribution

Estimated Human Volume of Distribution (>10 L/Kg[3])

Maximize systemic exposure for duration of dosing

Extensive volume of tissue distribution ensures optimal target coverage throughout dosing interval

PK Profile / dosing

Dose Dependent PK Exposure Response

Dose-dependent PK and emerging exposure-response relationship for adagrasib supports dose modification schema and selected combination strategies

NSCLC = non-small cell lung cancer; CSF = cerebrospinal fluid; CNS = central nervous system; POC = proof of concept

1.Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2019; 2. Stites and Shaw, CPT Pharmacometrics Syst. Pharmacol. (2018); 3. Estimated from nonclinical data and PBPK modeling;

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Adagrasib (MRTX849): *Advanced NSCLC*

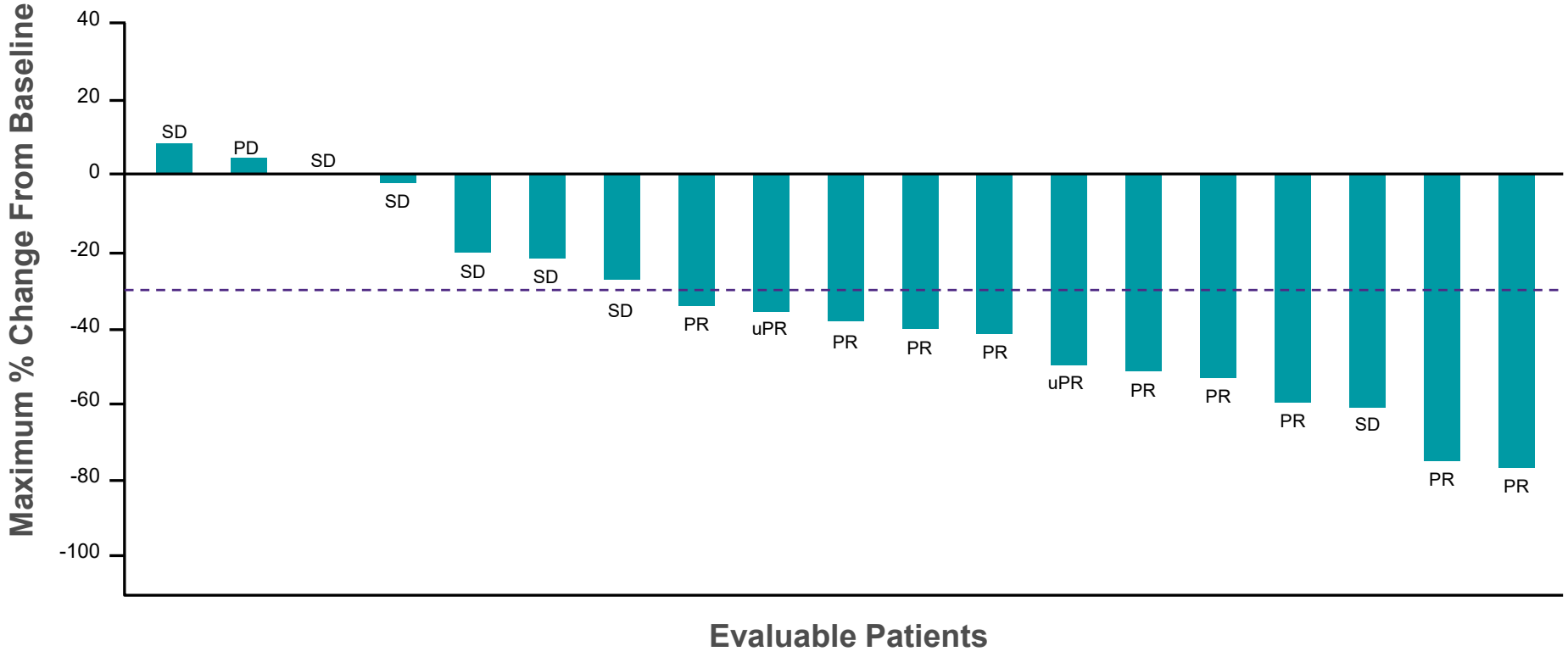
Adagrasib P2 Topline NSCLC Data

- Topline results from Phase 2 cohort of KRYSTAL-1 study in 2L+ NSCLC patients with the KRAS^{G12C} mutation evaluating adagrasib at 600mg BID:
  - Intent-to-treat population
  - Data cut off: June 15, 2021
  - Median follow-up: 9 months
- 43% ORR (confirmed based on central independent review)
  - 98.3% of patients received adagrasib following treatment with both immunotherapy and platinum chemotherapy
- Safety and tolerability profile consistent with previously reported findings for adagrasib in patients with advanced NSCLC
- NDA submission in Q4:2021

ORR = Objective Response Rate; NSCLC = Non-Small Cell Lung Cancer; NDA = New Drug Application

NSCLC: Phase 1/1b 2nd Line and Beyond: Best Overall Response Includes All Monotherapy Phase 1/1b 2L+ Patients Enrolled at 600mg BID (n=19)

Best Tumor Change From Baseline in All Patients Treated With Adagrasib 600 mg BID (n=19)

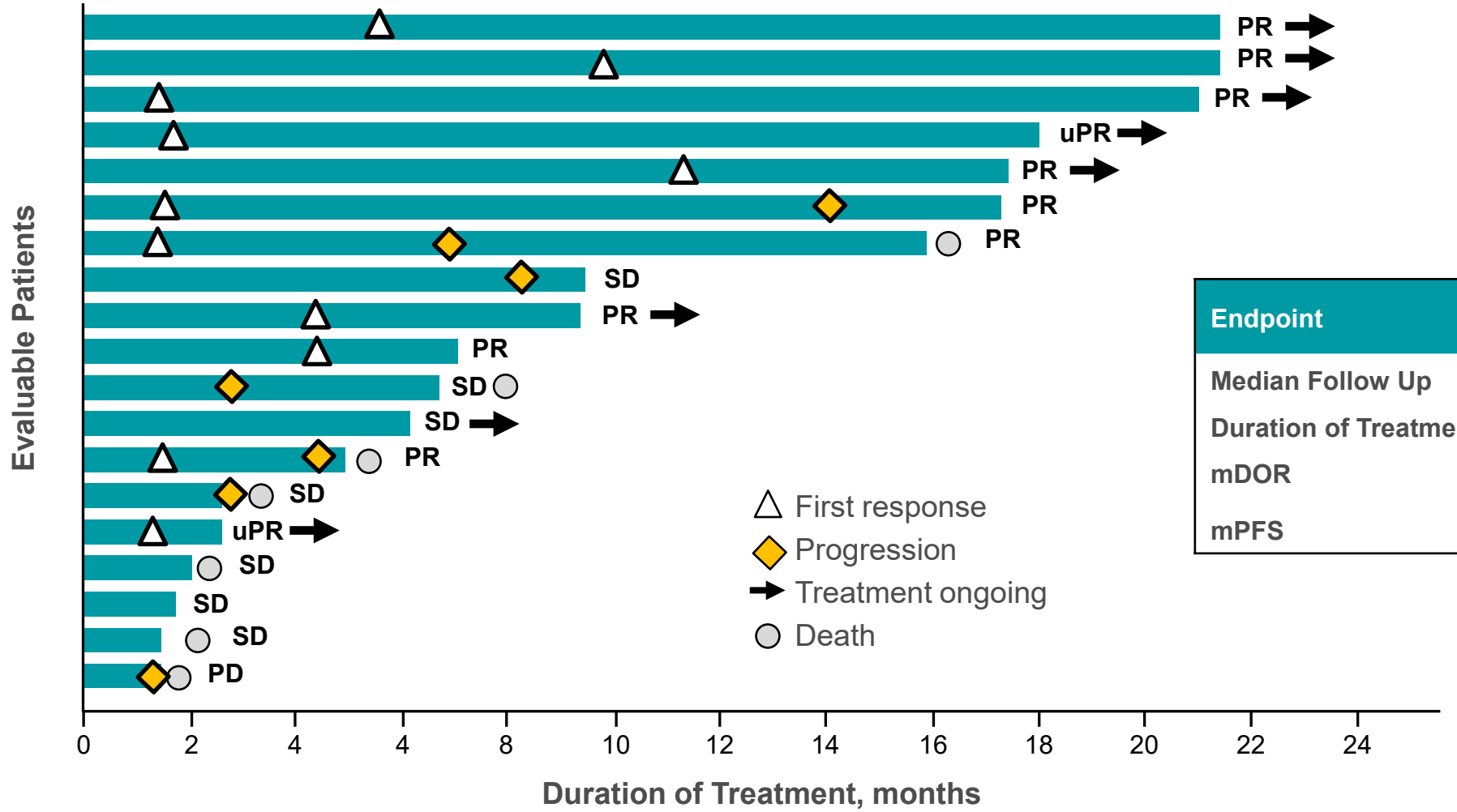


- Heavily pretreated (median of 2 prior lines of treatment), investigator-assessed ORR of 58%, including 2 responses that occurred after being on treatment for > 10 months[a]

[a]Two unconfirmed responses subsequently both confirmed; Data cut off: June 15, 2021

NSCLC: Phase 1/1b in the Second Line+ Setting: Duration of Treatment

Duration of Treatment in All Patients Treated With Adagrasib 600 mg BID (n=19)



Endpoint	Median (months) (range/95%CI)
Median Follow Up	17.3
Duration of Treatment	9.5 (2.6, NE)
mDOR	12.6 (3.1, NE)
mPFS	8.3 (2.8, NE)

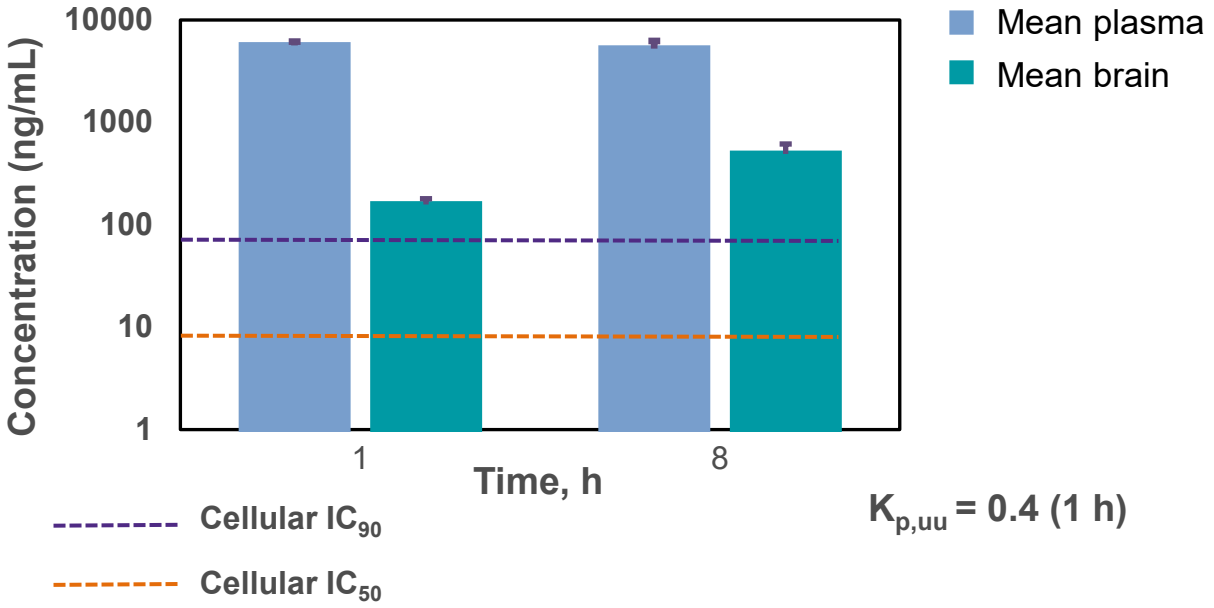
Data cutoff June 15, 2021

Adagrasib Clinical Activity in NSCLC Patients with Brain Metastases

Clinical activity in NSCLC patients with brain metastases with brain and CSF exposure in preclinical and clinical studies

- Preclinical research demonstrates adagrasib has dose dependent drug penetration in the CNS
  - Brain concentrations >IC90 achieved with dose comparable to human dose
- Heavily pre-treated KRAS^{G12C} mutated NSCLC patient with active brain metastases was evaluated following several cycles of adagrasib therapy
  - Patient experienced 63% reduction in size of primary lung tumor and disappearance of the active brain metastases
- Enrolling cohort of patients to assess adagrasib in NSCLC patients with a G12C mutation and active brain metastases

Mean Plasma and Brain Concentrations of Adagrasib After a Single 100 mg/kg Oral Dose in Mice



Kpuu[1] Comparison		
	Osimertinib	0.3
	Adagrasib preclinical	0.4
	Preliminary adagrasib clinical	0.47

[1]Kpuu is the concentration ratio of unbound drug in CSF to blood, to, as a measure of brain penetration
NSCLC: non-small cell lung cancer; CSF = cerebrospinal fluid; CNS = central nervous system

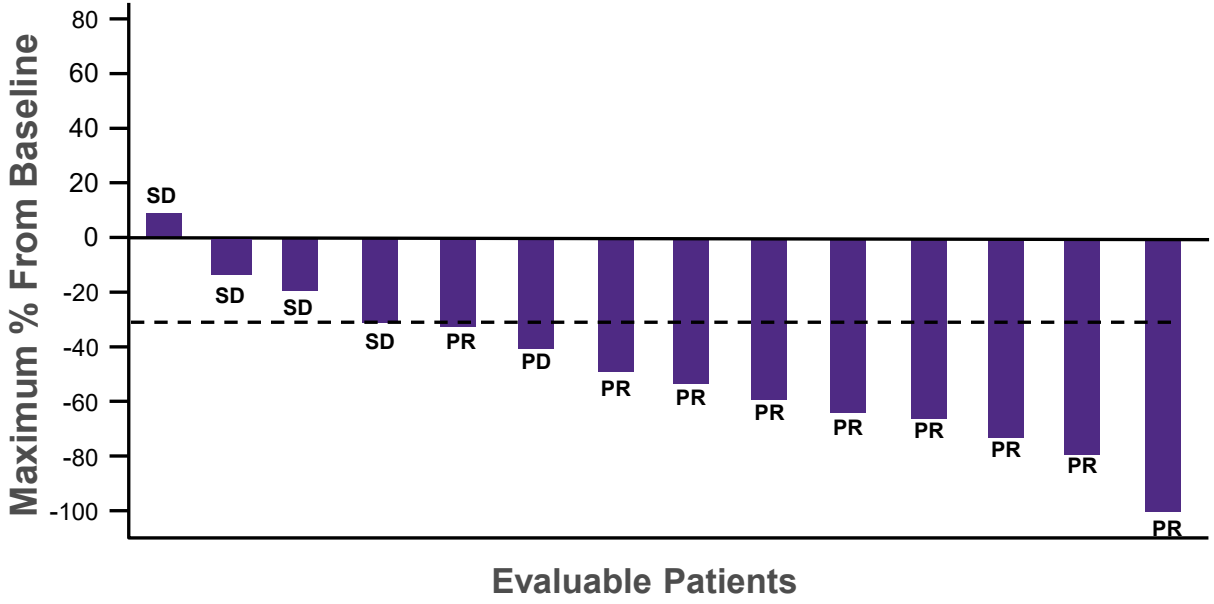
Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020

Adagrasib Clinical Activity in NSCLC in Patients with KRAS^{G12C} and STK11 Co-Mutations

Co-mutations in KRAS and STK11 in NSCLC Patients

- KRAS and STK11 co-mutations comprise approximately 30% of KRAS^{G12C} mutant NSCLC
- The co-occurrence of KRAS and STK11 mutations may cooperate to create an immune-suppressed tumor microenvironment
- Initial adagrasib clinical activity shows promising response
- **Potentially registration enabling Phase 2 monotherapy study in 1st line NSCLC patients with STK11 co-mutation initiated in Q1:2021**

Best Tumor Change From Baseline for Patients Harboring KRAS^{G12C} and STK11 Co-mutations Shows 64% (9 of 14 patients) ORR

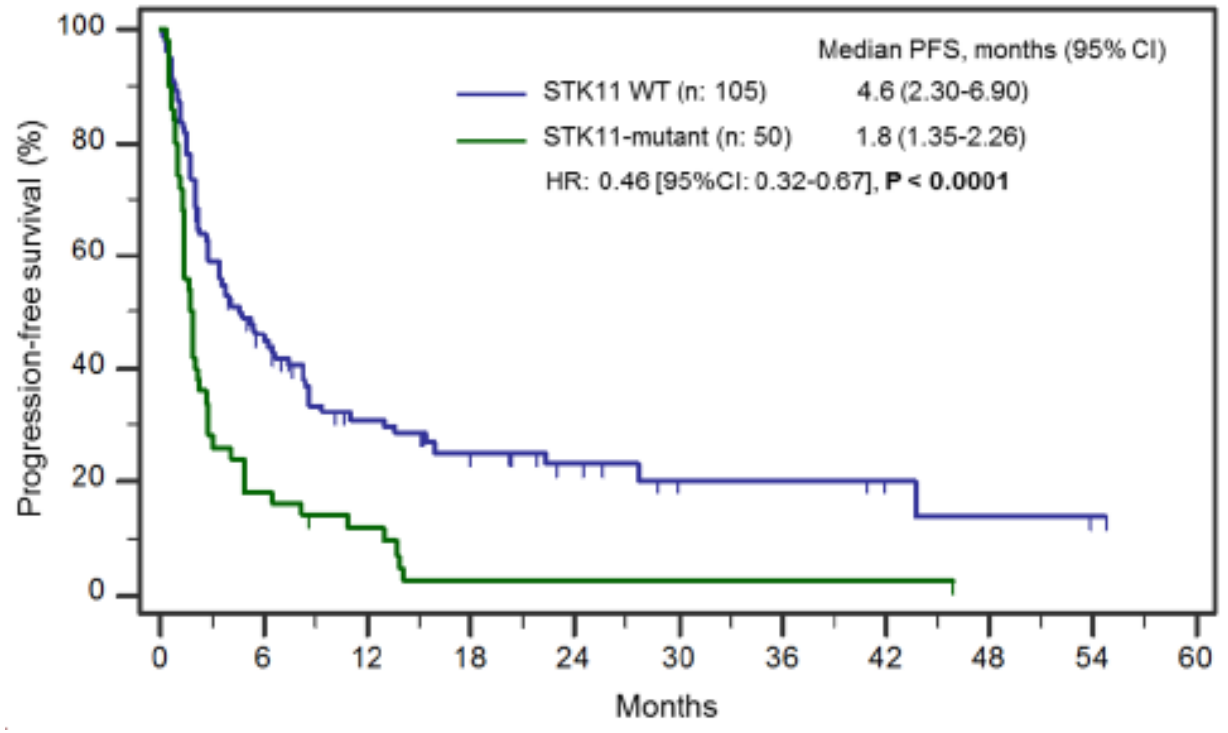


NSCLC: non-small cell lung cancer; ORR = overall response rate

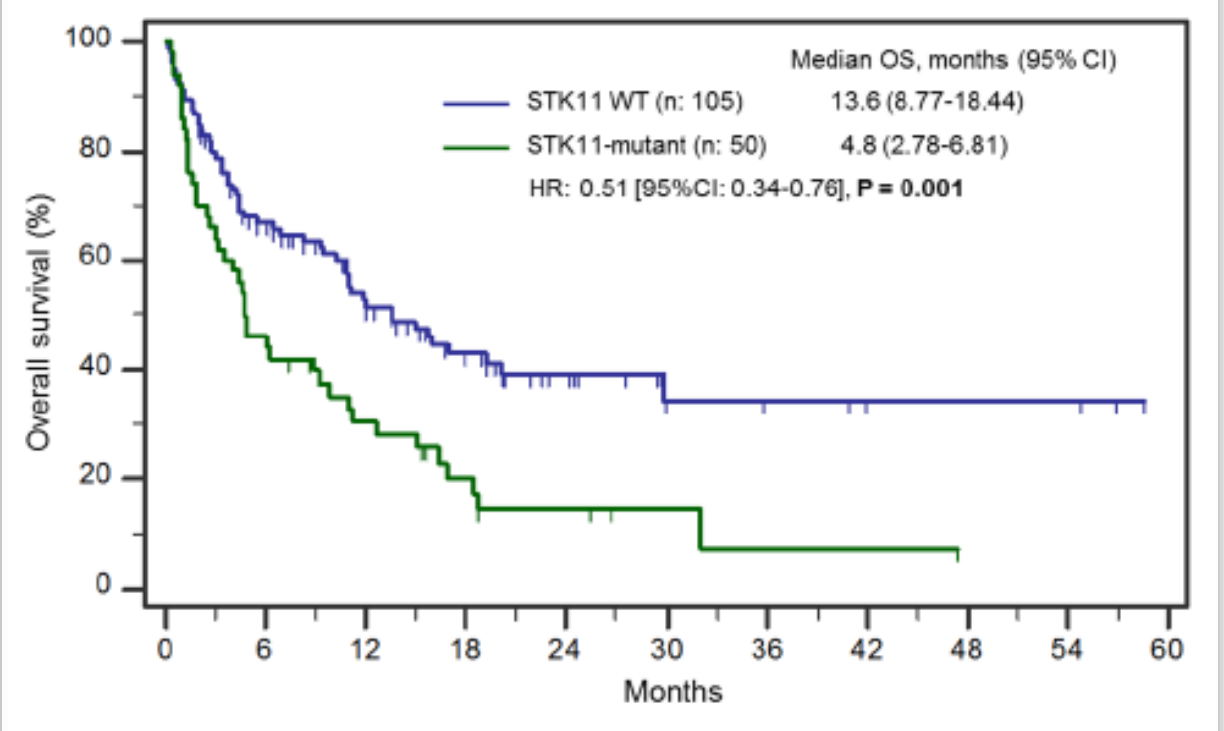
Presented at the 32nd EORTC-NCI-AACR Symposium, October 24-25, 2020

Co-mutations in KRAS and STK11 are Associated with Poor Prognosis and Outcomes on Checkpoint Inhibitor Therapy in NSCLC

Progression Free Survival



Overall Survival



Ricciuti et al. Journal of Clinical Oncology 37, no. 15_suppl (May 20, 2019); Skouldis et al. Cancer Discovery. 2018 Jul;8(7):822-835; Zehir et al. Nat Med. 2017 Aug 4;23(8):1004.

NSCLC = non-small cell lung cancer

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Adagrasib (MRTX849): Heavily Pretreated *CRC*

Prognosis on Standard of Care in CRC with KRAS^{G12C} Mutations Have Historically Been Worse Than the Broader CRC Population

Population	Historical Efficacy Outcomes 3rd Line and Beyond
KRAS-agnostic	• Regorafenib[1] or Trifluridine/Tipiracil[2,3]: – ORR: 1-2% – mPFS: 1.9-2.0 months – mOS: 6.4-8.0 months
KRAS-mutant	• Trifluridine/Tipiracil[3]: – KRAS-mut mOS = 6.5 months

- Patient outcomes in CRC have historically been poor and progressively worse in later lines of therapy
- KRAS-mutant CRC patients tend to have worse outcomes than the broader CRC patient population

[1] Obermannová R, et al. Ann Oncol. 2016;27(11):2082-2090. [2] Grothey A, et al. *Lancet*. 2013;381(9863):303-312. [3] Mayer RJ, et al. *N Engl J Med*. 2015;372(20):1909-1919. [3]Van Cutsem E, et al. *Eur J Cancer*. 2018;90:63-72.

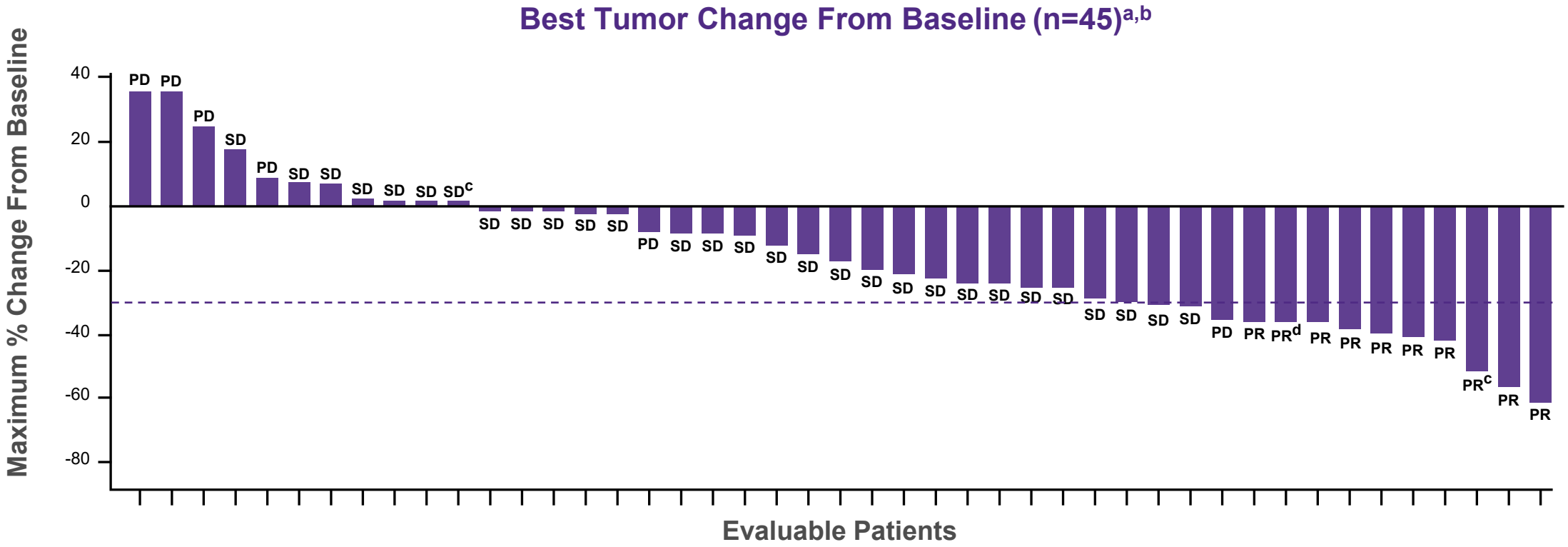
Studied CRC patients Were Heavily Pretreated; 90% of Patients in Combination Treatment Were 3rd Line or Beyond

	Adagrasib Monotherapy[a] (n=46)	Adagrasib + Cetuximab[b] (n=32)
Median age, y (range)	58 (29-79)	60 (41-74)
Female, n (%)	23 (50%)	17 (53%)
Race, n (%)		
White	35 (76%)	26 (81%)
Black	6 (13%)	4 (13%)
Asian	3 (7%)	2 (6%)
Other	2 (4%)	0 (0%)
ECOG PS, n (%)		
0	23 (50%)	14 (44%)
1	23 (50%)	18 (56%)
Prior lines of systemic anticancer therapy, median (range)	3 (1-10)	3 (1-8)
Prior lines of systemic anticancer therapy, %		
1/2/3/≥4	20%/26%/20%/35%	9%/25%/34%/31%
Prior systemic anticancer therapy, %		
Fluoropyrimidine/oxaliplatin/irinotecan	100%/98%/80%	100%/100%/88%
Anti-VEGF	83%	84%
Anti-EGFR biological therapy	2%	0%
Regorafenib and/or trifluridine/tipiracil	22%	19%
Molecular status, n (%)[c]		
BRAF V600E	0/44 (0%)	0/30 (0%)
MSI-H or dMMR	1/35 (3%)	0/19 (0%)
EGFR amplification	1/35 (3%)	1/28 (4%)
TP53	23/34 (68%)	18/26 (69%)
PIK3CA	5/36 (14%)	3/26 (12%)

[a]Adagrasib monotherapy was administered at a dose of 600 mg BID. [b]Adagrasib was administered at a dose of 600 mg BID. Cetuximab was administered IV at a dose of 400 mg/m^2 followed by 250 mg/m^2 QW, or 500 mg/m^2 Q2W (Phase 1b). [c]Molecular status includes patients with conclusively evaluable test results. Data as of 25 May 2021 for monotherapy (median follow-up: 8.9 months). Data as of 9 July 2021 for the cetuximab combination (median follow-up: 7 months).

Presented at the European Society for Medical Oncology (ESMO) Congress, 19 September 2021

Adagrasib Monotherapy in Patients With Advanced CRC: Best Overall Response

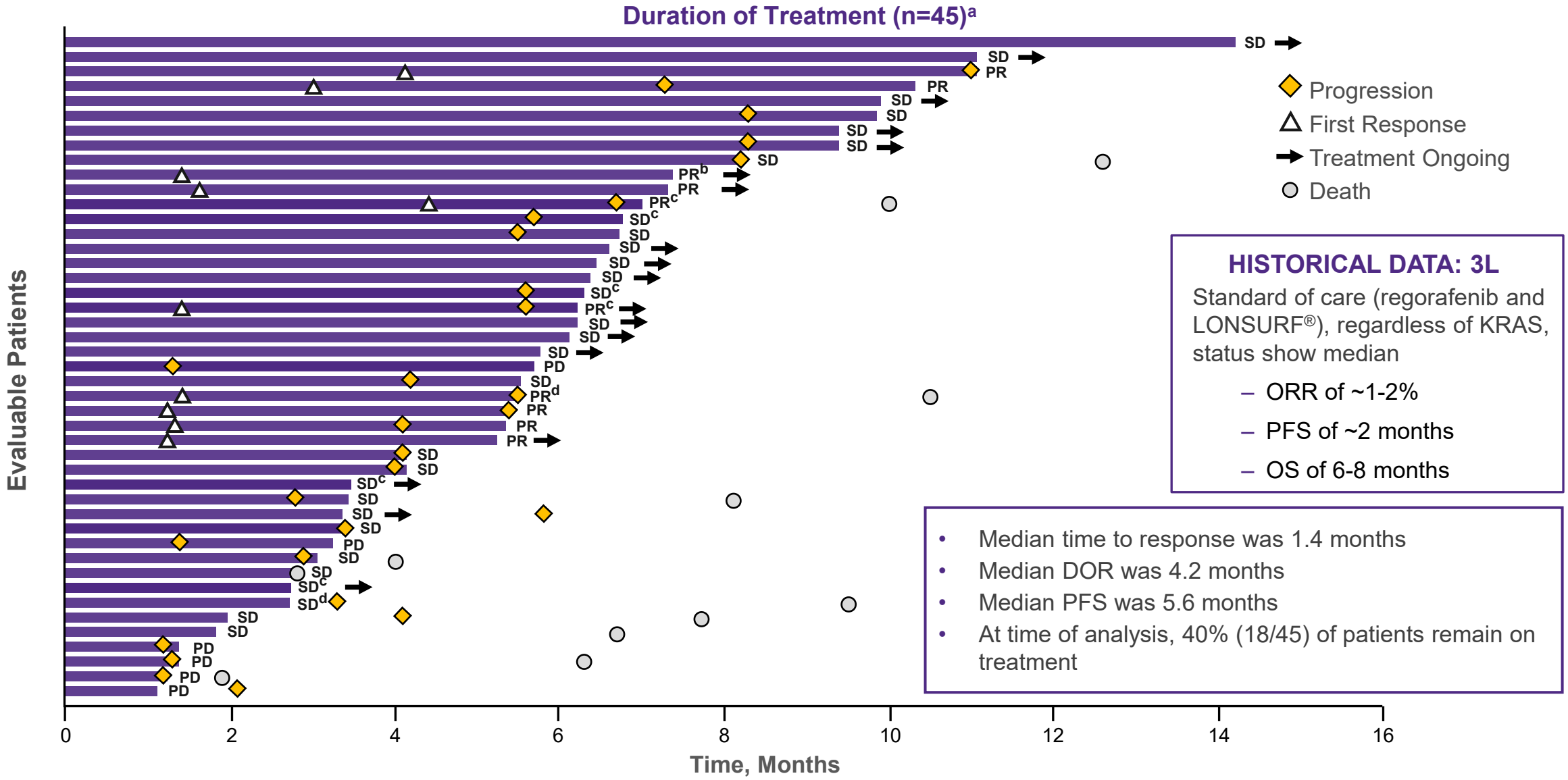


- No apparent association between response rate and molecular status was shown in an exploratory analysis
- Response rate was 22% (10/45), including 1 unconfirmed PR (unconfirmed response remains unconfirmed)[e]
- SD was observed in 64% (29/45) of patients[e]
- Clinical benefit (DCR) was observed in 87% (39/45) of patients[e]

[a]All results are based on investigator assessments. [b]Efficacy evaluable population (n=45) excludes 1 patient who withdrew consent prior to the first scan. [c]Phase 1/1b. [d]At the time of the 25 May 2021 data cutoff, the patient had uPR, After a follow-up scan after the data cut off, this response still remains unconfirmed, and the patient is still on therapy and will be evaluated with the next scan. [e]Among all enrolled Phase 1/2 monotherapy patients (n=46), ORR was 22% (10/46). Data as of 25 May 2021 for monotherapy (median follow-up: 8.9 months).

Presented at the European Society for Medical Oncology (ESMO) Congress, 19 September 2021

Adagrasib Monotherapy in Patients With Advanced CRC: Duration of Treatment



HISTORICAL DATA: 3L

Standard of care (regorafenib and LONSURF®), regardless of KRAS, status show median

- ORR of ~1-2%
- PFS of ~2 months
- OS of 6-8 months

- Median time to response was 1.4 months
- Median DOR was 4.2 months
- Median PFS was 5.6 months
- At time of analysis, 40% (18/45) of patients remain on treatment

[a]All results are based on investigator assessments. [b]At the time of the 25 May 2021 data cutoff, the patient had uPR. [c]Patients who crossed over to receive adagrasib + cetuximab. [d]Phase 1/1b. [e]Median duration of response is based on 9 confirmed responses. Data as of 25 May 2021 for monotherapy (median follow-up: 8.9 months).

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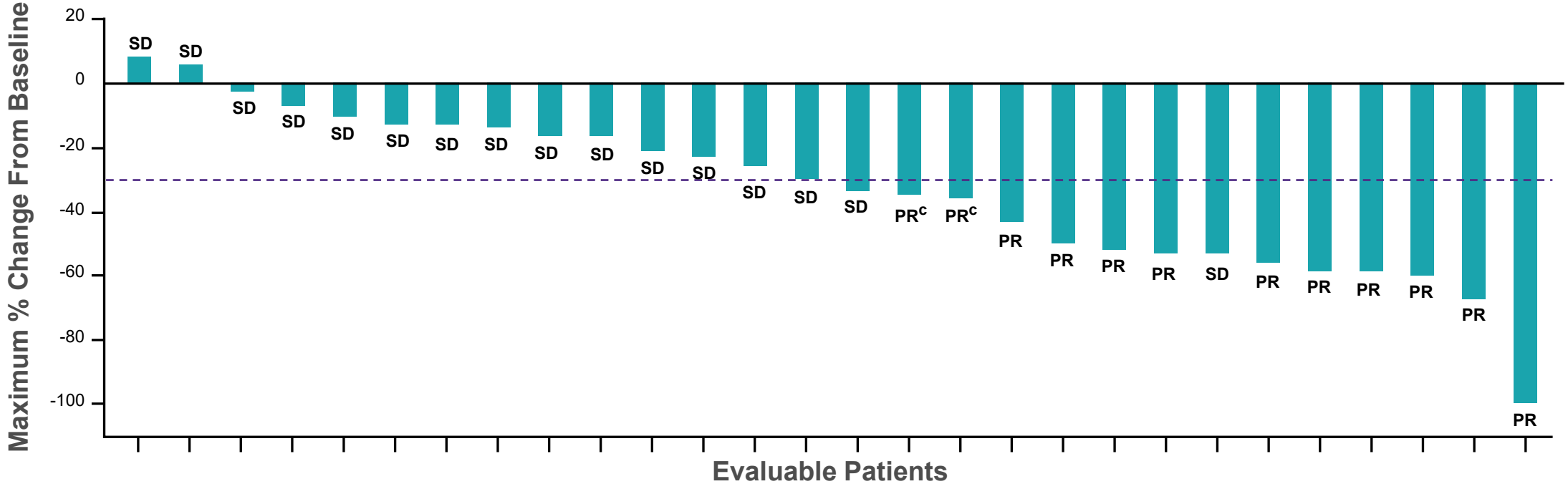
Adagrasib + Cetuximab in Patients with Advanced CRC: Best Overall Response

Best Tumor Change From Baseline (n=28)[a,b]



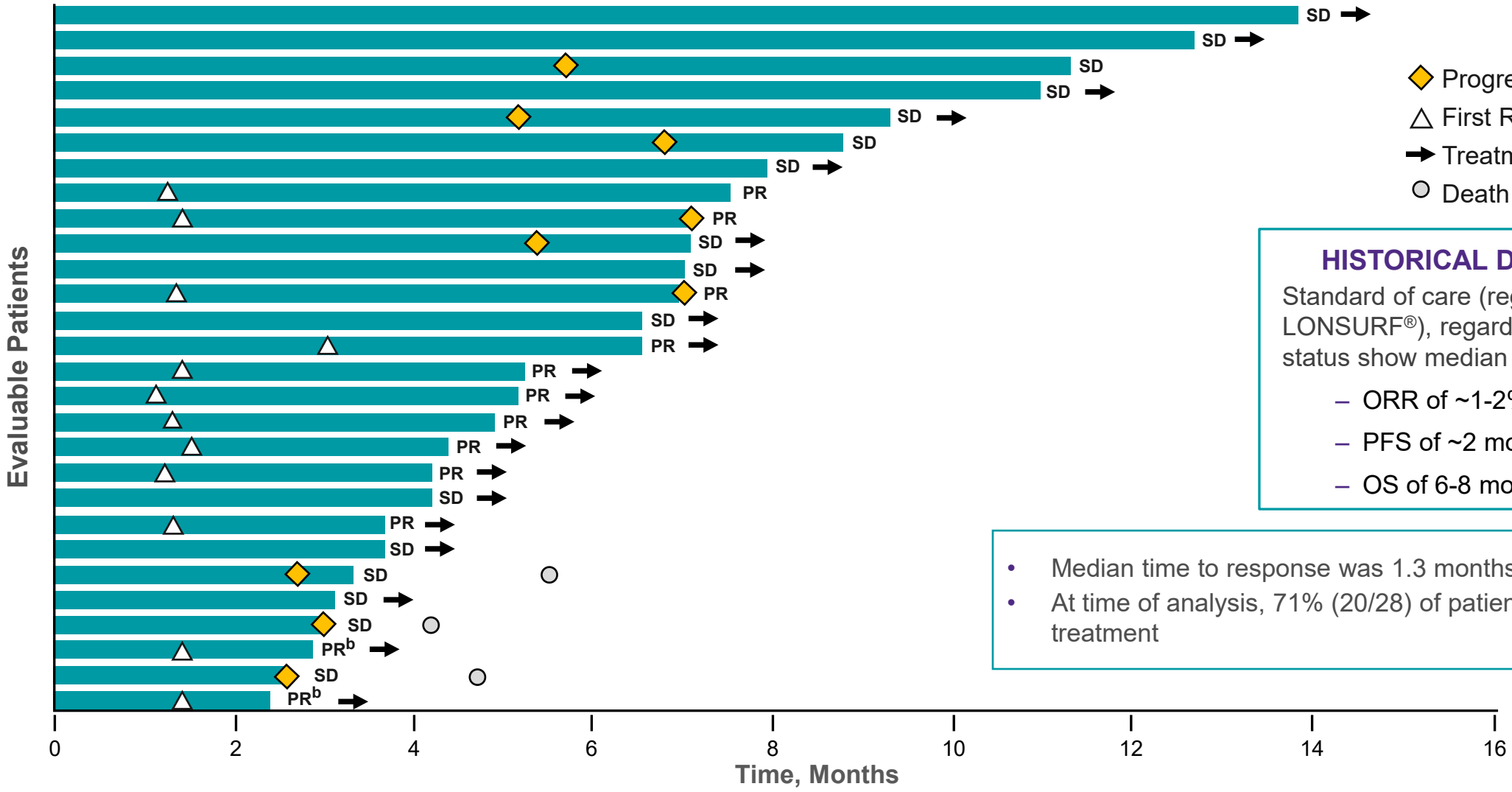
- Response rate was 43% (12/28), including 2 unconfirmed PRs[c]
  - Confirmed ORR of 39% (11/28) in the efficacy eligible and heavily pretreated population
- SD was observed in 57% (16/28) of patients
- Clinical benefit (DCR) was observed in 100% (28/28) of patients

[a]All results are based on investigator assessments. [b] Evaluable population (n=28) excludes 4 patients who withdrew consent prior to the first scan (1 withdrew due to unrelated pneumonia, 2 withdrew related to cetuximab, and 1 withdrew related to mailese from both cetuximab and adagrasib); [c]At the time of the 9 July 2021 data cutoff, 2 patients had uPRs (1 patient subsequently confirmed and 1 patient subsequently had progressive disease). [d]Among all enrolled Phase 1b combination patients (n=32). Data as of 9 July 2021 (median follow-up: 7 months).

Presented at the European Society for Medical Oncology (ESMO) Congress, 19 September 2021

Adagrasib + Cetuximab in Patients with Advanced CRC: Duration of Treatment

Duration of Treatment (n=28)[a]



HISTORICAL DATA: 3L

Standard of care (regorafenib and LONSURF®), regardless of KRAS, status show median

- ORR of ~1-2%
- PFS of ~2 months
- OS of 6-8 months

- Median time to response was 1.3 months
- At time of analysis, 71% (20/28) of patients remain on treatment

[a]All results are based on investigator assessments. [b]At the time of the 9 July 2021 data cutoff, 2 patients had uPRs.
Data as of 9 July 2021 (median follow-up: 7 months).

Adagrasib +/- Cetuximab in Patients With Advanced CRC: Treatment-Related Adverse Events

Most Frequent TRAEs	Adagrasib Monotherapy[a] (n=46)		Adagrasib + Cetuximab[b] (n=32)	
TRAEs,[c,d] %	**Any Grade**	**Grades 3-4**	**Any Grade**	**Grades 3-4**
Any TRAEs	91%	30%	100%	16%
Most frequent TRAEs, %				
Diarrhea	63%	7%	56%	3%
Nausea	57%	0%	63%	0%
Fatigue	46%	4%	47%	0%
Vomiting	46%	0%	50%	0%
Decreased appetite	15%	0%	16%	0%
Peripheral edema	15%	0%	19%	0%
AST increase	13%	4%	6%	0%
QT prolongation	13%	2%	16%	3%
ALT increase	11%	4%	13%	0%
Anemia	11%	2%	9%	0%
Dermatitis acneiform	0%	0%	44%	3%
Rash maculopapular	2%	0%	22%	0%
Infusion-related reaction	NA	NA	19%	3%

Adagrasib Monotherapy

- No Grade 5 TRAEs
- No TRAEs that led to discontinuation

Adagrasib + Cetuximab Combination

- No Grade 5 TRAEs
- 6% (n=2) of TRAEs led to discontinuation of treatment[e]

[a]Adagrasib monotherapy was administered at a dose of 600 mg BID. [b]Adagrasib was administered at a dose of 600 mg BID + cetuximab was administered IV at a dose of 400 mg/m^2 followed by 250 mg/m^2 QW, or 500 mg/m^2 Q2W. [c]Occurred in ≥10% of patients treated with adagrasib monotherapy and select TRAEs of interest in patients treated with adagrasib + cetuximab combination. [d]Includes events reported between the first dose and 25 May 2021 for adagrasib monotherapy (median follow-up: 8.9 months). Includes events reported between the first dose and 9 July 2021 for adagrasib + cetuximab combination (median follow-up: 7 months). [e]TRAEs leading to discontinuation were grade 2 treatment-related malaise and grade 2 cetuximab-related infusion-related reaction.

Presented at the European Society for Medical Oncology (ESMO) Congress, 18 September 2021

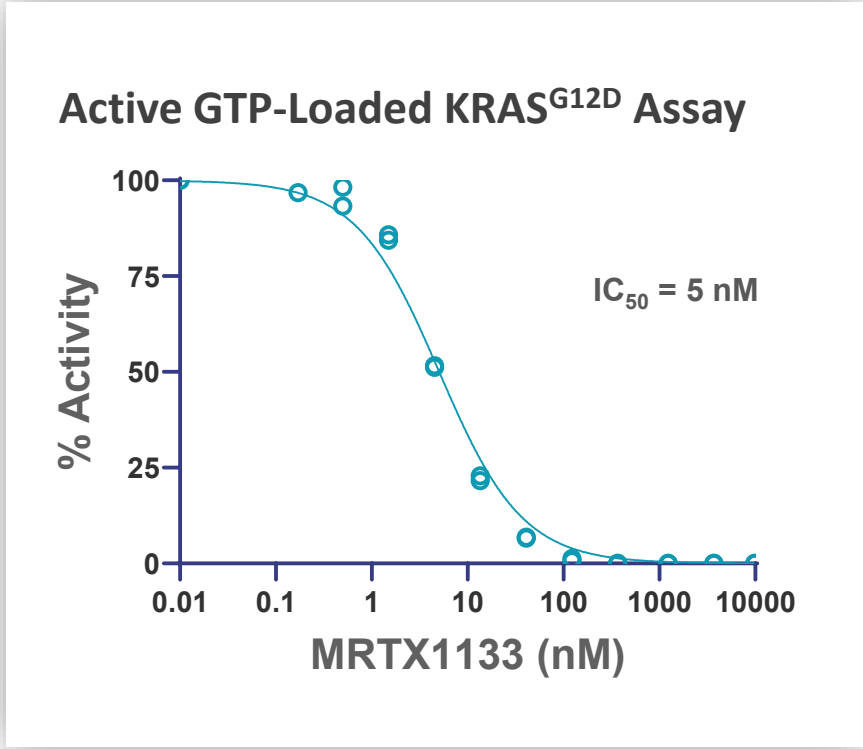
MIRATI THERAPEUTICS

MRTX1133:

KRAS^{G12D} Selective Inhibitor

MRTX1133: Potential First-in-Class KRAS^{G12D} Selective Inhibitor

Assay	Criteria	MRTX1133
KRAS^{G12D} cell activity	<10nM	**~5 nM**
Selectivity over KRAS^{WT}	>100-fold	**>1,000-fold**
Predicted human half-life	>24 hours	**~50 hours**
Low risk for hERG/off-target pharmacology	>10μM	✓
Drug-drug interaction (CYPs)	Low risk	✓



- MRTX1133 is a small molecule that selectively & reversibly binds to & inhibits KRAS^{G12D} in both active & inactive states
- MRTX1133 demonstrates selective inhibition of cell viability of KRAS^{G12D} mutant, but not KRAS wild-type, tumor cells

MRTX1133: Clinical Development Path and Design Principles

PATH TO CLINICAL DEVELOPMENT

- Optimizing target coverage throughout the dosing interval is important for maximizing antitumor activity in KRAS mutated cancers
- To ensure sustained therapeutic levels are achieved, evaluation is ongoing of drug delivery platforms, including long-acting IV injectables
- IV injectable route of administration commercially attractive and compatible with development as a monotherapy or in combination with standard of care regimens
- IND filing planned for 2022

CLINICAL TRIAL DESIGN PRINCIPLES

- Multi-cohort Phase 1 monotherapy trial comparable to adagrasib
  - Rapid dose escalation strategies to define a tolerated and active dose
- Multiple expansion cohorts for pancreatic, colon, lung and other G12D patients
- Rational combination approaches are similar to G12C and enabled in first-in-human clinical trials

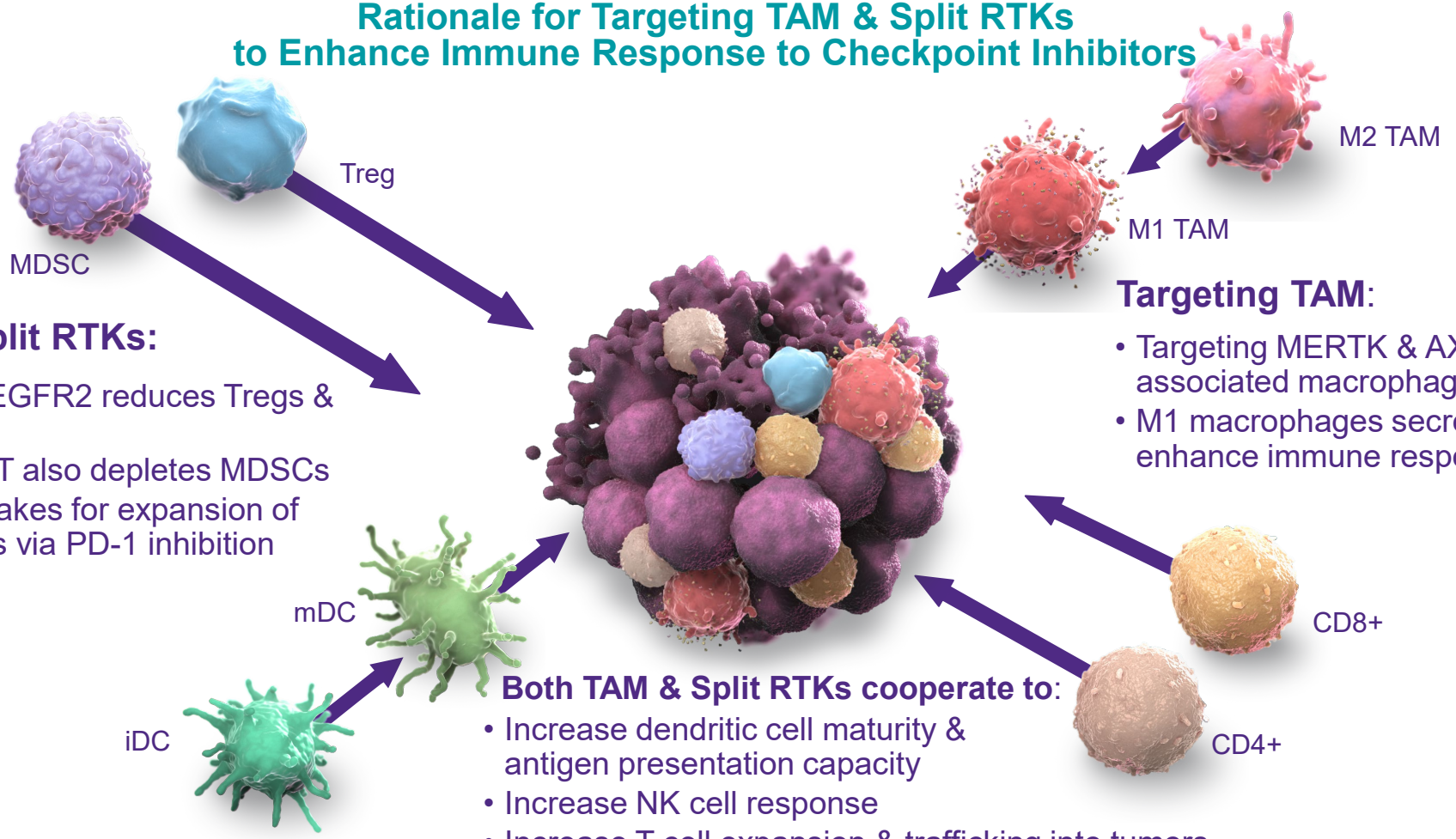
IND: investigational new drug; IV = intravenous

MIRATI THERAPEUTICS

Sitravatinib + Checkpoint Inhibitors

Sitravatinib Inhibits TAM (TYRO3, AXL and MER), VEGFR2, and KIT Receptors and May Restore Immune Response

Rationale for Targeting TAM & Split RTKs to Enhance Immune Response to Checkpoint Inhibitors



Targeting Split RTKs:

- Targeting VEGFR2 reduces Tregs & MDSCs
- Targeting KIT also depletes MDSCs
- Releases brakes for expansion of CD8+ T cells via PD-1 inhibition

Targeting TAM:

- Targeting MERTK & AXL shifts tumor associated macrophage (TAM) type to M1
- M1 macrophages secrete cytokines that enhance immune response (IL-12, TNF)

Both TAM & Split RTKs cooperate to:

- Increase dendritic cell maturity & antigen presentation capacity
- Increase NK cell response
- Increase T cell expansion & trafficking into tumors

Pircher et al., Synergies of Targeting Tumor Angiogenesis and Immune Checkpoints. Int J Mol Sci, 2017. 18(11).
Garton et al., Anti-KIT Monoclonal Antibody Treatment Enhances the Antitumor Activity of Immune Checkpoint Inhibitors by Reversing Tumor-Induced Immunosuppression. Mol Cancer Ther, 2017. 16(4)
Akalu, Y.T., C.V. Rothlin, and S. Ghosh, TAM receptor tyrosine kinases as emerging targets of innate immune checkpoint blockade for cancer therapy. Immunol Rev, 2017. 276(1)
Graham, D.K., D. DeRyckere, K.D. Davies, and H.S. Earp, The TAM family. Nat Rev Cancer, 2014. 14(12)
Du, W., Huang, H., Sorrelle, N., & Brekken, R. A. (2018). Sitravatinib potentiates immune checkpoint blockade in refractory cancer models. JCI Insight, 3(21).

MRTX-500: Phase 2, Open-Label Study of Sitravatinib + Nivolumab in Patients with Nonsquamous NSCLC with Prior Clinical Benefit from Checkpoint Inhibitor Therapy

Key Eligibility Criteria
(n=68)

- Advanced/metastatic nonsquamous NSCLC[a]
- No actionable driver mutations
- Anti–PD-1/L1 must be the most recent line of therapy
- Prior Clinical Benefit (PCB) to CPI: CR, PR, or SD ≥12 weeks from prior CPI therapy
- No uncontrolled brain metastases
- ECOG PS 0-2

Sitravatinib 120 mg QD + nivolumab

Primary Endpoint:
- Objective Response Rate[b] (ORR), as defined by RECIST 1.1

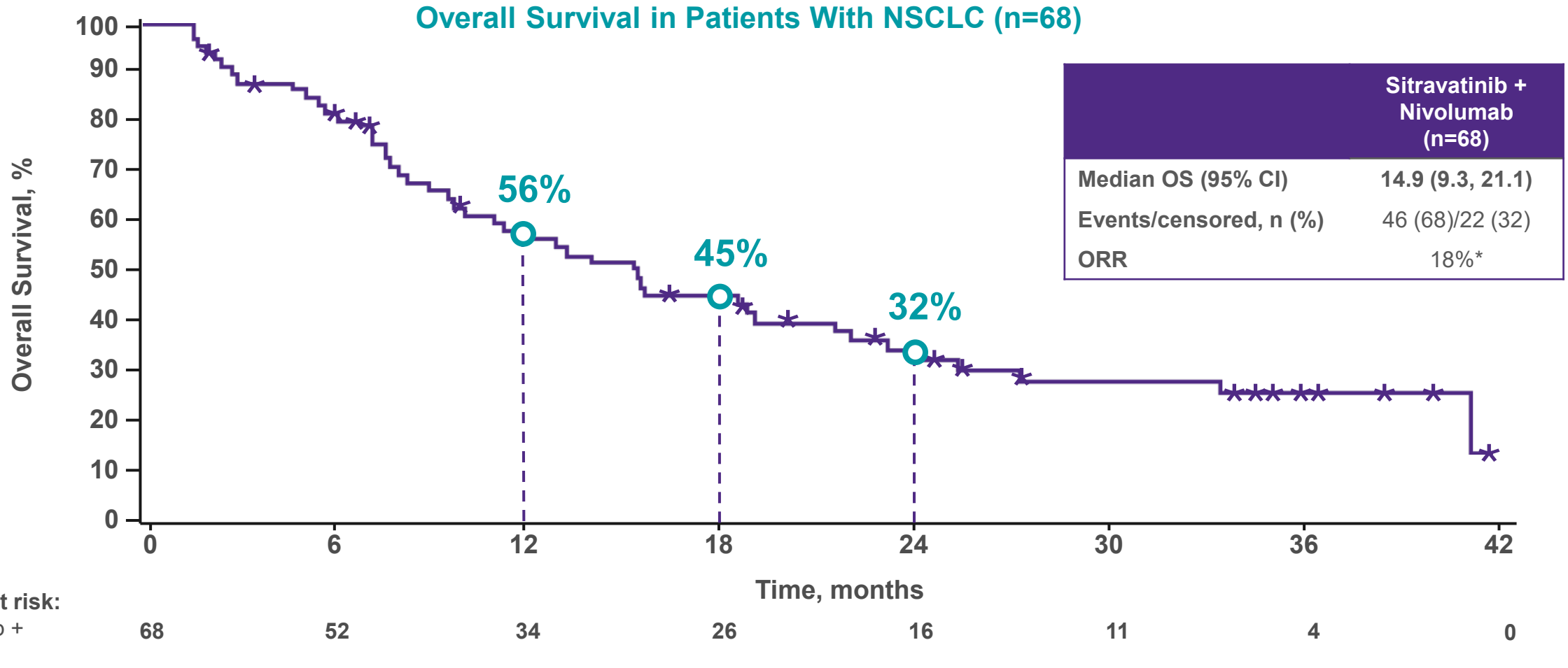
Secondary Endpoints:
- Safety and tolerability
- DOR
- CBR
- PFS
- OS
- 1-year survival rate

Data as of 1 June 2021

[a] Additional cohorts included a CPI-experienced cohort that did not receive prior clinical benefit from CPI therapy (radiographic progression of disease ≤12 weeks after initiation of treatment with CPI) and a CPI-naive cohort in patients that were previously treated with platinum-based chemotherapy. [b]Objective response rate based on investigator assessment. Dosing: sitravatinib free base formulation; nivolumab, 240 mg Q2W or 480 mg Q4W. Treatment discontinuation could be due to (but is not limited to) disease progression, global health deterioration, AEs, protocol violation, lost to follow-up, refusal of further treatment, study termination, or death.

Presented at the European Society for Medical Oncology (ESMO) Congress, 20 September 2021

Overall Survival with Sitravatinib + Nivolumab in Patients with Nonsquamous NSCLC With Prior Clinical Benefit From CPI Therapy



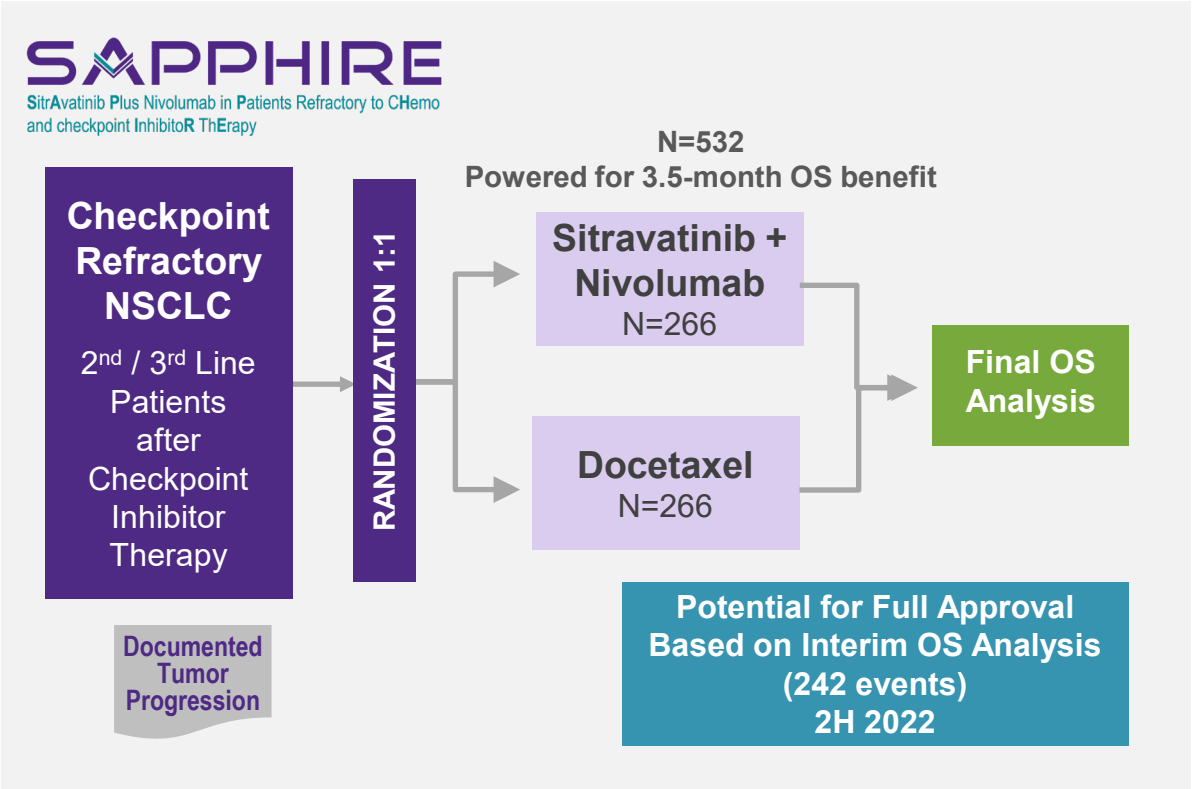
	Sitravatinib + Nivolumab (n=68)
Median OS (95% CI)	14.9 (9.3, 21.1)
Events/censored, n (%)	46 (68)/22 (32)
ORR	18%*

Median follow-up in PCB cohort: 33.6 months.
Data as of 1 June 2021.
* ORR of 18% included 2 complete responses (3%) and 10 partial responses (15%)

Presented at the European Society for Medical Oncology (ESMO) Congress, 20 September 2021

Compelling Phase 2 Results Support and Inform SAPPHIRE Phase 3 Trial in 2nd / 3rd Line Non-Squamous NSCLC

- **Encouraging Overall Survival (OS)** data from Phase 2 trial [1]
  - Median OS of 14.9 months[1] in 2L or 3L patients with Prior Clinical Benefit (PCB) on a prior checkpoint inhibitor (CPI) and subsequent disease progression (n=68)
    - 56% and 32% of patients alive at 1- and 2-years, respectively
- Phase 3 SAPPHIRE clinical trial inclusion criteria in PCB patients who received the combination as either 2nd or 3rd line therapy after progressing on treatment with checkpoint inhibitor
- **Potential to establish sitravatinib + nivolumab as new standard of care after checkpoint inhibitor failure**
  - >2nd line NSCLC U.S. & EU Populations (circa 2020): over 100,000 patients with ~70,000 being non-squamous



1. MRTX-500 Phase 2 trial: full Prior Benefit Cohort (PCB) (n=68), data cut-off of June 1, 2021, and presented at European Society for Medical Oncology (ESMO) Congress on September 18, 2021. Patients with PCB on a checkpoint inhibitor as part of their last treatment regimen prior to enrollment. PCB is defined as either complete response, partial response or stable disease for ≥12 weeks. PCB patients who received the combination as either 2nd or 3rd line of therapy after progressing on treatment with a checkpoint inhibitor. [a]10 (14.7%) patients were not evaluable for ORR: 8 patients without post-baseline scan, 1 patient without measurable disease at baseline, and 1 patient for whom all post-baseline scans were NE. Median follow-up in the PCB cohort was 33.6 months. OS: overall survival; NSCLC: non-small cell lung cancer
2. Data represented are from the CheckMate 057,KEYNOTE 010 and OAK studies and do not reflect results that might have been obtained from head-to-head studies. Results from Mirati's on-going Phase 3 SAPPHIRE trial comparing sitravatinib + nivolumab to docetaxel may differ materially from prior studies presented.
3. Borghaei H, et al. *New England Journal of Medicine* 2015;373:1627-1639, Herbst RS, et al. *Lancet*. 2016;387:1540-1550, Rittmeyer A, et al. *Lancet*. 2017;389:255-265.

MIRATI THERAPEUTICS

PRMT5 Inhibitor

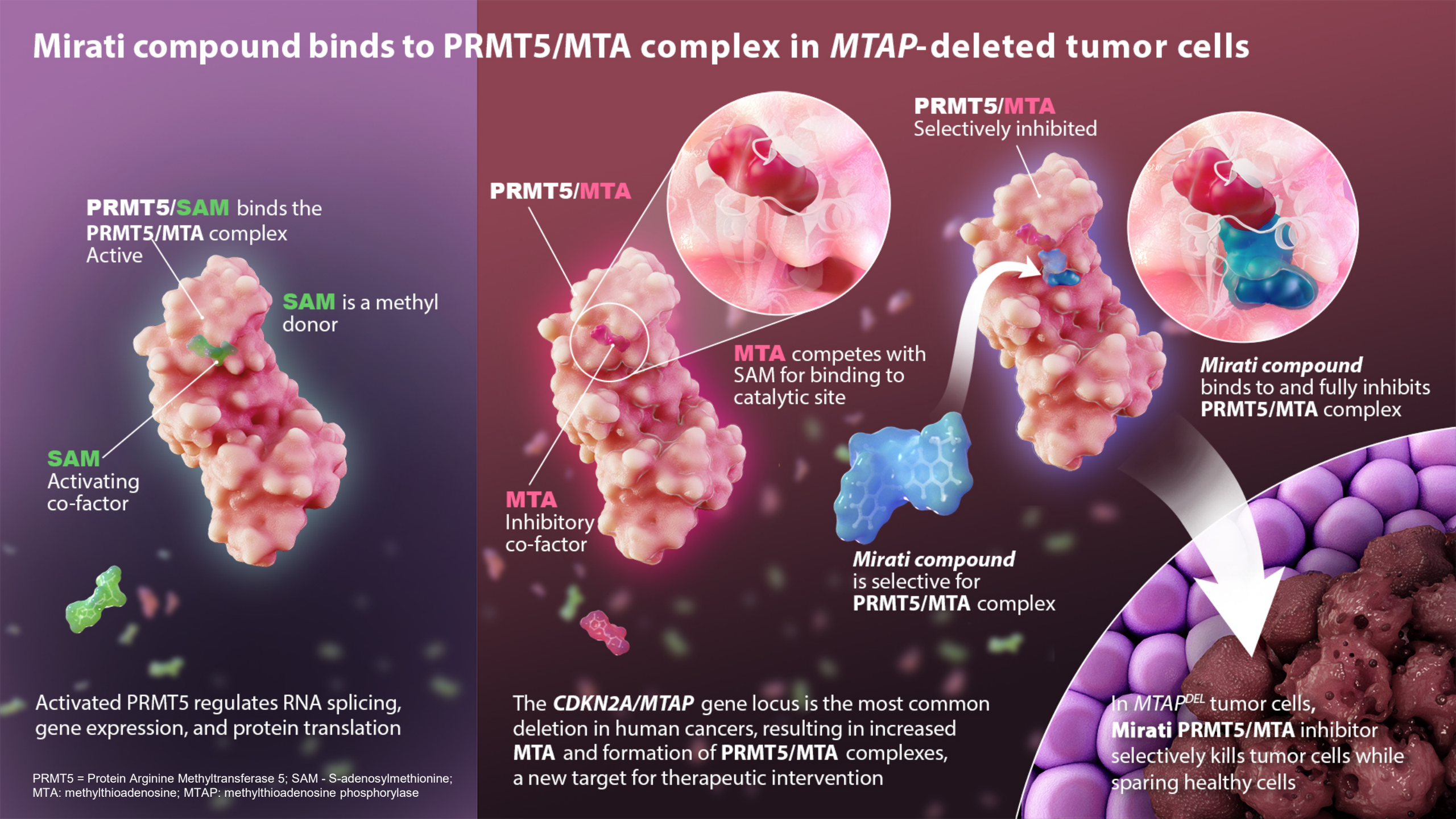
Potential First-in-class PRMT5 Inhibitor Selective for MTAP-deleted Cancers

- *MTAP* deletions occur in up to 10%[1] of all human cancers including pancreatic, lung, and bladder
  - Patients have a poor prognosis, representing a significant unmet medical need
- Internally discovered PRMT5 inhibitor represent a potential precision medicine for *MTAP*-deleted cancers
  - Program leverages a synthetic lethal approach and selectively targets the PRMT5/MTA complex in *MTAP*-deleted cancer cells
  - Designed to spare normal human cells and demonstrates improved therapeutic index in preclinical studies relative to first generation approaches
- MRTX1719 selected as clinical candidate with IND filing anticipated by year-end 2021

[1] cBioPortal

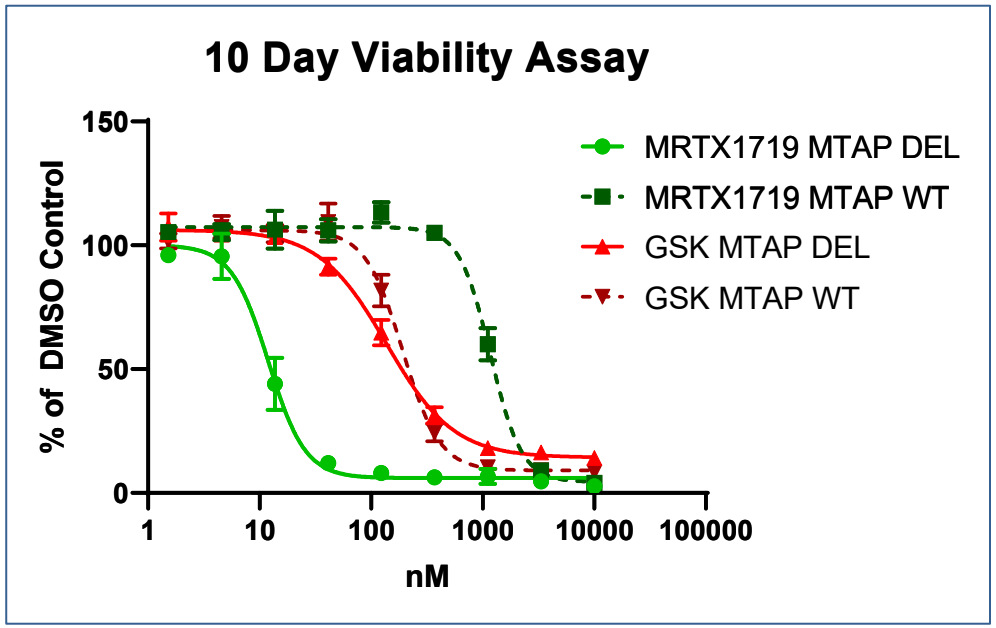
PRMT5 = Protein Arginine Methyltransferase 5; SAM - S-adenosylmethionine; MTA: methylthioadenosine; MTAP: methylthioadenosine phosphorylase; IND: investigational new drug

Mirati compound binds to PRMT5/MTA complex in *MTAP*-deleted tumor cells



MRTX1719: Potential First-in-class Selective Inhibitor of the PRMT5/MTA Complex

Assay	Criteria	MRTX1719
PRMT5/MTA *MTAP*^{DEL} SDMA cell activity	<15nM	**<10 nM**
Selectivity for *MTAP*^{WT} cells (SDMA)	>20-fold	**>70-fold**
Drug-drug interaction (CYPs)	Low risk	✓
Favorable bioavailability	Low risk ADME	✓



- MRTX1719 selectively inhibits the PRMT5/MTA complex with a very slow off rate and tight binding leads to prolonged PD effects in preclinical models
- Greater inhibition of PRMT5 in *MTAP*-deleted (tumor) cells suggest the potential for an increased therapeutic index with fewer adverse events (e.g., bone marrow suppression) compared to non-PRMT5/MTA selective inhibitors

WT = wild type; ADME: absorption, distribution, metabolism, and excretion; PD = pharmacodynamic; SDMA = symmetric dimethylarginine; PRMT5 = Protein Arginine Methyltransferase 5; MTAP: methylthioadenosine phosphorylase

MIRATI THERAPEUTICS

Financial Update

Select Company Financials

NASDAQ	**MRTX**
Cash as of June 30, 2021*	$1.2B
Shares outstanding as of June 30, 2021**	59.2M
Q2 2021: Operating Expenses	$164.2M
Q2 2021: Operating Expenses net of stock-based compensation***	$136.2M

* This amount is comprised of cash, cash equivalents and short-term investments.

** Shares outstanding as of June 30, 2021, includes 51.6 million shares of common stock outstanding and pre-funded warrants to purchase a total of 7.6 million shares of common stock. The pre-funded warrants have a per share exercise price of $0.001.

*** Amount disclosed is calculated as Q2 2021 operating expenses ($164.2M) less Q2 2021 stock-based compensation expense ($28.0M).

NASDAQ: MRTX

MIRATI THERAPEUTICS

Targeting the genetic and immunological drivers of cancer

Corporate Overview Presentation
September 2021