



Next-Generation Precision Oncology Medicines

AACR-NCI-EORTC Investor Meeting

October 7, 2021

Forward-Looking Statements

Statements in this Presentation that are not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding our research and clinical development activities, plans and projected timelines, business strategy and plans, regulatory matters, objectives of management for future operations, market size and opportunity, our ability to complete certain milestones and our expectations regarding the relative benefits of our drug candidates versus competitive therapies. Words such as “believe,” “can,” “continue,” “anticipate,” “could,” “estimate,” “plan,” “predict,” “expect,” “intend,” “will,” “may,” “goal,” “upcoming,” “near term”, “milestone”, “potential,” “target” or the negative of these terms or similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include, without limitation: our preclinical studies and clinical trials may not be successful; regulatory authorities, including the U.S. Food and Drug Administration (FDA) may not agree with our interpretation of the data from clinical trials of our drug candidates; we may decide, or regulatory authorities may require us, to conduct additional clinical trials or to modify our ongoing clinical trials; we may experience delays in the commencement, enrollment, completion or analysis of clinical testing for our drug candidates, or significant issues regarding the adequacy of our clinical trial designs or the execution of our clinical trials may arise, which could result in increased costs and delays, or limit our ability to obtain regulatory approval; our drug candidates may not receive regulatory approval or be successfully commercialized; unexpected adverse side effects or inadequate therapeutic efficacy of our drug candidates could delay or prevent regulatory approval or commercialization; the COVID-19 pandemic may disrupt our business and that of third parties on which we depend, including delaying or otherwise disrupting our research and development activities; and we may not be able to obtain additional financing. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any assurance or guarantee that the assumptions on which such forward-looking statements have been made are correct or exhaustive. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this Presentation is given. Other risks and uncertainties affecting us are described more fully in our filings with the Securities and Exchange Commission. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

This Presentation discusses drug candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these drug candidates for the use for which such drug candidates are being studied.



Agenda

Introduction

Athena Countouriotis, M.D., President & CEO

Repotrectinib TRIDENT-1 Presented Data

ROS1+ TKI-pretreated NSCLC

Mohammad Hirmand, M.D., Chief Medical Officer

Elzovantinib (TPX-0022) SHIELD-1 Presented Data

Solid Tumors with MET Genetic Alterations

Mohammad Hirmand, M.D., Chief Medical Officer

Q&A Panel

Athena Countouriotis, M.D., President & CEO

Mohammad Hirmand, M.D., Chief Medical Officer

Alexander Drilon, M.D.

Chief, Early Drug Development Service, Memorial Sloan Kettering Cancer Center

David S. Hong, M.D.

Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center

Clinical data for repotrectinib from the NTRK-positive TKI-naïve and TKI-pretreated advanced solid tumor cohorts of TRIDENT-1 will be presented at a late breaker plenary presentation on October 8 at 10:05 am ET at the AACR-NCI-EORTC conference.



Introduction

Athena Countouriotis, M.D.
President & Chief Executive Officer



Robust Pipeline with Four Clinical Stage Drug Candidates

Lead Candidate: Repotrectinib with 2 Breakthrough Therapy Designations¹

Inhibitor of ROS1 and TRK²



NSCLC

Other
Solid
Tumors

Best-in-class potential in TKI-naïve and TKI-pretreated *ROS1*+ NSCLC, and TKI-pretreated *TRK*+ solid tumors

Inhibitor of JAK2, SRC and FAK



Pancreatic

CRC

NSCLC Endometrial

Other
Solid
Tumors

Combination potential with *KRAS*-targeting agents, with first cohort planned in *KRAS mutant G12D* solid tumors

Developing **potential best-in-class** drug candidates

Deep expertise in tumor biology and **structure-based drug design**

Leveraging strategies for **rapid proof-of-concept data** and **accelerated paths to market**

Development and commercial synergies across the portfolio

\$1.1 billion in cash, cash equivalents and marketable securities, as of 30-Jun-2021, expected to fund current operations into 2024

Early Stage Pipeline

Elzovantinib (TPX-0022)

Inhibitor of MET, CSF1R and SRC



NSCLC

Gastric

Other
Solid
Tumors

Encouraging early clinical activity, supporting development as monotherapy and in combinations

TPX-0046

Inhibitor of RET



NSCLC

Thyroid

Other
Solid
Tumors

Encouraging early clinical activity, supporting development in TKI-naïve and TKI-pretreated settings

TPX-0131

Inhibitor of ALK



NSCLC

Highly potent and CNS penetrant in preclinical studies

¹ Breakthrough Therapy designation granted in (1) *ROS1*+ metastatic NSCLC patients who have not been treated with a *ROS1* TKI; and (2) patients with adv. solid tumors that have an NTRK gene fusion who have progressed following treatment with 1 or 2 prior TRK TKIs, with or without prior chemotherapy, and have no satisfactory alternative treatments. ² Also being studied in pediatric patients harboring ALK, *ROS1* or NTRK1-3 alterations.



Ongoing Clinical Studies Against Well Validated Oncogenic Targets

	Discovery	Preclinical	Early Stage Clinical Development	Late Stage Clinical Development
Repotrectinib (ROS1/TRK)				
TRIDENT-1: Advanced NSCLC (ROS1) and solid tumors (NTRK)				
CARE: Pediatric advanced solid tumors				
TRIDENT-2: KRAS-targeting combination				
Elzovantinib (TPX-0022) (MET)				
SHIELD-1: Advanced solid tumors				
SHIELD-2: EGFR combination				
TPX-0046 (RET)				
Advanced solid tumors				
TPX-0131 (ALK)				
Advanced NSCLC				
Discovery Programs				
KRAS G12D				
p21 Activated Kinase				
Multiple GTPase Oncology Targets				

Note: Turning Point retains worldwide rights for all pipeline assets, except for repotrectinib and elzovantinib (TPX-0022) in Greater China (partnered with Zai Lab).



Highlights at AACR-NCI-EORTC Virtual International Conference on Molecular Targets and Cancer Therapeutics

Poster Presentations

- Update from the Phase 2 registrational trial of repotrectinib in TKI-pretreated patients with ROS1+ advanced non-small cell lung cancer and with NTRK+ advanced solid tumors (TRIDENT-1)¹
- Preliminary interim data of elzovantinib (TPX-0022), a novel inhibitor of MET/SRC/CSF1R, in patients with advanced solid tumors harboring genetic alterations in MET: Update from the Phase 1 SHIELD-1 trial²

Plenary Presentation, Session 2: New Drugs on the Horizon I

- Repotrectinib in patients with NTRK fusion-positive advanced solid tumors: update from the registrational phase 2 TRIDENT-1 trial³
Friday, October 8 at 10:05 am ET

¹ P224; Authors: J. Lin, et al.

² P225; Authors: David S. Hong, et al.

³ LB #6545; Authors: Benjamin Besse, et al.



Repotrectinib: Data from TRIDENT-1
ROS1+ TKI-pretreated NSCLC

Mohammad Hirmand, M.D.
Chief Medical Officer



MOLECULAR TARGETS AND CANCER THERAPEUTICS

October 7-10, 2021



Poster #: P224

Update from the Phase 2 registrational trial of repotrectinib in TKI-pretreated patients with *ROS1*+ advanced non-small cell lung cancer and with *NTRK*+ advanced solid tumors (TRIDENT-1)

Jessica J. Lin,¹ Byoung Chul Cho,² Christoph Springfield,³ D. Ross Camidge,⁴ Benjamin Solomon,⁵ Christina Baik,⁶ Vamsidhar Velcheti,⁷ Young-Chul Kim,⁸ Victor Moreno,⁹ Anthonie J. van der Wekken,¹⁰ Enriqueta Felip,¹¹ Dipesh Uprety,¹² Denise Trone,¹³ Shanna Stopatschinskaja,¹³ Alexander Drilon¹⁴

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Repotrectinib: Potent ROS1 Inhibitor in TKI-Naïve and TKI-Pretreated *ROS1*+ NSCLC

- ROS1 fusions have been identified as oncogenic drivers in 1-2% of NSCLC^{1,2}
- Crizotinib and entrectinib are FDA approved TKIs for *ROS1*+ NSCLC.³ ROS1 resistance mutations including solvent front mutations (SFMs) can emerge in up to 28% of entrectinib-treated patients and 53% of crizotinib-treated patients^{4,5}
- There are currently no FDA approved targeted treatments for TKI-pretreated *ROS1*+ NSCLC
- Repotrectinib is a next-generation TKI with a compact macrocyclic structure that binds completely inside the ATP binding pocket even in the presence of mutations⁶
- Repotrectinib (IC₅₀ < 0.2 nM) is more potent in wildtype ROS1 than crizotinib (IC₅₀ 14.6 nM) and entrectinib (IC₅₀ 10.5 nM), and is active against ROS1 resistance mutations including SFM G2032R (IC₅₀ 3.3 nM)⁷
- Preliminary data with repotrectinib in *ROS1*+ TKI-naïve NSCLC showed a cORR of 91% (N=22).⁸ Repotrectinib was granted Breakthrough Therapy Designation in this setting
- Preliminary data also showed promising activity in *ROS1*+ TKI-pretreated NSCLC including patients with known SFMs.^{7,8} Repotrectinib was granted two Fast Track Designations for *ROS1*+ TKI-pretreated NSCLC (with and without prior platinum-based chemotherapy)

1. Pan Y, et al. *Lung Cancer*. 2014;84:121-126. 2. IASLC atlas of ALK and ROS1 testing in lung cancer. In: Tsao MS, Hirsch FR, Yatabe Y ed. *International Association for the Study of Lung Cancer*; 2016. 3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer, Version 5.2021. 4. Doebele R, et al. *ESMO 2019. Abstract LBA28*. 5. Gainor JF, et al. *JCO Precis Oncol*. 2017;2017:PO.17.00063. 6. Drilon A, et al. *Cancer Discov*. 2018;8(10):1227-1236. 7. Drilon A, et al. *ESMO 2019. Abstract 4536*. 8. Cho BC, et al. *WCLC 2020 Annual Meeting. Abstract MA11.07*.



TRIDENT-1 Phase 2 Study Design

ROS1+ Advanced NSCLC				NTRK+ Advanced Solid Tumors	
EXP-1 ROS1 TKI naïve (n=55)	EXP-2 1 prior ROS1 TKI AND 1 platinum-based chemotherapy (n=60)	EXP-3 2 prior ROS1 TKIs AND No prior chemotherapy (n=40)	EXP-4 1 prior ROS1 TKI AND No prior chemotherapy (n=60)	EXP-5 TRK TKI naïve (n=55)	EXP-6 TRK TKI pretreated (n=40)
	Treated (n=21)	Treated (n=11)	Treated (n=44)	Data from NTRK+ cohorts (EXP-5 and EXP-6) will be presented at LB# 6546 during Plenary Session 2: New Drugs on the Horizon I	
	Efficacy Evaluable (n=16)	Efficacy Evaluable (n=9)	Efficacy Evaluable (n=36)		

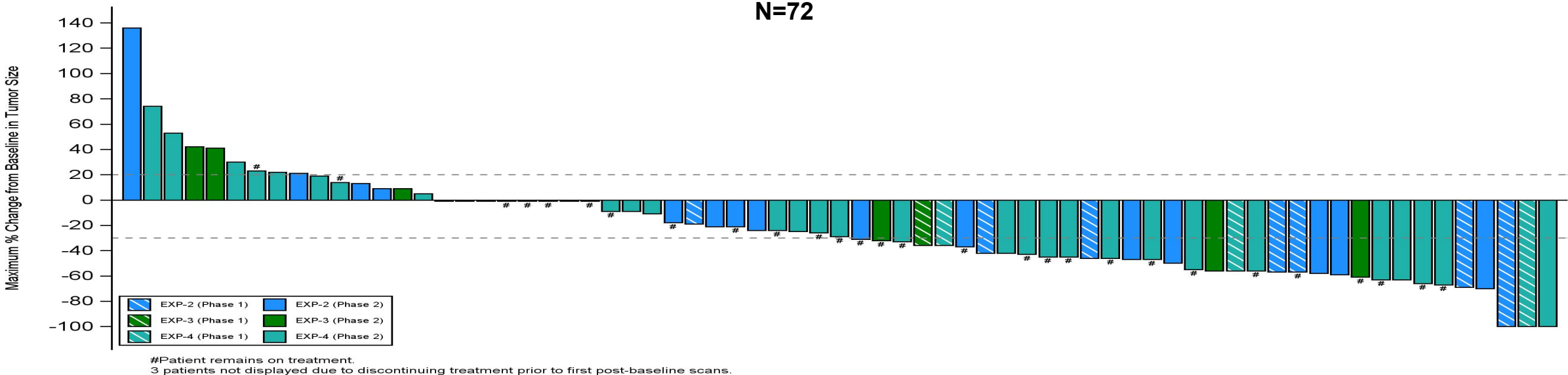
Today's presentation will focus on updated **ROS1+** TKI-pretreated cohorts (EXP-2, EXP-3 and EXP-4) in a total of n=61 efficacy evaluable patients in Phase 2

Efficacy evaluable for Phase 2: patients with baseline measurable disease and ≥ 1 post-baseline scan, or off treatment prior to first post-baseline scan.
Response based on RECIST v1.1 for Phase 2 assessed by Physician Assessment with data cutoff date of 26-Aug-2021.



Preliminary Efficacy: Patients with *ROS1*+ TKI-Pretreated Advanced NSCLC

Overall Response (Phase 1 + Phase 2)
N=72

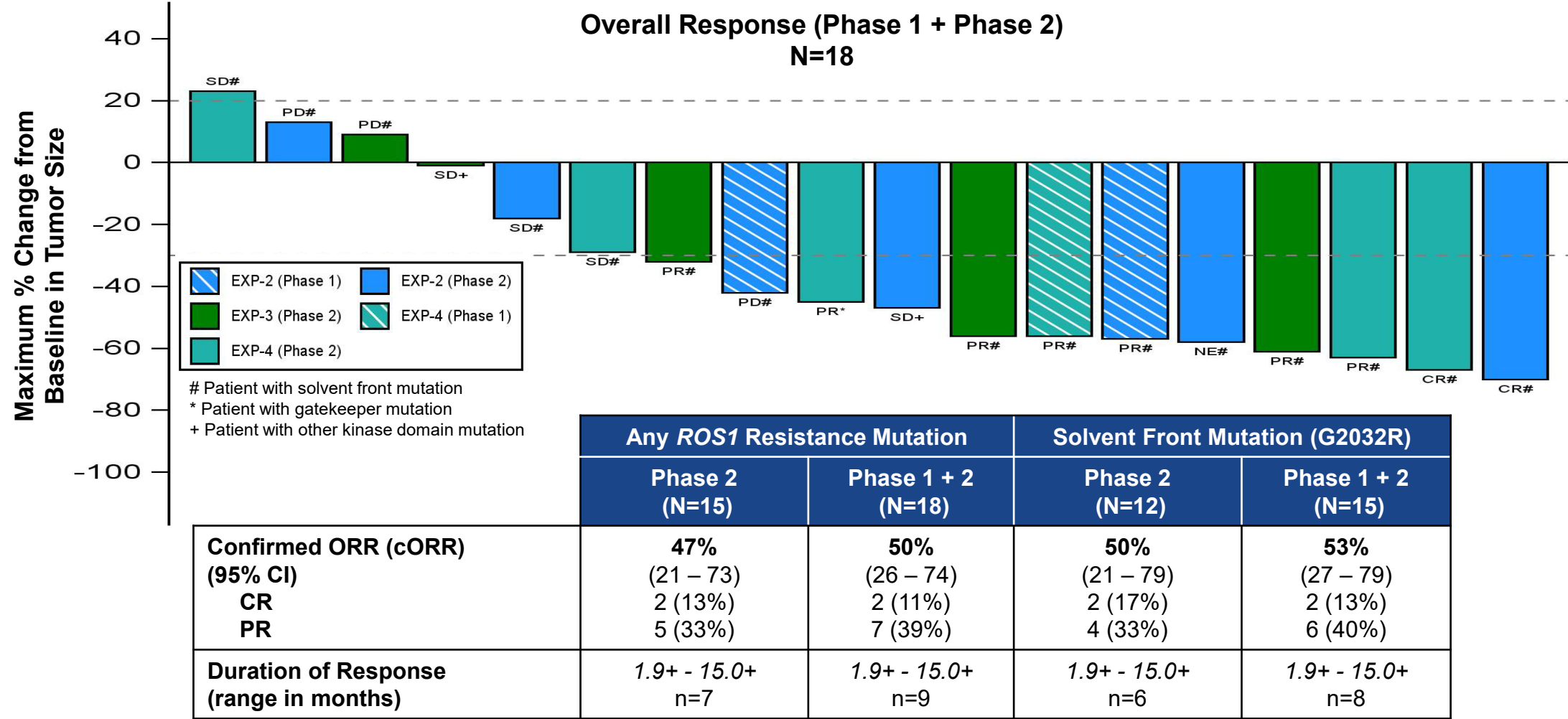


	EXP-2		EXP-3		EXP-4	
	Phase 2 (N=16)	Phase 1 + 2 (N=23)	Phase 2 (N=9)	Phase 1 + 2 (N=10)	Phase 2 (N=36)	Phase 1 + 2 (N=39)
Confirmed ORR (cORR) (95% CI)	31% (11 – 59)	39% (20 – 61)	33% (7 – 70)	30% (7 – 65)	36%* (21 – 54)	38%* (23 – 55)
Duration of Response (range in months)	1.8+ – 9.2 n=5	1.8+ – 11.1 n=9	1.9+ – 12.9+ n=3	1.9+ – 12.9+ n=3	1.7+ – 15.0+ n=13	0.8+ – 15.0+ n=15

* At time of the 26-Aug-2021 data cutoff, 3 patients in Ph 2 EXP-4 had unconfirmed PR (uPR). All 3 uPRs have been confirmed since the 26-Aug-2021 data cutoff and are included in the cORR. Ph 2: RECIST v1.1 assessed by Physician Assessment with a data cutoff date of 26-Aug-2021. Ph 1: RECIST v1.1 assessed by Blinded Independent Central Review (BICR) with data cutoff date of 22-Jul-2019 for patients with baseline measurable disease and ≥ 1 post-baseline scan. Ph 1 patients treated at or above the Ph 2 recommended dose. EXP-4 data updated since pre-recorded presentation at the AACR-NCI-EORTC conference.

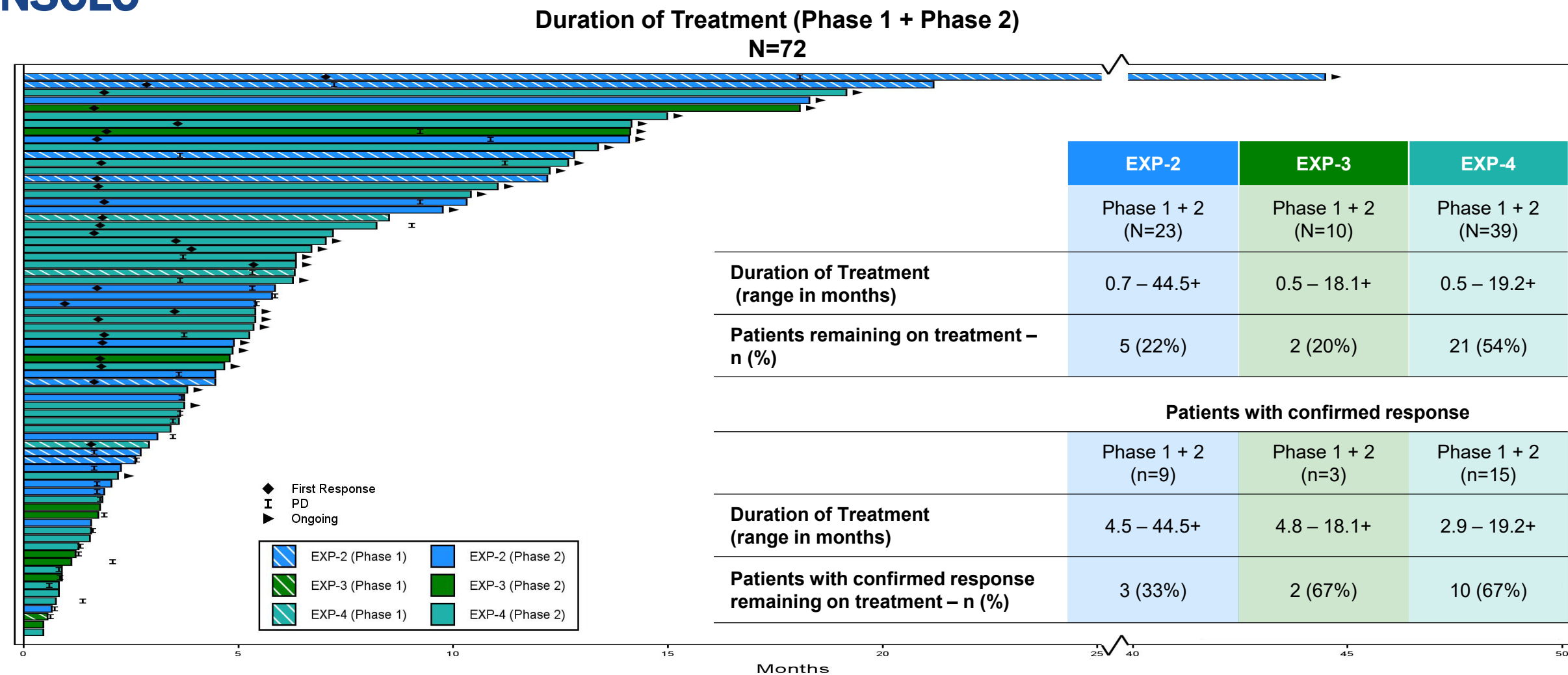


Preliminary Efficacy: Patients with *ROS1*+ TKI-Pretreated Advanced NSCLC and Baseline *ROS1* Resistance Mutations



Note: 15 of 18 resistance mutations were G2032R solvent front mutations; the other 3 included 1 gatekeeper (L2026M) and 2 other kinase domain mutations (F2004I and L2086F). 2 patients with CR had lymph node response and therefore not at -100% change from baseline. Data cutoff date 26-Aug-2021 for Phase 2 and 22-Jul-2019 for Phase 1.

Duration of Treatment: Patients with *ROS1*+ TKI-Pretreated Advanced NSCLC



Note: Phase 2 data cutoff date 26-Aug-2021 (responses confirmed by Physician Assessment). Phase 1 data cutoff date 22-Jul-2019 for responses confirmed by BICR and 26-Aug-2021 for duration of treatment. EXP-4 data updated since pre-recorded presentation at the AACR-NCI-EORTC conference.

Safety Summary: Phase 1 and Phase 2 Combined

All Treated Patients (N=301)					
Adverse Events	TEAEs (≥15% of patients)			TRAEs	
	All Grades n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 3 n (%)	Grade 4 n (%)
Dizziness	181 (60.1)	7 (2.3)	0	7 (2.3)	0
Dysgeusia	132 (43.9)	1 (0.3)	0	1 (0.3)	0
Constipation	101 (33.6)	1 (0.3)	0	0	0
Paraesthesia	87 (28.9)	3 (1.0)	0	3 (1.0)	0
Dyspnoea ^a	84 (27.9)	18 (6.0)	3 (1.0)	1 (0.3)	0
Anaemia	82 (27.2)	24 (8.0)	1 (0.3)	10 (3.3)	0
Fatigue	73 (24.3)	5 (1.7)	0	2 (0.7)	0
Nausea	62 (20.6)	3 (1.0)	0	0	0
Muscular weakness	57 (18.9)	5 (1.7)	0	3 (1.0)	0
Ataxia	51 (16.9)	0	0	0	0

^a One patient reported Grade 5 dyspnoea.

Note: 2 Grade 4 TRAEs of transient CPK increase and no Grade 5 TRAEs. TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event. Data cutoff date 26-Aug-2021.

- Repotrectinib was generally well tolerated
- Most TRAEs were Grade 1 or 2
- The most commonly-reported TEAE remains low-grade dizziness (60%)
 - 76% (138/181) were Grade 1
 - 11 (4%) patients reported ataxia in the absence of dizziness
 - No events of dizziness or ataxia led to treatment discontinuation
- Dose modifications due to TEAEs
 - 27% with TEAEs that led to dose reduction
 - 11% with TEAEs that led to drug discontinuation



Conclusions

- Repotrectinib is a next-generation ROS1/TRK inhibitor
- Repotrectinib was generally well-tolerated
- In the setting of *ROS1*+ TKI pretreated advanced NSCLC with limited treatment options, repotrectinib demonstrated clinical activity in Phase 1 and Phase 2
 - EXP-2: N=23, cORR 39% (95% CI: 20 – 61)
 - EXP-3: N=10, cORR 30% (95% CI: 7 – 65)
 - EXP-4: N=39, cORR 38% (95% CI: 23 – 55)
 - In TKI-pretreated NSCLC and *ROS1* G2032R SFM (N=15): cORR 53% (95% CI: 27 – 79)
- Enrollment is ongoing in the registrational Phase 2 TRIDENT-1 study evaluating repotrectinib for the treatment of TKI-naïve and TKI-pretreated patients with *ROS1*+ advanced NSCLC and *NTRK*+ advanced solid tumors
- Data for *NTRK*+ cohorts (EXP-5 and EXP-6) will be presented at LB# 6546 during Plenary Session 2: New Drugs on the Horizon I



**Elzovantinib (TPX-0022): Data from
SHIELD-1**
***Solid Tumors with MET Genetic
Alterations***

Mohammad Hirmand, M.D.
Chief Medical Officer



MOLECULAR TARGETS AND CANCER THERAPEUTICS

October 7-10, 2021



Poster #: P225

Preliminary interim data of elzovantinib (TPX-0022), a novel inhibitor of MET/SRC/CSF1R, in patients with advanced solid tumors harboring genetic alterations in *MET*: Update from the Phase 1 SHIELD-1 trial

David S. Hong¹, Daniel Catenacci², Lyudmila Bazhenova³, Byoung Chul Cho⁴, Mariano Ponz-Sarvis⁵, Rebecca Heist⁶, Victor Moreno⁷, Gerald Falchook⁸, Viola W. Zhu⁹, Aurélie Swald¹⁰, Benjamin Besse¹¹, Dong-Wan Kim¹², Shinkyoo Yoon¹³, Xiuning Le¹, Tingting Zhao¹⁴, Justine Lam¹⁴, Zachary Zimmerman¹⁴, Jeeyun Lee¹⁵

¹The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ²University of Chicago Medical Center, Chicago, IL, USA; ³UC San Diego Moores Cancer Center, San Diego, CA, USA; ⁴Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; ⁵Clinica Universidad de Navarra, Pamplona, Spain; ⁶Massachusetts General Hospital, Boston, MA, USA; ⁷Fundación Jiménez Díaz - START Madrid, Madrid, Spain; ⁸Sarah Cannon Research Institute at HealthONE, Denver, CO, USA; ⁹University of California Irvine, Orange, CA, USA; ¹⁰Centre de Lutte Contre le Cancer - Centre Leon Berard, Lyon, France; ¹¹Institut Gustave Roussy, Villejuif Cedex, France; ¹²Seoul National University Hospital, Seoul, Republic of Korea; ¹³Asan Medical Center, Seoul, Republic of Korea; ¹⁴Turning Point Therapeutics, Inc., San Diego, CA, USA; ¹⁵Samsung Medical Center, Seoul, Republic of Korea

Phase 1 SHIELD-1 Study Design

Population

- Adults with advanced solid tumors
- MET genetic alterations assessed by local testing (exon 14 deletion, amplification, fusion, or oncogenic kinase domain mutation)
- Asymptomatic CNS disease allowed

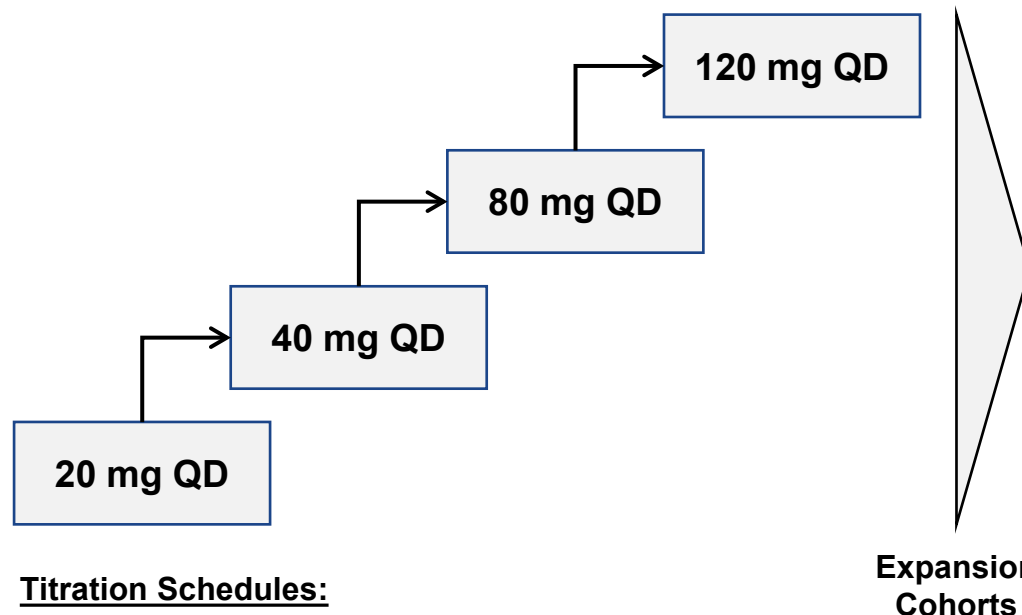
Design

- 3+3 with expansion allowed at doses where clinical activity is observed
- Response evaluation by RECIST v1.1

Primary Objectives

- Evaluate safety/tolerability and determine MTD and RP2D

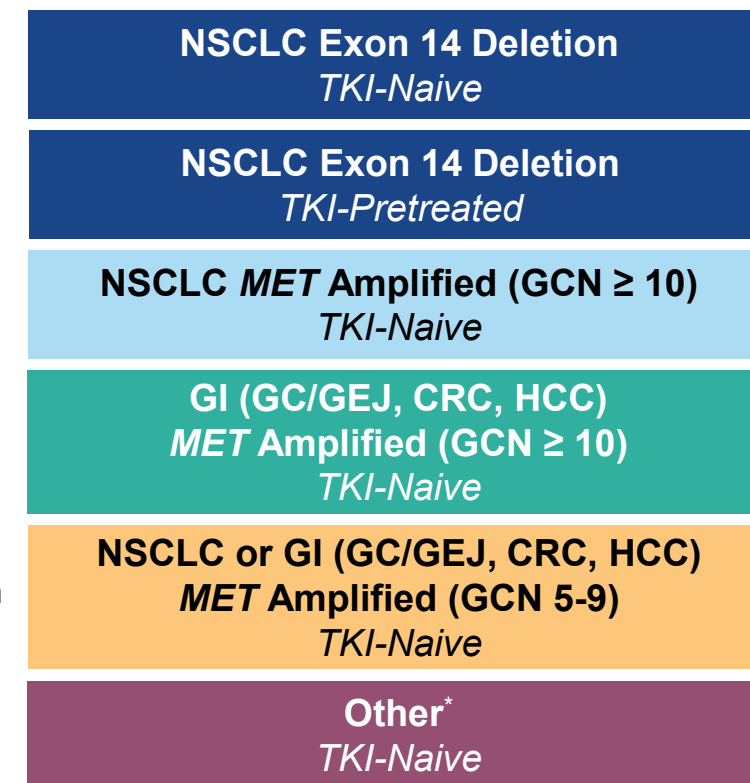
Dose Finding



Titration Schedules:

- 80 mg QD (14 days) → 120 mg QD
- 40 mg QD (14 days) → 40 mg BID
- 40 mg QD (14 days) → 80 mg QD

Dose Expansion



*Solid Tumors with MET Fusions or Oncogenic KD Mutations OR MET-amplified other than GI/NSCLC OR otherwise eligible for Cohorts I, III, or IV and >2 lines prior systemic therapy.

BID, twice daily; CNS, central nervous system; CRC, colorectal cancer; GC, gastric cancer; GEJ, gastroesophageal junction; GI, gastrointestinal; HCC, hepatocellular carcinoma; KD, kinase domain; MET, mesenchymal-epithelial transition factor; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; QD, once daily; RECIST v1.1, response evaluation criteria in solid tumors version 1.1; RP2D, recommended phase 2 dose.



Subject Disposition

**Phase 1 Dose Finding
All Treated Patients**

N=54

31 NSCLC, 9 GC/GEJ, 5 CRC, 9 Other*

Evaluable Patients[†]

N=46

TKI-Naïve (N=32)

11 NSCLC, 9 GC/GEJ, 5 CRC, 7 Other‡

TKI-Naïve NSCLC and GC/GEJ (n=20)

TKI-Pretreated (N=14)

13 NSCLC, 1 Liver

Non-Evaluable Patients

**Off Treatment Prior to
1st Evaluable Scan
N=7**

**No Baseline
Measurable Disease
N=1**

Data cut-off date August 23, 2021

*Includes 2 liver cancers, 2 melanoma, 1 esophageal cancer, 1 glioblastoma multiforme, 1 ovarian/fallopian tube/peritoneal cancer, 1 pancreatic cancer, 1 uterine cancer.

†Patients with baseline measurable disease and at least one post-baseline evaluable scan. ‡Includes 1 esophageal cancer, 1 glioblastoma multiforme, 1 liver cancer, 2 melanoma, 1 pancreatic cancer, 1 uterine cancer.

CRC, colorectal cancer; GC/GEJ, gastric cancer/gastroesophageal junction; NSCLC, non-small cell lung cancer

Note: CRC includes colorectal adenocarcinoma and rectal neuroendocrine tumor.



Demographics and Baseline Characteristics

All Treated Patients (N=54)	
Age (years)	
Median (range)	63 (33–84)
Sex, n (%)	
Female	27 (50.0)
ECOG Performance Status, n (%)	
0	15 (27.8)
1	39 (72.2)
Baseline Brain Metastasis, n (%)	
Yes	9 (16.7)
Number of Prior Regimens, n (%)	
0	3 (5.6)
1	9 (16.7)
2	19 (35.2)
≥3	23 (42.6)
Median (range)	2 (0–6)
Prior MET TKI Treatment, n (%)	
Yes	18 (33.3)
Type of Cancer, n (%)	
NSCLC	31 (57.4)
GC/GEJ Cancer	9 (16.7)
CRC*	5 (9.3)
Other†	9 (16.7)

Data cut-off date August 23, 2021

CRC, colorectal cancer; GC/GEJ, gastric cancer/gastroesophageal junction; NSCLC, non-small cell lung cancer. *CRC includes colorectal adenocarcinoma and rectal neuroendocrine tumor.

†Other includes 2 liver cancers, 2 melanoma, 1 esophageal cancer, 1 glioblastoma multiforme, 1 ovarian/fallopian tube/peritoneal cancer, 1 pancreatic cancer, 1 uterine cancer.



Preliminary Safety Summary

Adverse Events	All Treated Patients (N=54)			
	TEAEs (≥15% of patients)		TRAEs	
	All Grades	Grades≥3	All Grades	Grades≥3 [^]
	n (%)	n (%)	n (%)	n (%)
Dizziness	35 (64.8)	2 (3.7)	31 (57.4)	1 (1.9)
Constipation	18 (33.3)	1 (1.9)	3 (5.6)	-
Fatigue	17 (31.5)	3 (5.6)	12 (22.2)	2 (3.7)
Lipase increased	17 (31.5)	3 (5.6)	17 (31.5)	2 (3.7)
Anaemia	16 (29.6)	5 (9.3)	2 (3.7)	-
Amylase increased	15 (27.8)	1 (1.9)	13 (24.1)	1 (1.9)
Nausea	12 (22.2)	1 (1.9)	7 (13.0)	-
Vomiting	12 (22.2)	3 (5.6)	4 (7.4)	-
Oedema peripheral	11 (20.4)	-	9 (16.7)	-
Abdominal pain	10 (18.5)	2 (3.7)	1 (1.9)	-

- Elzovantinib was generally well tolerated
- Most common TEAE was dizziness, likely due to off target TRK inhibition
- Dose modifications due to TEAE
 - 21 (38.9%) patients with TEAEs leading to dose reduction
 - 3 (5.6%) patients with TEAEs leading to drug discontinuation
- 2 DLTs at 120 mg QD*
- All Grade peripheral edema in 11 (20.4%) patients (no Grade ≥ 3 event)
- No ILD/pneumonitis of any Grade
- No related Grade ≥ 3 ALT/AST elevation

Data cut-off date August 23, 2021.

[^] Other reported Grade 3 TRAEs are: asthenia, blood creatine phosphokinase increased, delirium, vertigo, vestibular disorder. No Grade 4 or 5 TRAEs. * Grade 3 vertigo and Grade 2 dizziness.

ALT, alanine transaminase; AST, aspartate transaminase; BID, twice daily; DLT, dose-limiting toxicity; ILD, interstitial lung disease; QD, once daily; TEAE, treatment emergent adverse event; TRAE, treatment related adverse event.



Preliminary Efficacy by Investigator Assessment

TKI-Naïve Efficacy Evaluable Patients (N=32)			
Efficacy Outcomes	NSCLC (N=11)	GC/GEJ (N=9)	Other Tumor Types (N=12)
Best Overall Response			
PR – n (%)	4 (36)	3 (33)	1 (8)
SD – n (%)	3 (27)	3 (33)	7 (58)
PD – n (%)	4 (36)	3 (33)	4 (33)
cORR	36%	33%	8%
CBR	64%	67%	67%

TKI Pre-treated Efficacy Evaluable (N=14)

Among 14 TKI-pretreated efficacy evaluable patients (13 NSCLC and 1 liver cancer), 36% received at least 5 lines of prior therapy (median: 3; range: 1-6), 7 NSCLC patients achieved SD as best overall response for a CBR of 54% in NSCLC.

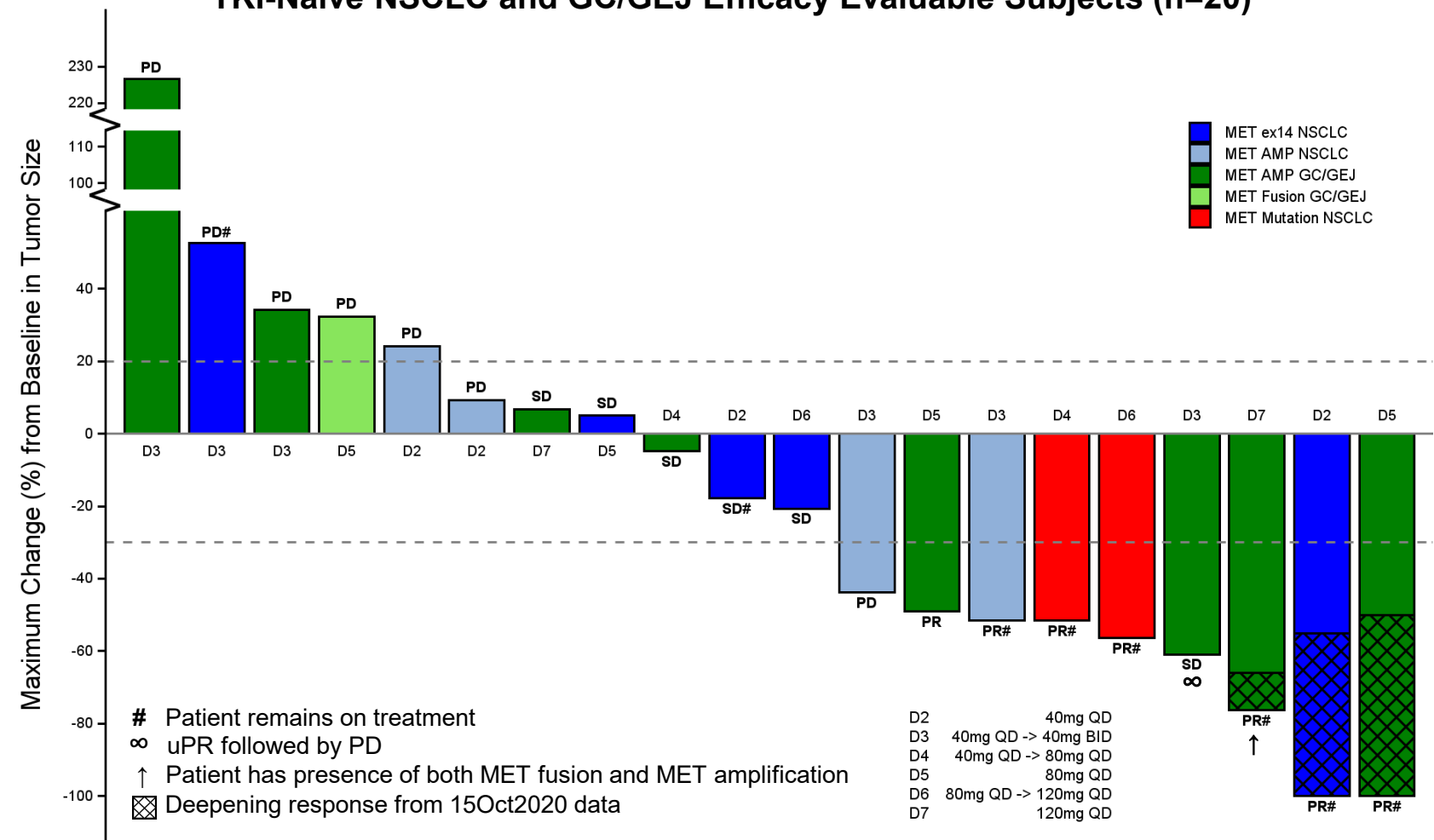
Data cut-off date August 23, 2021. CBR = PR + SD

CBR, clinical benefit rate; cORR, confirmed objective response rate; GC/GEJ, gastric cancer/gastroesophageal junction; NSCLC, non-small cell lung cancer; PD, progressive disease; PR, partial response; SD, stable disease.



Preliminary Efficacy by Investigator Assessment

TKI-Naïve NSCLC and GC/GEJ Efficacy Evaluable Subjects (n=20)



Preliminary Efficacy	TKI-Naïve Efficacy Evaluable	
	NSCLC	GC/GEJ
All Dose Levels, N	11	9
cORR (95% CI)	36% (11 - 69)	33% (7 - 70)
CBR (95% CI)	64% (31 - 89)	67% (30 - 93)

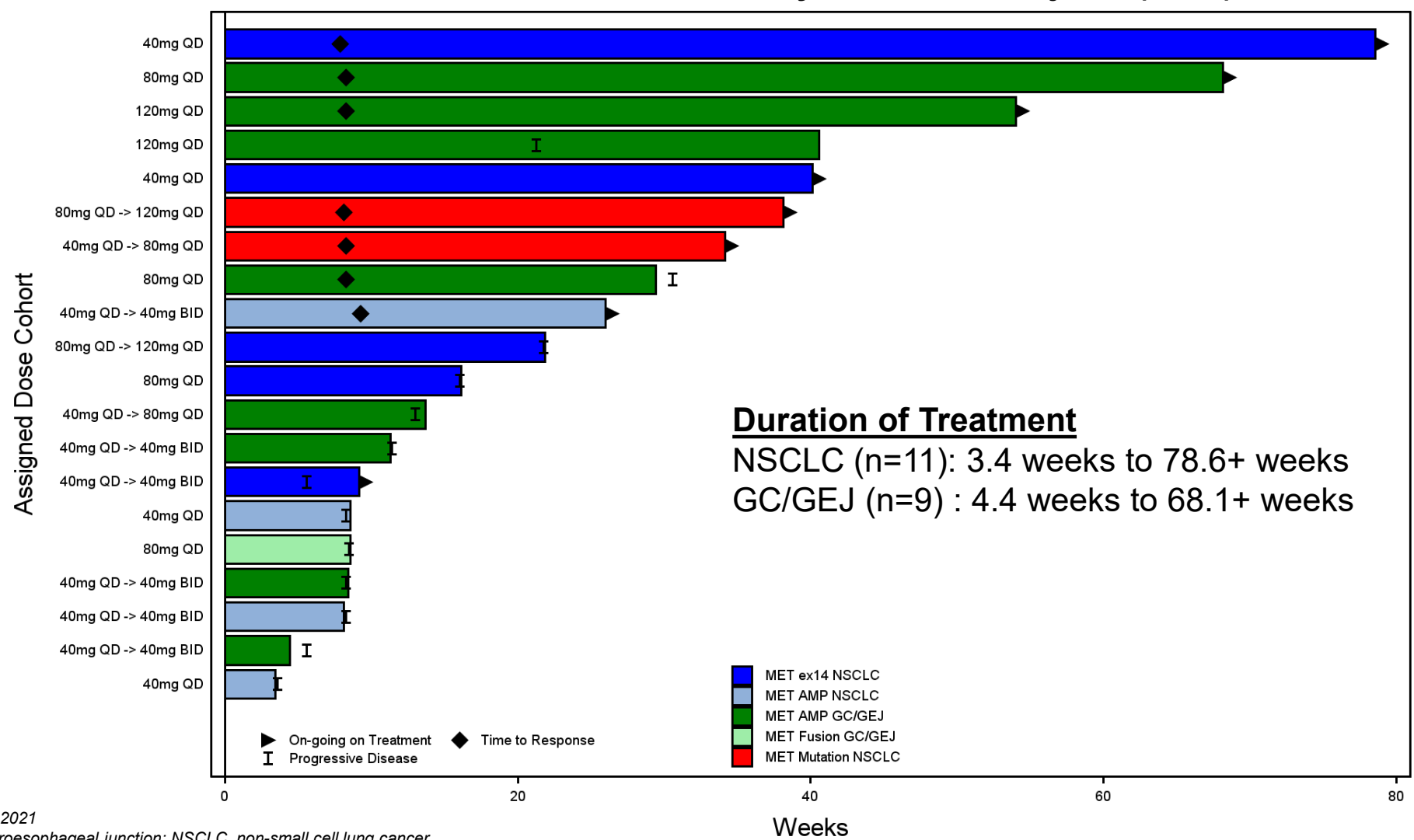
Note:

- 95% patients received prior Chemo/IO therapy
- DOR for 7 PRs were 15+, 12.9+, 9.2+, 5.6+, 5.6+, 5.2, and 1.8+ months
- MET amplification: 4 PRs (GCN: 7, 12, 14, and 25); 8 non-responders (GCN: n=6 had <10; n=1 had ≥6; n=1 had >13)

Data cut-off date August 23, 2021
CBR, clinical benefit rate; cORR, confirmed objective response rate; DOR, duration of response; GC/GEJ, gastric cancer/gastroesophageal junction adenocarcinoma; GCN, gene copy number; IO, immunotherapy; NSCLC, non-small cell lung cancer; PD, progressive disease; RP2D, recommended phase 2 dose.

Duration of Treatment

TKI-Naïve NSCLC and GC/GEJ Efficacy Evaluable Subjects (n=20)



Data cut-off date August 23, 2021
GC/GEJ, gastric cancer/gastroesophageal junction; NSCLC, non-small cell lung cancer.

Conclusions

- Elzovantinib was generally well tolerated
- Responses in MET TKI-naïve NSCLC and GC/GEJ cancers
 - 95% patients received prior Chemo/IO therapy
 - NSCLC: cORR 36% (all dose levels)
 - GC/GEJ Cancer: cORR 33% (all dose levels)
- Limited activity in heavily pretreated MET TKI-pretreated patients (36% with ≥ 5 lines of prior therapy) with a CBR of 54% in NSCLC patients



Regulatory Updates

Repotrectinib

- At the anticipated meeting with the FDA in 1H 2022 to discuss the topline BICR results from EXP-1 of the TRIDENT-1 study, plan to also discuss available BICR data in at least 50 patients from the ROS1-positive TKI-pretreated NSCLC cohorts of the study (EXP-2, EXP-3, EXP-4), with at least 6 months of follow-up for the majority of responders

Elzovantinib (TPX-0022)

- Recent End of Phase 1 meeting with the FDA focused on next steps in patients with NSCLC
- In initial feedback, FDA recommended exploring an intermediate dose level using the QD titration to BID dosing strategy in at least 6 to 10 patients prior to starting the Phase 2 portion of the study
 - Plan to enroll at least 6 to 10 patients at 60 mg QD (14 days) → 60 mg BID in Phase 1
- Plan to revise SHIELD-1 into a potentially registrational Phase 1/2 study and initiate the Phase 2 portion in 2022, pending FDA feedback on data from the intermediate dose level
- FDA feedback focused on gastric/gastroesophageal junction cancer (GEJ) is pending
- Plan to initiate the SHIELD-2 combination study with an EGFR targeted therapy in 2022, pending filing of an IND application by the FDA





***Thank you to the patients and investigators for participating
in the TRIDENT-1 and SHIELD-1 studies***



Next-Generation Precision Oncology Medicines

AACR-NCI-EORTC Investor Meeting

October 7, 2021