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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

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Disclosures

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- ***Other ownership interests:*** Molecular Match (Advisor), OncoResponse (Founder), Telperian Inc (Advisor)

- **TPX-0022 is investigational and not approved for the treatment of any condition in any jurisdiction**

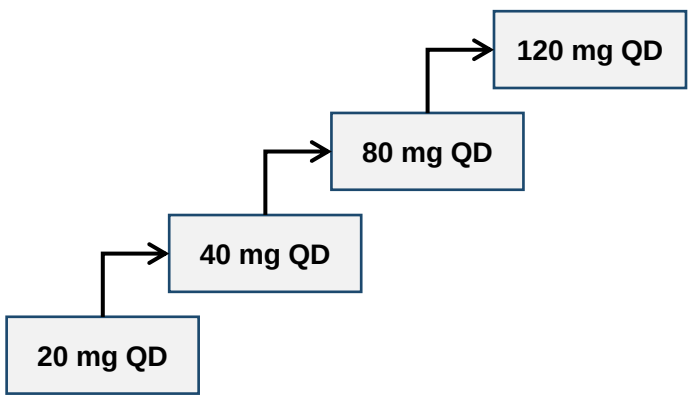
Phase 1 SHIELD-1 Study Design

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 – Enrollment Complete



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**

Expansion Cohorts

Dose Expansion – Enrolling

- **NSCLC Exon 14 Deletion** *TKI-Naive*
- **NSCLC Exon 14 Deletion** *TKI-Pretreated*
- **NSCLC *MET* Amplified (GCN ≥ 10)** *TKI-Naive*
- **GI (GC/GEJ, CRC, HCC) *MET* Amplified (GCN ≥ 10)** *TKI-Naive*
- **NSCLC or GI (GC/GEJ, CRC, HCC) *MET* Amplified (GCN 5-9)** *TKI-Naive*
- **Other*** *TKI-Naive*

Proposed RP2D of 40 mg QD → 40 mg BID determined and enrollment into Dose Expansion cohorts initiated

*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.

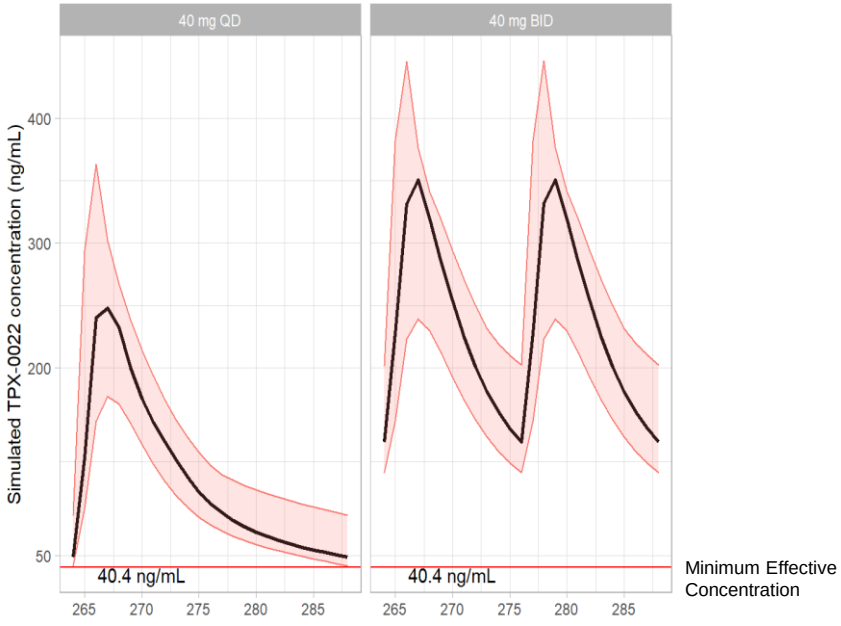
Demographics and Baseline Characteristics

	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.

PK Coverage at Proposed RP2D



The lines represent the median and shaded ribbons represent 95% confidence interval

Dose (mg)	Median $C_{trough,ss}$ (ng/mL)	Fold Coverage over MEC	% of Subjects with $C_{trough,ss}$ above MEC
20 QD	28.9	0.71	25.0
40 QD	58.4	1.45	73.1
40 BID	144	3.56	94.2
80 QD	119	2.95	92.3
120 QD	181	4.48	94.2

- 40 mg QD dose is predicted to result in trough concentration that is 1.45-fold above the minimum effective concentration (MEC) at steady state
- 40 mg BID dose is predicted to result in trough concentration that is 3.56-fold above the MEC at steady state

Preliminary Safety Summary

	All Treated Patients (N=54)			
	TEAEs (≥15% of patients)		TRAEs	
Adverse Events	All Grades n (%)	Grades≥3 n (%)	All Grades n (%)	Grades≥3^ 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)	-

- TPX-0022 was generally well tolerated
- Most common TEAE was dizziness, likely due to off target TRK inhibition
  - All Grade dizziness at proposed RP2D (40 mg QD → 40 mg BID) in 46.7% of patients (no Grade ≥ 3 event)
- 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 related Grade ≥ 3 ALT/AST elevation
- No ILD/pneumonitis of any Grade

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.

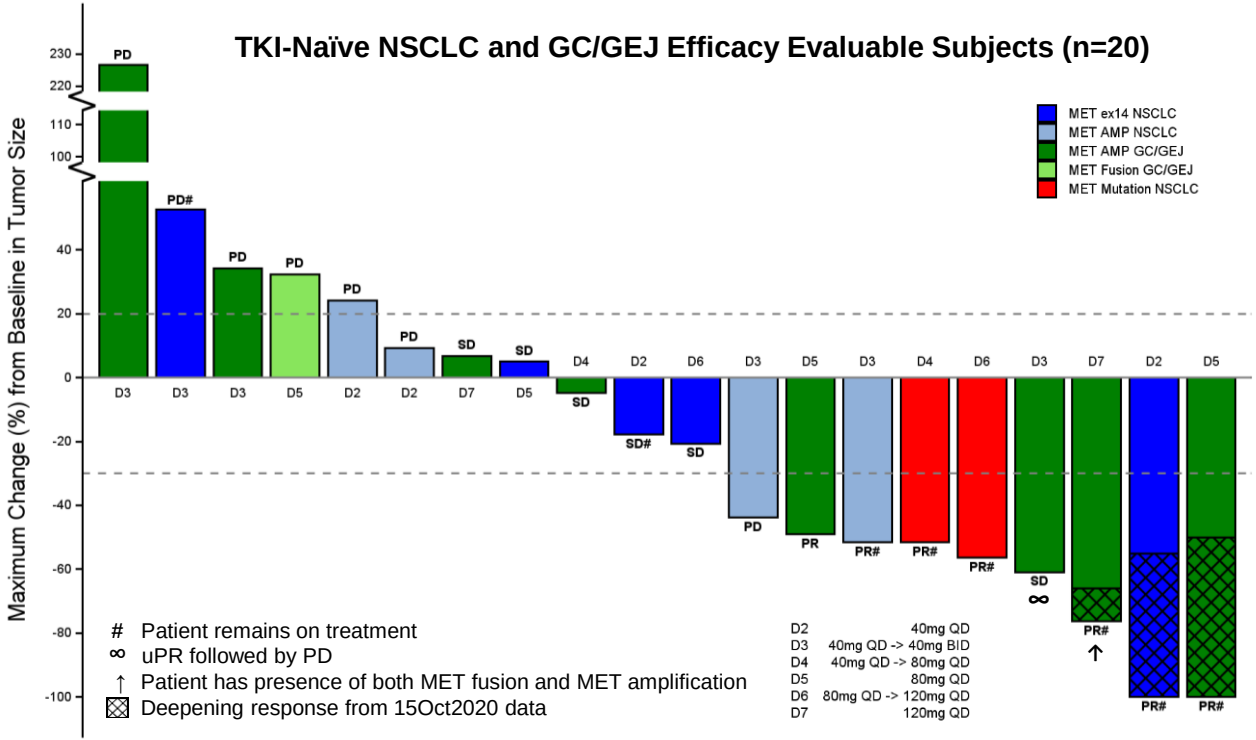
Preliminary Efficacy by Investigator Assessment

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.

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

Preliminary Efficacy by Investigator Assessment



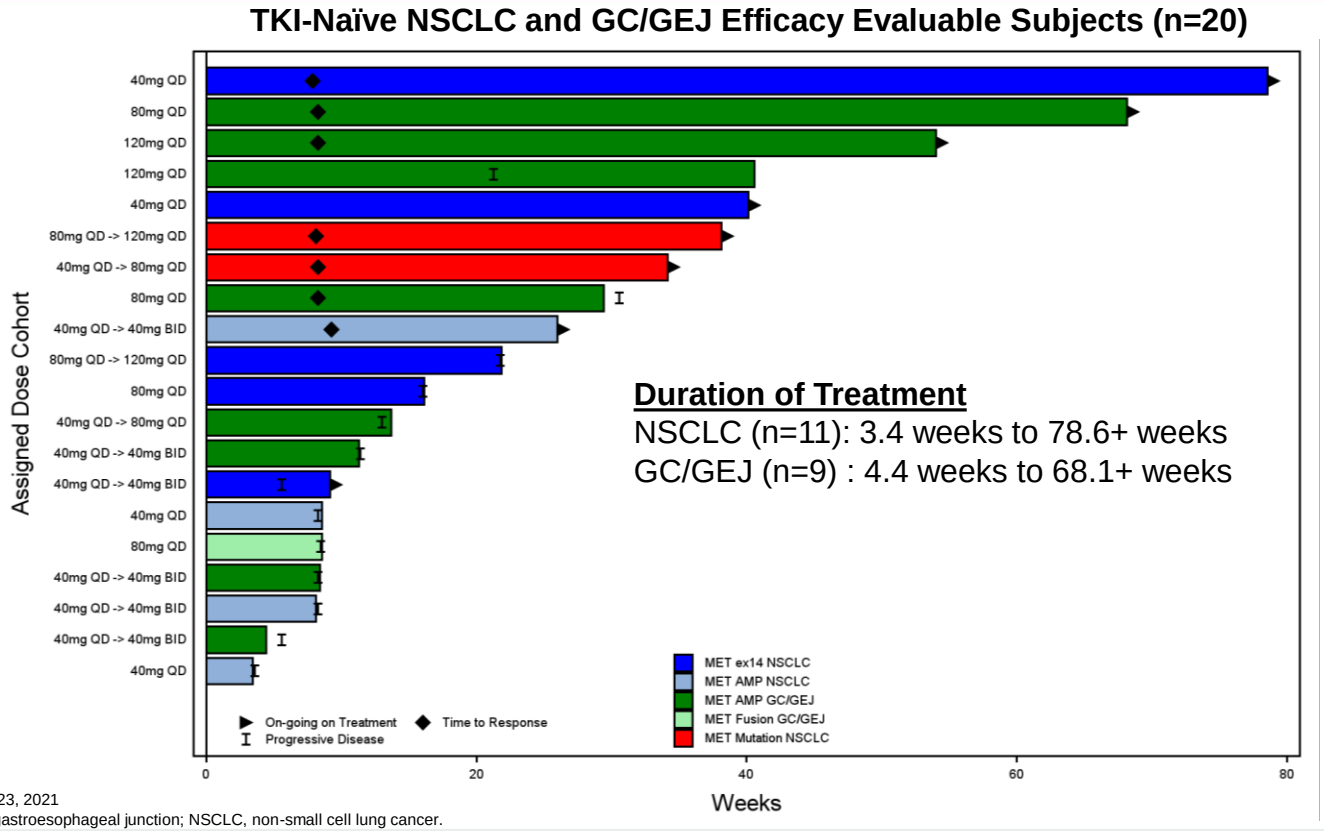
Preliminary Efficacy	TKI-Naïve Efficacy Evaluable NSCLC	TKI-Naïve Efficacy Evaluable GC/GEJ
All Dose Levels, N	**11**	**9**
cORR (95% CI)	**36% (11 - 69)**	**33% (7 - 70)**
CBR (95% CI)	64% (31 - 89)	67% (30 - 93)
RP2D & Above, N	**7**	**9**
cORR (95% CI)	**43% (10 - 82)**	**33% (7 - 70)**
CBR (95% CI)	71% (29 - 96)	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



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

Conclusions

- TPX-0022 was generally well tolerated
- SHIELD-1 dose expansion is ongoing at the proposed RP2D of 40 mg QD → 40 mg BID
- Responses in MET TKI-naïve NSCLC and GC/GEJ cancers
  - 95% patients received prior Chemo/IO therapy
  - NSCLC: cORR 36% (all dose levels); cORR 43% (proposed RP2D & above)
  - GC/GEJ Cancer: cORR 33% (all dose levels and proposed RP2D & above)
- Limited activity in MET TKI-pretreated patients (36% with ≥5 lines of prior therapy)
- Subject to FDA feedback, including agreement on the proposed RP2D, the company plans to revise the study into a Phase 1/2 trial and proceed to multi-cohort Phase 2

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For further questions please contact:
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