Abstract 3255

Phase 1/2 TRIDENT-1 Study of Repotrectinib in Patients with *ROS1*+ or *NTRK*+ Advanced Solid Tumors

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Financial Disclosures

Commercial Interest	Relationship(s)
Research funding	Novartis, Bayer, AstraZeneca, MOGAM Institute, Dong-A ST, Champions Oncology, Janssen, Yuhan, Ono, Dizal Pharma, MSD, Abbvie, Medpacto, GIInnovation, Eli Lilly, Blueprint Medicines, Interpark Bio Convergence Corp
Consulting role	Novartis, AstraZeneca, Boehringer-Ingelheim, Roche, BMS, Ono, Yuhan, Pfizer, Eli Lilly, Janssen, Takeda, MSD, Janssen, Medpacto, Blueprint Medicines
Stock ownership	TheraCanVac Inc, Gencurix Inc, Bridgebio Therapeutics, KANAPH Therapeutics Inc, Cyrus Therapeutics, Interpark Bio Convergence Corp.
Scientific Advisory Board	KANAPH Therapeutics Inc, Bridgebio Therapeutics, Cyrus Therapeutics, Guardant Health
Board of Directors	Gencurix Inc, Interpark Bio Convergence Corp.
Royalty	Champions Oncology
Founder	DAAN Biotherapeutics

This study was sponsored by Turning Point Therapeutics, Inc. Repotrectinib is not approved for the treatment of any indication in any jurisdiction by any health authority

TRIDENT-1 Study Design and Early Interim Phase 2 Data as of August 2020

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)
ORR **86% (6/7)** 95% CI, 42–100	**ORR** **40% (2/5)** 95% CI, 5–85	**ORR** **40% (2/5)** 95% CI, 5–85	**ORR** **67% (4/6)** 95% CI, 22–96	**Not Reported**	**ORR** **50% (3/6)** 95% CI, 12–88

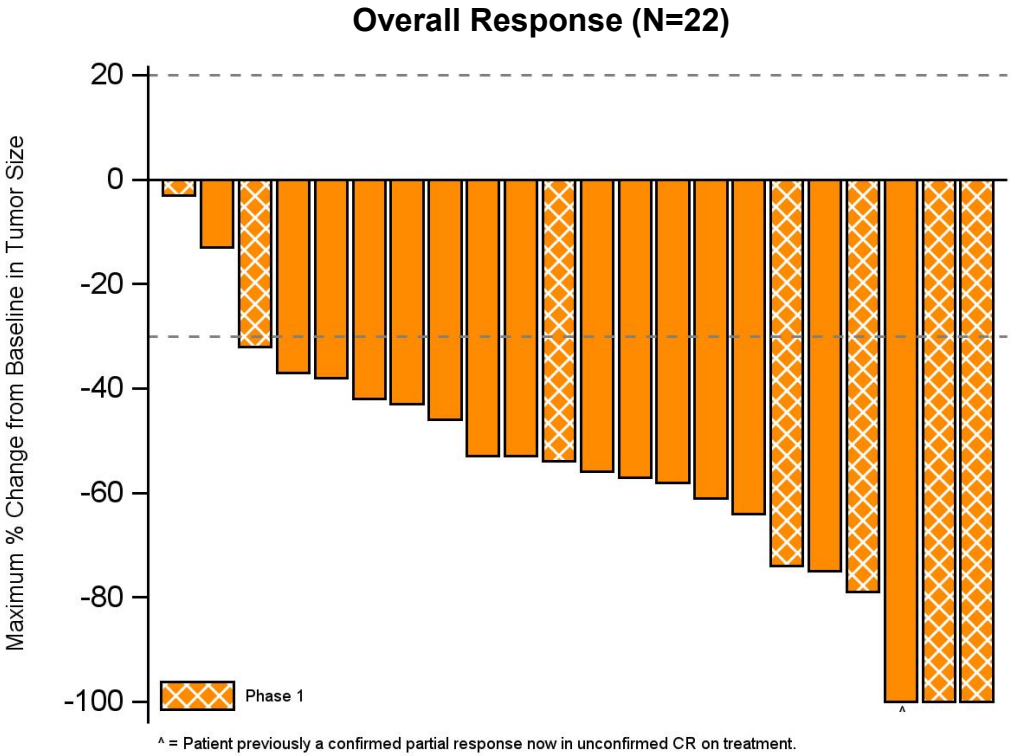
Today's presentation will focus on UPDATED Phase 2 EXP-1 data (N=15) utilizing a data cutoff of 31 December 2020:
- Median age 58 (range 30-76); ECOG PS 1 = 60%; Prior Chemotherapy Use = 20%

Previously reported Phase 1 *ROS1*+ TKI-Naïve results (N=11) based on data cutoff by BICR of 22 July 2019:

- ORR: 91% (10/11) (95% CI: 59 – 100)
  - ORR 86% (6/7) at or above the Phase 2 recommended dose
- Median DOR (95% CI): 23.1 months (5.6 - NR)
- Median PFS (95% CI): 24.6 months (7.2 - NR)

Phase 2 data cut-off date December 31, 2020, responses confirmed by investigator assessment. Phase 1 data cut-off date July 22, 2019 responses confirmed by BICR, and December 31, 2020 for duration of treatment. Phase 1 data includes only patients treated at or above repotrectinib RP2D.
BICR, blinded independent central review; CI, confidence interval; DOR, duration of response; EXP, expansion; NR, not reached; NSCLC, non-small cell lung cancer; ORR, overall response rate; PFS, progression-free survival; RP2D, recommended Phase 2 dose; TKI, tyrosine kinase inhibitor

Clinical Activity in *ROS1*+ TKI Naïve Advanced NSCLC Patients



^ = Patient previously a confirmed partial response now in unconfirmed CR on treatment.

	Phase 2 N=15	Phase 1+2 N=22
Confirmed ORR, % (95% CI)	93% (68–100)	91% (71–99)

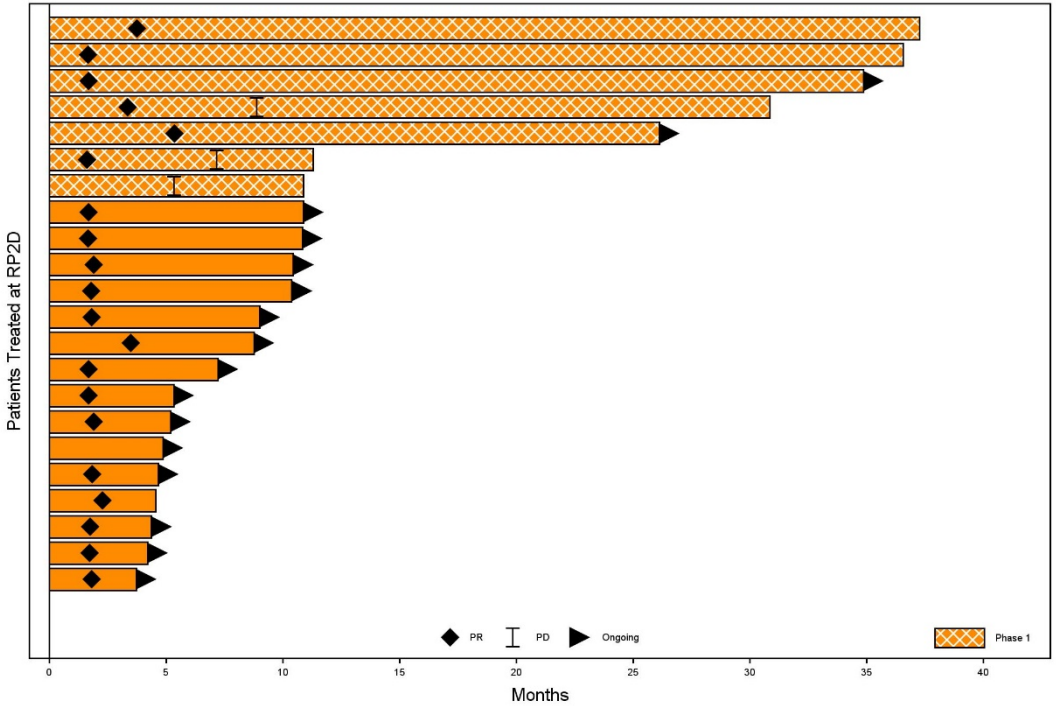
N=22 patients with baseline and at least two post baseline scans
- *N=15 Phase 2 patients*
- *N=7 Phase 1 patients treated at or above the Phase 2 recommended dose*

As of 31 December 2020, the 16th patient in Phase 2 has an unconfirmed PR and is on treatment awaiting a second post-baseline confirmatory scan.

cORR, confirmed overall response rate; ORR, overall response rate.

Duration of Treatment in *ROS1*+ TKI Naïve Advanced NSCLC Patients

Duration of Treatment (N=22):†



	Phase 1 n=7	Phase 2 n=15
Remaining on treatment, n (%)	2 (29)	14 (93)
On treatment >30 months, n (%)	4 (57)	–
Median Time on treatment, months (range)	30.9 (10.9–37.3)	5.3 (3.7+–10.9+)

†Includes patients with a baseline and at least two post-baseline scans; Phase 1 data includes only patients treated at or above repotrectinib RP2D; PD, progressive disease; PR, partial response; RP2D, recommended Phase 2 dose

TRIDENT-1 Safety Summary: Phase 1 and Phase 2 Combined Treatment-Emergent and Treatment-Related AEs

	All treated patients (N=185)				
	TEAEs (≥15% of patients)			TRAEs	
Adverse event, n (%)	All grades	Grade 3	Grade 4	Grade 3	Grade 4
Dizziness	108 (58.4)	4 (2.2)	–	4 (2.2)	–
Dysgeusia	80 (43.2)	–	–	–	–
Constipation	60 (32.4)	–	–	–	–
Dyspnea	58 (31.4)	13 (7.0)	3 (1.6)	1 (0.5)	–
Fatigue	50 (27.0)	3 (1.6)	–	–	–
Paresthesia	47 (25.4)	–	–	–	–
Anemia	41 (22.2)	15 (8.1)	–	6 (3.2)	–
Nausea	37 (20.0)	2 (1.1)	–	-	–
Muscular weakness	30 (16.2)	3 (1.6)	–	1 (0.5)	–

- Repotrectinib was generally well tolerated
- Most TRAEs were Grade 1 or 2
- There were no Grade 4 or 5 TRAEs
- The most commonly-reported TEAE remains low-grade dizziness
  - 79% (85/108) were Grade 1
  - No cases of dizziness led to treatment discontinuation
- Infrequent dose modifications due to TEAEs
  - 33 (17.8%) patients with TEAEs that led to dose reduction
  - 16 (8.6%) patients with TEAEs that led to drug discontinuation

Data cut-off date October 30, 2020.
AE, adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event

Conclusions

- **Repotrectinib has been granted Breakthrough Therapy Designation by FDA in *ROS1+* TKI-naïve patients with metastatic NSCLC**

- **Preliminary TRIDENT-1 data support repotrectinib as a potential best-in-class treatment in *ROS1+* advanced NSCLC**
  - In Phase 1 repotrectinib demonstrated encouraging results in TKI-naïve NSCLC patients
    - 91% cORR, 23.1 months median DOR, 24.6 months median PFS
  - Updated Phase 2 data continues to support strong clinical activity in TKI-naïve patients
    - 93% cORR including 1 uCR

- **Repotrectinib was generally well tolerated**
  - Most commonly reported TEAE was low grade dizziness. No cases of dizziness led to treatment discontinuation

- **TRIDENT-1 trial is currently enrolling at approximately 90 sites worldwide**