Phase 1 Clinical Testing of a First-in-Class Antisense Oligonucleotide Therapeutic against Advanced Solid Tumors of Multiple Tissue Origins

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PURPOSE

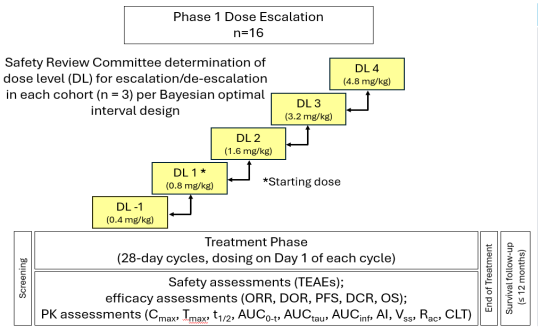
TTX-MC138 a microRNA-10b (miR-10b) inhibitor, was evaluated in an ongoing Phase 1a Multicenter, Open-Label, Dose-Escalation and Expansion Study in Subjects with Advanced Solid Tumors.

BACKGROUND

TransCode Therapeutics, Inc. is developing TTX-MC138, an antisense oligonucleotide (ASO) therapeutic targeting miR-10b, a critical driver of metastatic disease progression. Several in vivo preclinical studies with TTX-MC138 have successfully demonstrated its delivery to metastatic lesions, its activity against metastatic cancers of multiple tissue origins, and its capacity to elicit disease regression and long-term overall survival (1-3). In a Phase 0 clinical study in a patient with metastatic breast cancer, accumulation of TTX-MC138 in metastatic lesions was demonstrated. TTX-MC138 is currently being evaluated in a Phase 1a Multicenter, Open-Label, Dose-Escalation and Expansion Study in Subjects with Advanced Solid Tumors (NCT06260774). A total of sixteen patients were treated across four escalating dose levels. Primary objectives of the study focused on the safety, tolerability, PK and establishment of a Phase 2 dose (RP2D). Data from the dose-escalation phase only are presented in this poster.

METHODS

OBJECTIVES	ENDPOINTS
Primary Objectives	**Primary Endpoint**
Evaluate safety and tolerability of TTX-MC138 to determine the MTD and select an RP2D (or doses)	Incidence of TEAEs
Secondary Objectives	**Secondary Endpoints**
Evaluate anti-tumor activity of TTX-MC138	ORR, DCR, DoR, PFS, OS
Characterize the PK profile of TTX-MC138	PK parameters versus time data: AUC_t, AUC_{inf}, AUC_{TAU}, AI, C_{max}, T_{max}, $t_{1/2}$, Vss, and CLT.
Note: Dose expansion phase objectives and endpoints are not presented (Dose expansion phase has not been initiated); dose escalation phase objectives and endpoints without data to present are not presented.	



KEY INCLUSION	KEY EXCLUSION
• Histologically or cytologically confirmed diagnosis of relapsed/ refractory metastatic or locally advanced solid tumor with failed standard therapy. • Measurable or evaluable disease per RECIST version 1.1 • ECOG PS of 0 or 1 • Adequate organ function per protocol definitions	• Anticancer therapy (not immunotherapy/Ab therapies) ≤ 14 days or 5 half-lives before study drug • Prior antibody therapy ≤ 28 days before study drug • History of second primary malignancy diagnosed or required active therapy within past year. • Clinically significant, uncontrolled cardiovascular disease • Symptomatic CNS metastases or primary CNS tumor associated with progressive neurologic symptoms or requires ongoing corticosteroids to control CNS disease

Abbreviations: AI: accumulation index; AUC_{inf}: area under the curve from the time of dosing extrapolated to infinity; AUC_t: area under the concentration-time curve from the time of dosing to the time of the last observation; AUC_{TAU}: area under the curve from time zero to the end of the dosing interval; CLT: total body clearance; C_{max}: maximum observed concentration; CNS: central nervous system; DCR: disease control rate; DoR: duration of response; ECOG PS: Eastern Cooperative Oncology Group performance status; MTD: maximum tolerated dose; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; RECIST: Response Evaluation Criteria in Solid Tumors; RP2D: recommended Phase 2 dose; TEAE: treatment-emergent adverse event; $t_{1/2}$: terminal elimination half-life; T_{max}: time of the maximum observed concentration; Vss: steady-state volume of distribution.

RESULTS

No significant treatment related safety events or dose limiting toxicities were observed. To date, seventy-seven doses of TTX-MC138 have been administered. The median treatment duration was four months. Importantly, the duration of treatment for all patients ranged from two to twelve cycles indicative of durability, tolerability, and disease control. Three patients remain on study. One thyroid cancer patient with historic evidence of an increase in thyroglobulin levels, demonstrated a reversal of the trend during treatment and presented at the most recent measurement with undetectable thyroglobulin levels. Forty-four per cent or seven out of the sixteen patients were noted to have stable disease lasting 4 months or longer.

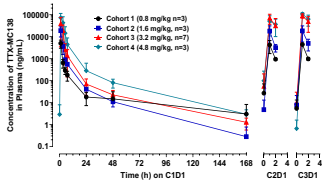


Figure 1. Mean Plasma TTX-MC138 Concentration Time Profiles. Preliminary data are illustrated as mean concentrations in ng/mL for 4 treatment cohorts (0.8 mg/kg, 1.6 mg/kg, 3.2 mg/kg, and 4.8 mg/kg) in linear scale. Error bars represent standard errors of mean. Exposure increases with dose administration consistently on all cycles tested.

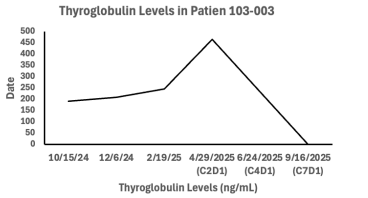


Figure 2. Thyroglobulin levels in patient 103-003 with thyroid cancer. Patient with historic evidence of an increase in thyroglobulin levels, demonstrated a reversal of the trend during treatment and presented at the most recent measurement with undetectable thyroglobulin levels.

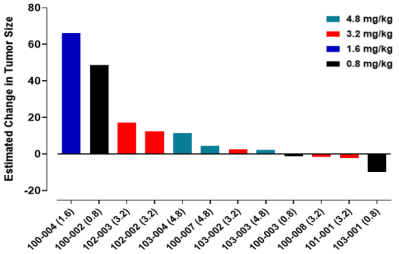


Figure 3. Estimated Tumor Size Change in Patients Treated with TTX-MC138. Preliminary data are illustrated per patient.

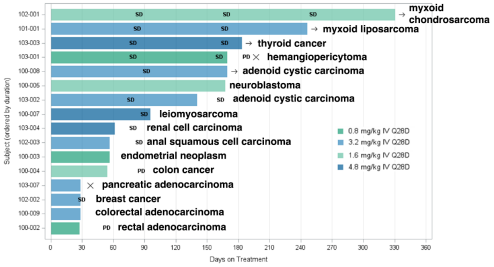


Figure 4. Swimmer Plot of Tumor Response. Preliminary data are illustrated per patient. SD, stable disease; PD, progressive disease; IV, intravenous; Q28D, every 28 days. Data as of October 1, 2025

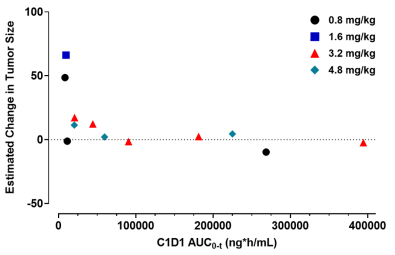


Figure 5. Estimated Change in Tumor Size in response to exposure at Cycle 1 Day 1. Preliminary data are illustrated per cohort.

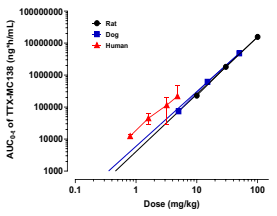


Figure 6. TTX-MC138 Exposure. Data are illustrated as mean exposure of TTX-MC138 in human, dog, and rat per dose level.

CONCLUSIONS

- Phase 1a preliminary data show apparent stable disease lasting over 4 months in 44% (7 out of 16) patients. Three patients still on study.
- One thyroid cancer patient with historic evidence of an increase in thyroglobulin levels, demonstrated a reversal of the trend during treatment and presented at the most recent measurement with undetectable thyroglobulin levels.
- No DLTs were reported in patients treated with TTX-MC138. A strong safety and durability profile was observed.
- Preliminary PK analysis in all 16 patients showed predictable systemic exposure and positive pharmacodynamic effects over a wide dose range, consistent with preclinical models and TransCode's Phase 0 clinical trial.

Funding and Disclosures

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