The Metabo-Oncology Company™

SDX-7320 elicits improvements in tumor-related and metabolic biomarkers: Results of a phase 1 dose-escalation study in patients with advanced refractory or late-stage solid tumors

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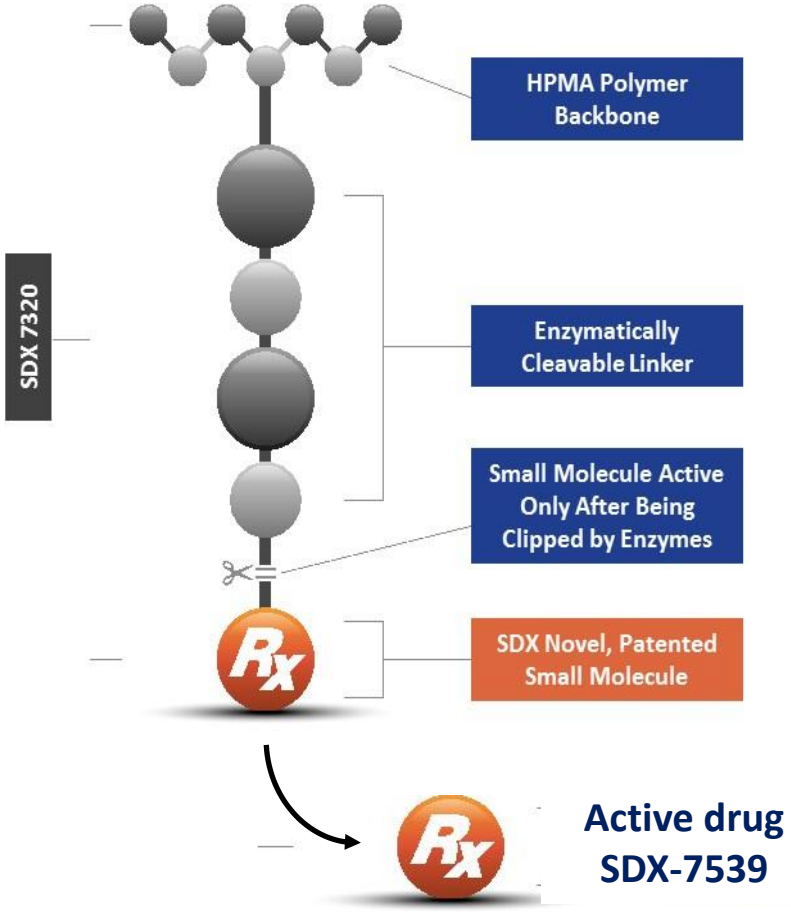
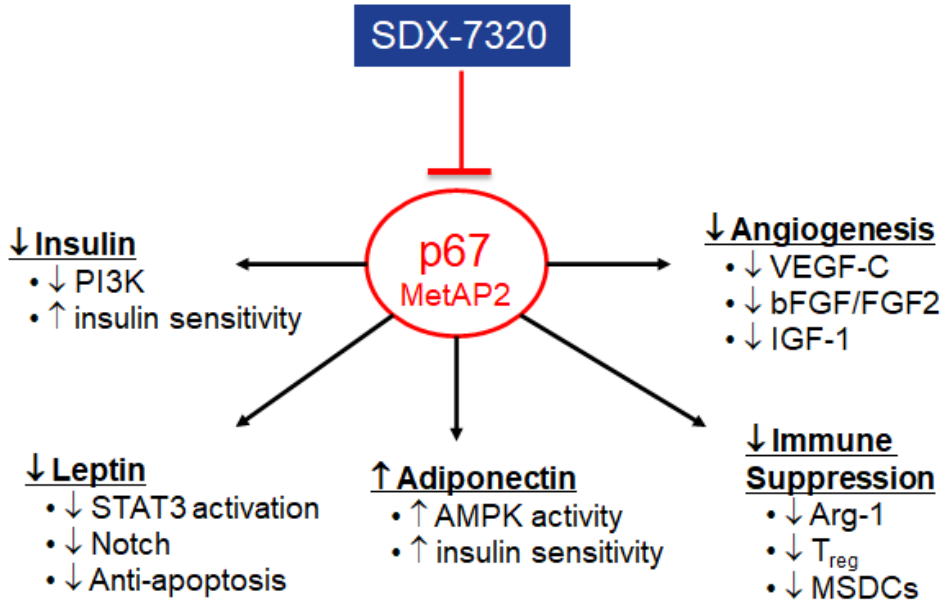
Phase 1 Trial of SDX-7320

Polymer-conjugated inhibitor of methionine aminopeptidase 2 (MetAP2)

SDX-7320 (prodrug) Produces SDX-7539



Pleiotropic Mechanism of Action



Efficacy demonstrated in preclinical oncology, metabolic disease models:

- Xenograft (A549, BT474)
- Syngeneic (B16F10, EO771)
- Diet-induced obese mice, rats

Source: SDX Internal data

Phase 1 Design, Patients

All comers, solid tumors

Phase I Trial Design

- Patients with advanced cancer
- Solid tumors only; no CNS tumors
- Sub-cutaneous administration, dose-escalation on a Q7D schedule (28 days/cycle) until >G2 AE, then expand to 3+3
- Switched to Q14D dosing schedule after encountering a DLT @ 49 mg/m^2 Q7D
- Target engagement was measured in whole blood with a custom ELISA
- Biomarkers were measured in serum using specific immunoassays
- PK for both SDX-7320 (pro-drug/polymer conjugate) as well as SDX-7539 (released active small molecule) was assessed in plasma using LC/MS

Patient Demographics

- 32 patients enrolled (14 male, 18 female)
- Mean age: 66 years (49 – 79)
- Mean # prior lines of therapy: 5.8 (1 – 17)
- Mean time since diagnosis: 6 years (0.6 – 24)
- Cancer types (n): lung (9), colon (6), breast (4), rectal (3), pancreatic (2), appendiceal (2), and one each of carcinoid, cholangiocarcinoma, cervical, endometrial, hepatocellular, urothelial

Source: SDX Internal data

Phase 1 Safety Profile: TEAEs

Relatively well-tolerated

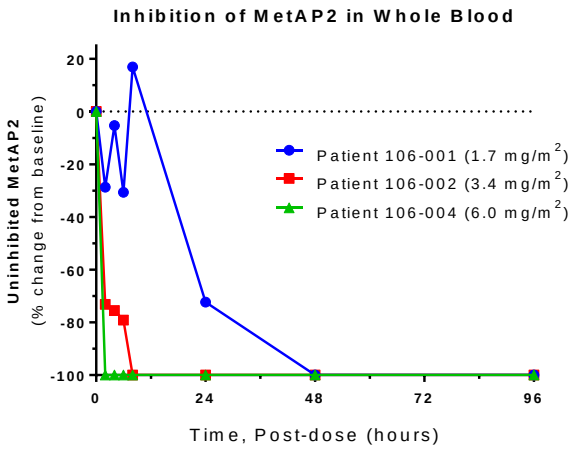
Dose	N	All Drug-Related TEAEs (%)	Drug-Related TEAEs ≥ G2 (%)	Drug-Related TEAEs ≥ G3 (events/patients)	AE Description (≥ G3)
1.7 – 36 mg/m² (Q7D)	10	7 (70)	2 (20)	0	
49 mg/m² (Q7D)	5	5 (100)	5 (100)	5/3	Thrombocytopenia
36 mg/m² (Q14D)	6	5 (83)	4 (67)	1/1	Vasculitis
49 mg/m² (Q14D)	6	5 (83)	4 (67)	0	
65 mg/m² (Q14D)	5	4 (80)	3 (60)	1/1	Thrombocytopenia
All Patients	32	25 (78)	17 (53)	7/4	

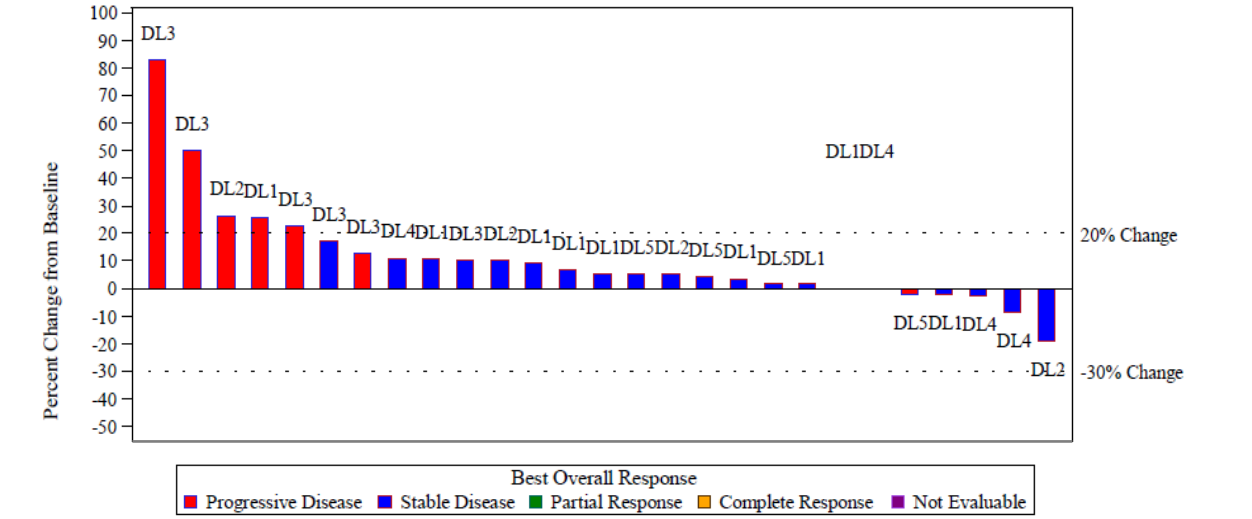
- Thrombocytopenia was reversible upon cessation of dosing
- No injection site reactions ≥ G2

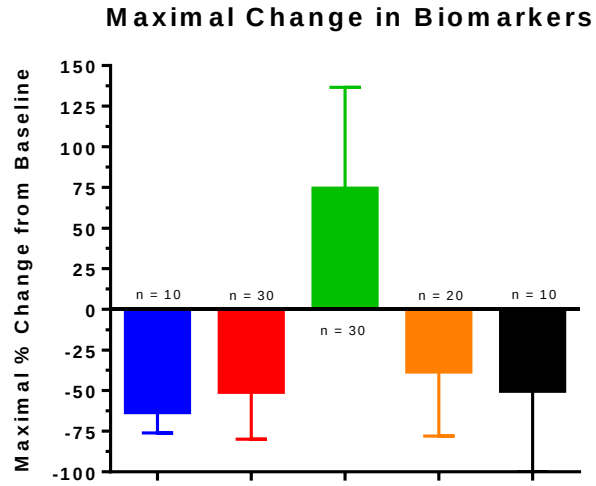
Source: SDX Internal data

Phase 1: Stable Disease in 76% of Patients, Cycle 2

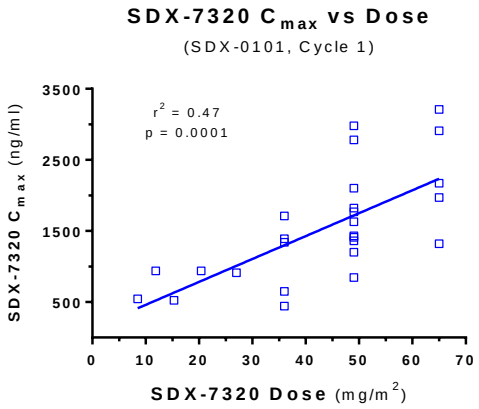
Target engagement in whole blood; PK data, key biomarker changes

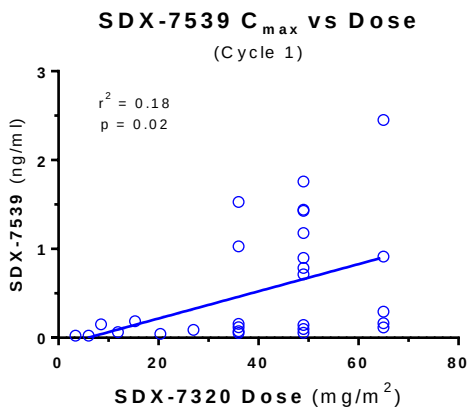


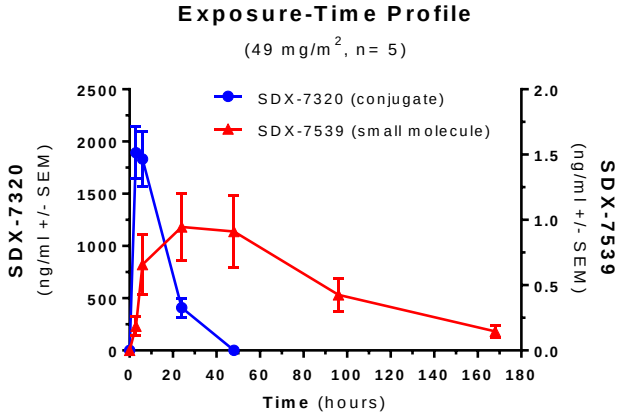




Insulin (>20 µU/ml at baseline)
Leptin
Adiponectin
VEGF-C (i>200 pg/ml at baseline)
bFGF (> 5 pg/ml at baseline)







Source: SDX Internal data

Phase 1 Summary

Ph I Safety Summary

- Most common AEs (in >10% of patients – mostly G1/2) were anemia (1 G3 event), constipation, diarrhea, nausea, vomiting, abdominal pain, decreased appetite, injection site reactions, alopecia and fatigue (1 G3 event)
- TEAEs ≥G3 possibly related to study drug were thrombocytopenia (4 patients) and vasculitis (1 patient)
- DLT was thrombocytopenia (G3, 4)
- RP2D is 49 mg/m2, Q14D

PK Summary

- Exposure of SDX-7320 (pro-drug) was proportional to dose (r^2 = 0.47), whereas levels of the released small molecule were more variable (r^2 = 0.18)
- Prolonged exposure of small molecule (SDX-7539) relative to polymer conjugate prodrug (SDX-7320)

PD Summary:

- Stable disease in 50% of patients; longest duration was 9 cycles; median = 6 cycles (95% CI = 3.8, 8.8); n = 28 patients
- Stable disease in 64% non-target lesions (n=16)
- Improvements in key biomarkers:
  - *Metabolic markers: -63% insulin, -51% leptin, +74% adiponectin*
  - *Cancer markers: -50% bFGF, -38% VEGF-C*

Ph Ib/2 Plans

- Leverage the anti-angiogenic/positive metabolic effects of SDX-7320 in a combination trial in patients with ER+/Her2- mBC
  - SDX-7320 + PI3Kα inhibitor + fulvestrant
  - Offset the negative metabolic effects of PI3Kα inhibitors (i.e., hyperglycemia, hyperinsulinemia) to extend PFS

Source: SDX Internal data

THANKS TO OUR PRESENTER

PRESENTER INFORMATION

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