SNDX-6352-0502 - A phase 1, open-label, dose escalation trial to investigate the safety, tolerability, pharmacokinetics and pharmacodynamic activity of axatilimab (SNDX-6352) monotherapy in patients with unresectable, recurrent, locally-advanced, or metastatic solid tumors

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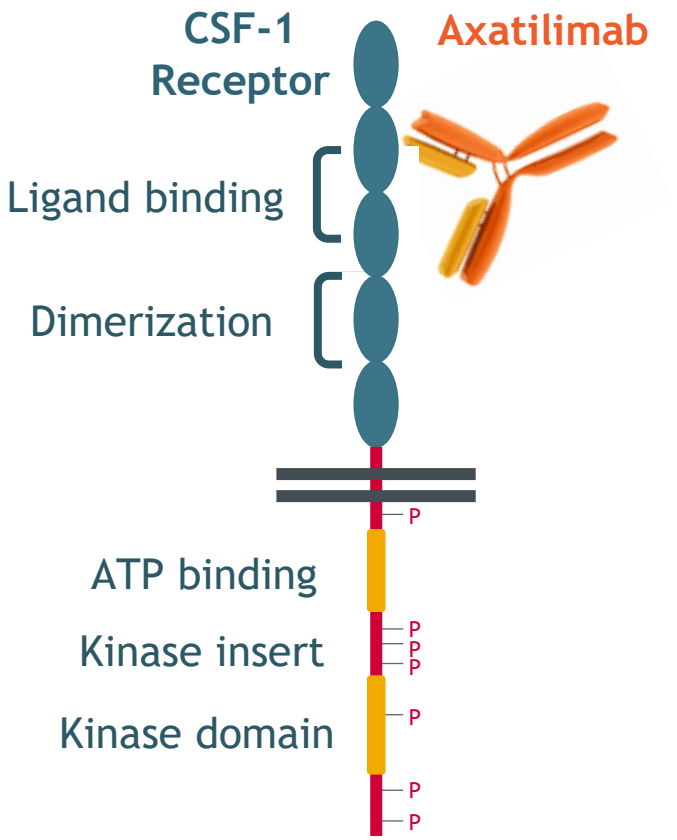
SNDX-6352-0502: Phase 1 dose escalation in solid tumors



- **Axatilimab (SNDX-6352) is a high affinity, dual ligand blocking IgG4 mAb targeting CSF-1R**
- **CSF-1 / CSF-1R signaling regulates monocyte proliferation and differentiation to tumor associated macrophages (TAMs)**
- **Blocking TAM activity through CSF-1R inhibition in preclinical studies enhances anti-tumor immune response**
- **Primary objective - safety; MTD & RP2D in advanced solid tumor patients as monotherapy and combination with durvalumab**

Dose / schedule	Enrolled / evaluable / DLT	On Study
1mg/kg q2wk	7 / 6 / 0	0
2mg/kg q2wk	3 /3 / 1	0
3mg/kg q2wk	9 / 6 / 0	0
6mg/kg q2wk	8 / 6 / 1	0
6mg/kg q4wk	6 / 6 / 0	2

- Standard “3+3” dose escalation design
- Patients receive treatment until unacceptable toxicity or progressive disease

Safety - Tolerated well with no unexpected AEs

- Adverse event profile consistent with class effects
- Dose dependent transient elevation in LFTs, amylase, lipase, CK related to inhibition of Kupffer cells and not associated with liver / organ damage
- Minimal pruritis /dermatologic adverse events observed

Treatment related adverse events (>10%) any grade

Preferred Term	1 mg/kg q2w n (%)	2 mg/kg q2w n (%)	3 mg/kg q2w n (%)	6 mg/kg q2w n (%)	6 mg/kg q4w n (%)	Total n (%)
Periorbital oedema	1 (14)	2 (67)	0	4 (50)	5 (83)	12 (36)
Blood CK Increased	0	0	4 (44)	2 (25)	4 (67)	10 (30)
Fatigue	3 (43)	2 (67)	4 (44)	0	1 (17)	10 (30)
AST increased	0	1 (33)	2 (22)	2 (25)	4 (67)	9 (27)
Amylase increased	0	0	2 (22)	0	2 (33)	4 (12)
Decreased appetite	0	1 (33)	3 (33)	0	0	4 (12)
Nausea	0	1 (33)	2 (22)	0	1 (17)	4 (12)
Oedema peripheral	0	0	1 (11)	2 (25)	1 (17)	4 (12)

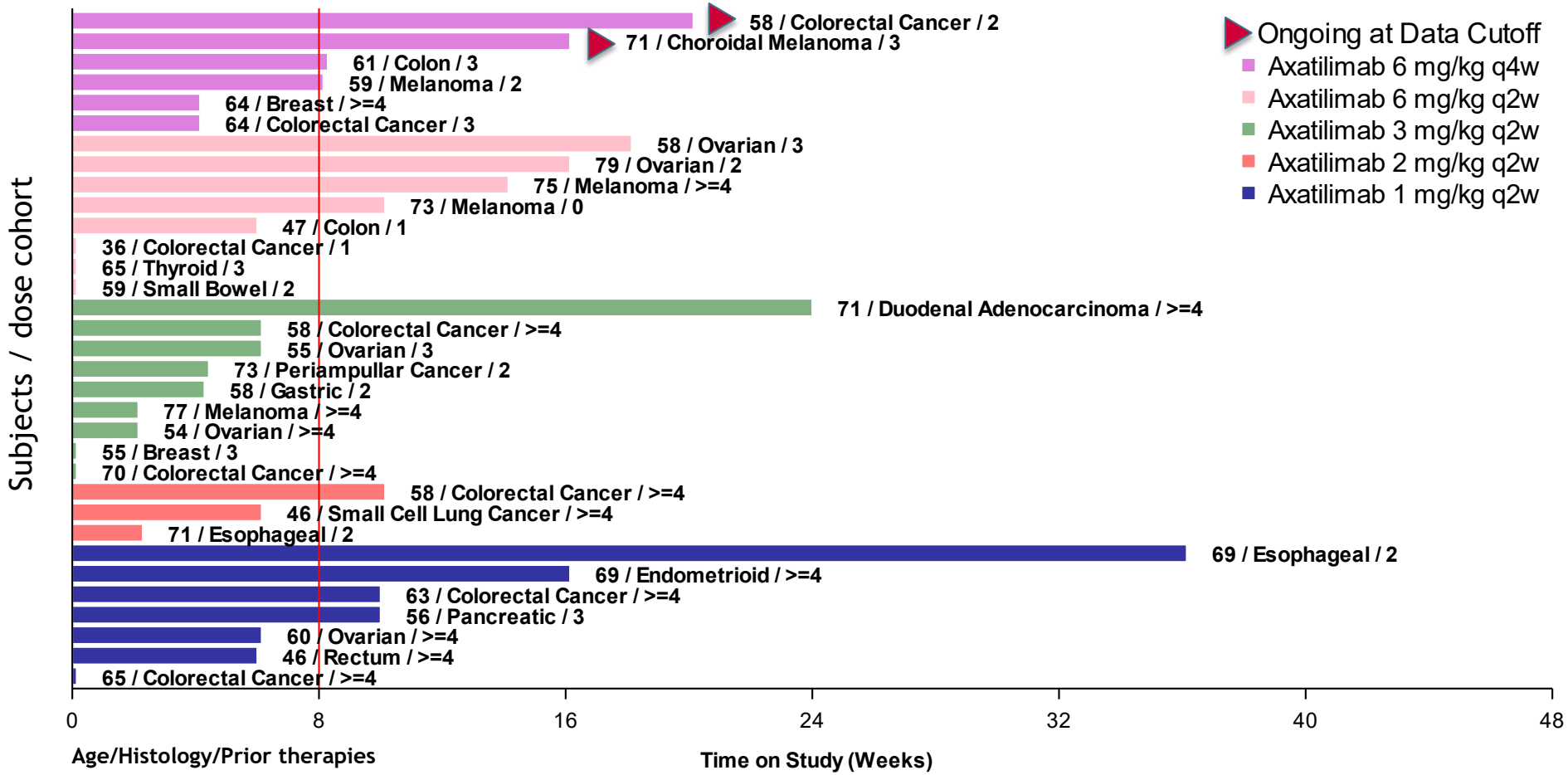
Treatment related adverse events ≥ Gr 3

Preferred Term	1 mg/kg q2w n (%)	2 mg/kg q2w n (%)	3 mg/kg q2w n (%)	6 mg/kg q2w n (%)	6 mg/kg q4w n (%)	Total n (%)
Subjects With TREAE ≥ Gr3	0	1 (33)	6 (67)	2 (25)	3 (50)	12 (36)
Periorbital oedema	0	1 (33)	0	0	0	1 (3)
Blood CK increased	0	0	4 (44)	1 (13)	1 (17)	6 (18)
Fatigue	0	1 (33)	0	0	0	1 (3)
AST increased	0	0	2 (22)	0	1 (17)	3 (9)
Amylase increased	0	0	2 (22)	0	1 (17)	3 (9)
Pneumonitis	0	0	0	1 (13)	0	0
Lipase increased	0	0	2 (22)	0	0	0
Anemia	0	0	1 (10)	0	0	0

Known class effect / consistent with MOA

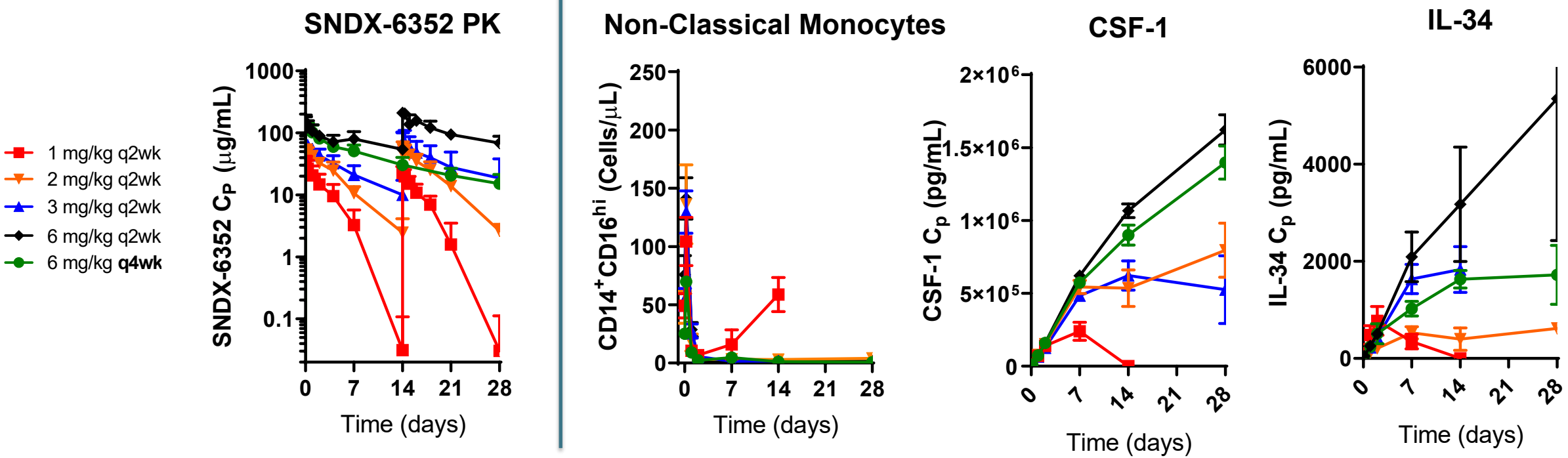
Exposure and demographics

- Advanced solid tumor subjects with median of 3 prior lines of therapy
- Prolonged disease stabilization (> 2 months) observed in multiple tumor types and across dose cohorts



Pharmacokinetics and pharmacodynamics

- Dose-proportional increase in plasma conc with drug accumulation observed at > 1 mg/kg
- Circulating non-classical monocytes ($CD14^{+}CD16^{hi}$) were ablated at all dose levels within 24 hrs and remained suppressed at all doses >1 mg/kg
- Plasma CSF1 and IL-34 concentrations increased with treatment and remained elevated at all doses > 1 mg/kg



SNDX-6352-0502 summary

- Axatilimab demonstrates tolerability at the highest dose level evaluated (6 mg/kg q2wk) with robust PD biomarker modulation at doses as low as 1 mg/kg
- No unexpected AEs with mild periorbital edema and transient elevation in circulating enzyme levels as most frequent treatment related AEs
  - Transient elevations in LFTs consistent with MOA related inhibition of Kupffer cell mediated clearance and not associated with liver injury
  - Minimal skin related AEs
- Rapid and sustained depletion of circulating pro-inflammatory monocytes observed at all doses
- RP2D for monotherapy in solid tumors – 6 mg/kg Q4WKs

Acknowledgements:

We thank the patients and their families for participating in this study and the clinical caregivers for their dedication to improving their patient's lives

For questions, please contact:

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