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

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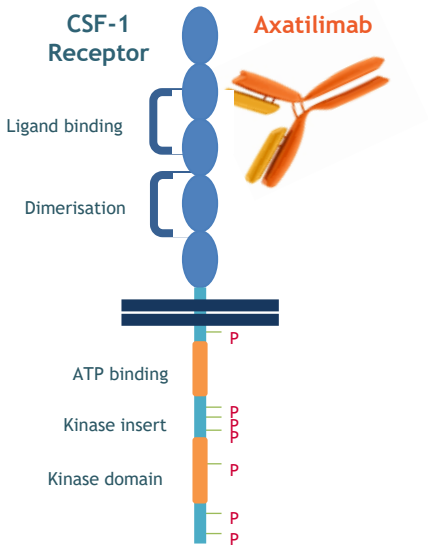
# SNDX-6352-0502 : Phase 1b dose escalation in solid tumors in combination with durvalumab

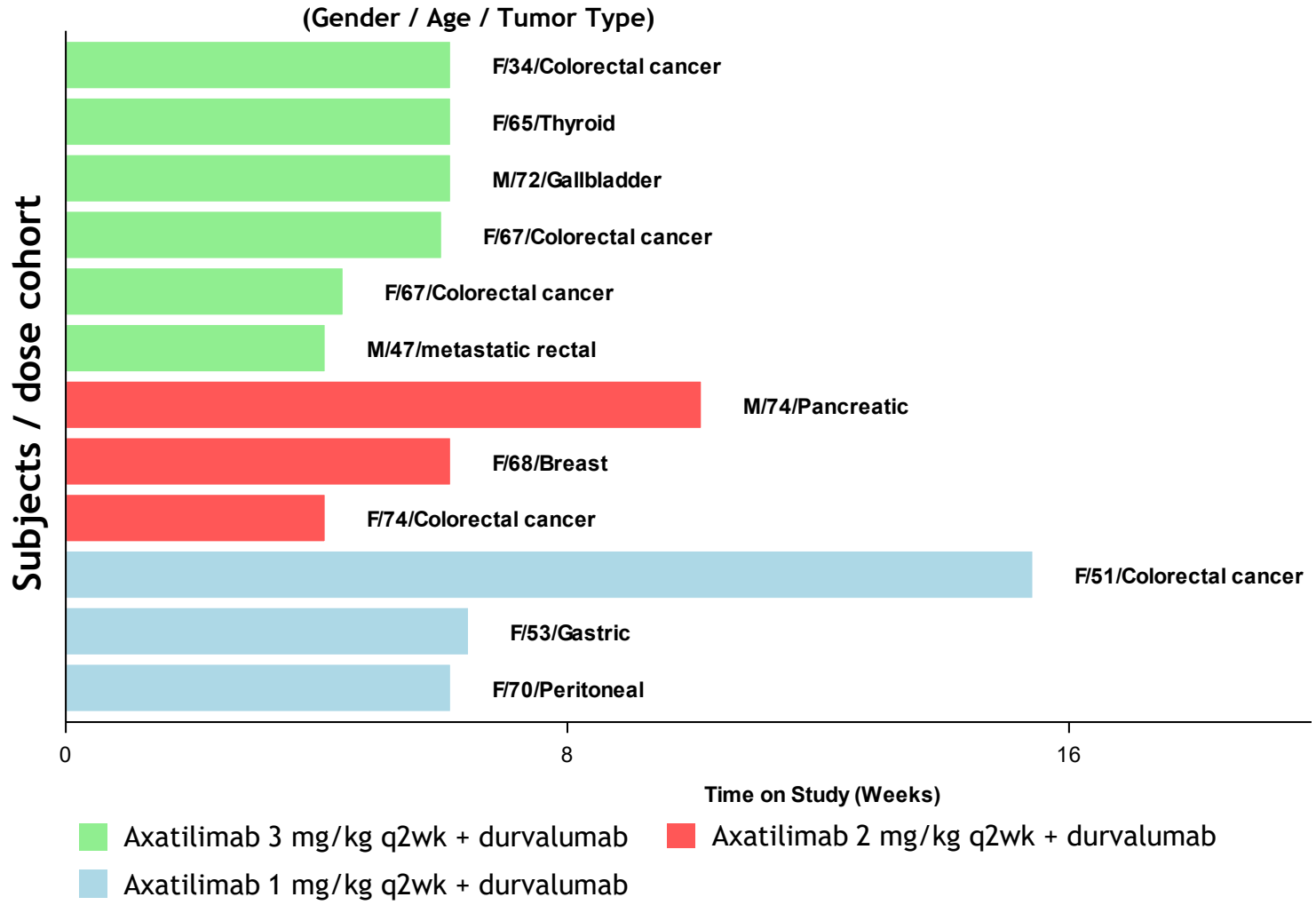



| Dose | Schedule | Enrolled / evaluable / DLT / on study |
|---|---|---|
| 1mg/kg | q2wk | 3 / 3 / 0 / 0 |
| 2mg/kg | q2wk | 3 /3 / 0 / 0 |
| 3mg/kg | Q2wk | 6 / 6 / 0 / 0 |

- 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 when combined with immune checkpoint inhibitors
- Phase 1b trial tested combination with durvalumab in patients with advanced solid tumors
- Primary objective – safety; Standard “3+3” dose escalation
- Patients receive treatment until unacceptable toxicity or progressive disease

# Exposure and Demographics

- Advanced solid tumor subjects with median of 3.5 prior lines of therapy
- Prolonged disease stabilization observed as best response in patients not predicted to respond to anti-PD-L1 alone



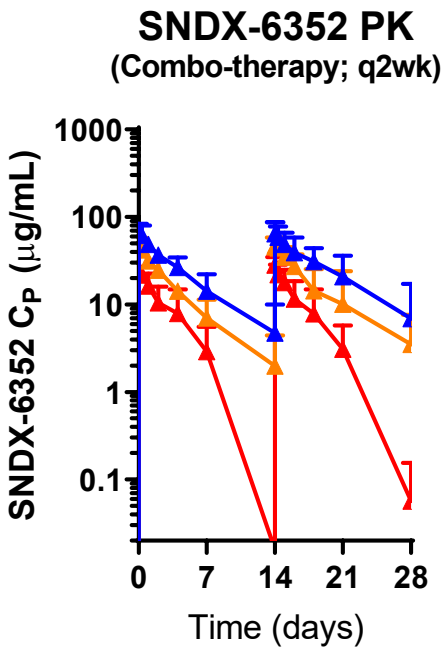
# Safety - Treatment-Related Adverse Events of Severity ≥ Grade 2

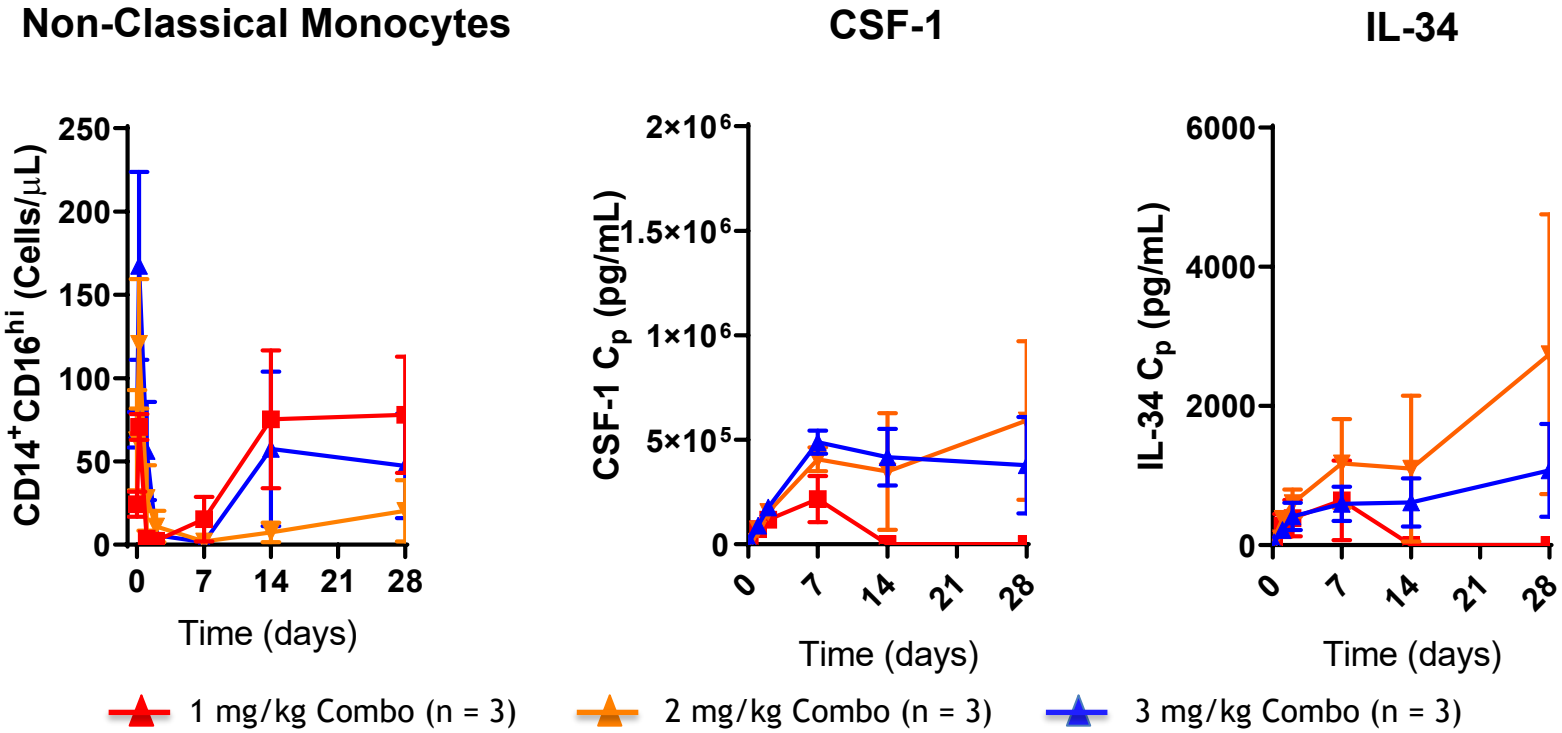
- Axatilimab is tolerated well in combination with durvalumab
- No unexpected adverse events from combining anti-CSF1R with anti-PD-L1
- No obvious increase in immune-related adverse events

| | Axa 1mg/kg + Durva 1500 mg n = 3; n (%) | | Axa 2mg/kg + Durva 1500 mg n = 3; n (%) | | Axa 3mg/kg + Durva 1500 mg n = 6; n (%) | |
|---|---|---|---|---|---|---|
| Preferred Term | Gr 2 | ≥ Gr 3 | Gr 2 | ≥ Gr 3 | Gr 2 | ≥Gr 3 |
| Subjects With ≥ 1 Gr 2 TREAE | 1 (33) | 0 | 1 (33) | 0 | 0 | 4 (67) |
| Amylase increased | 0 | 0 | 0 | 0 | 1 (17) | 1 (17) |
| Blood CK increased | 0 | 0 | 1 (33) | 0 | 1 (17) | 0 |
| Abdominal pain upper | 0 | 0 | 0 | 0 | 1 (17) | 0 |
| Anaemia | 0 | 0 | 0 | 0 | 0 | 1 (17) |
| Arthralgia | 1 (33) | 0 | 0 | 0 | 0 | 0 |
| AST increased | 0 | 0 | 0 | 0 | 1 (17) | 0 |
| Bone pain | 1 (33) | 0 | 0 | 0 | 0 | 0 |
| Decreased appetite | 0 | 0 | 1 (33) | 0 | 0 | 0 |
| Diarrhoea | 0 | 0 | 0 | 0 | 0 | 1 (17) |
| Fatigue | 0 | 0 | 0 | 0 | 1 (17) | 0 |
| GGT increased | 0 | 0 | 0 | 0 | 1 (17) | 0 |
| Hypothyroidism | 1 (33) | 0 | 0 | 0 | 0 | 0 |
| Lipase increased | 0 | 0 | 0 | 0 | 1 (17) | 0 |
| Oedena peripheral | 0 | 0 | 0 | 0 | 1 (17) | 0 |
| Rash pruritic | 0 | 0 | 0 | 0 | 0 | 1 (17) |

# Pharmacokinetics and Pharmacodynamics of SNDX-6352

- Dose-proportional increase in plasma conc consistent with axatilimab monotherapy with drug accumulation observed at > 1 mg/kg
- Circulating non-classical monocytes ($CD14^{+}CD16^{hi}$) were depleted for up to 14 days per dose level
- Plasma CSF1 and IL-34 concentrations increased with treatment and remained elevated at doses > 1 mg/kg



# SNDX-6352-0502 Phase 1b summary

Axatilimab is a potent CSF1R antagonist that demonstrates tolerability and robust PD biomarker modulation in combo w/ durva

<u>No unexpected AEs for combo:</u>

- Most frequent treatment related AEs: Transient elevation in circulating enzyme levels
- Transient elevations in LFTs consistent with CSF-1Ri MOA related inhibition of Kupffer cell mediated clearance -- not associated with liver injury
- Minimal skin related AEs

Rapid and sustained depletion of circulating pro-inflammatory monocytes observed at all doses

**RP2D for Durva combo in solid tumors – 3 mg/kg q2WKs**

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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