SIERRA ONCOLOGY

AZD5153: Sierra's Newest Development Asset

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Delivering on our Mission to Develop Targeted Therapies for Rare Cancers

Successfully executing on MOMENTUM pivotal clinical trial

- Over-enrolled (ahead of anticipated timing)
- Data expected 1Q 2022
- NDA filing expected mid-2022

Data analyses from SIMPLIFY-1 and -2 have reinforced our conviction that MMB could become the cornerstone therapy for patients with myelofibrosis

In-licensing AZD5153 supports our mission

- Potential to improve outcomes in MF patients with MMB / 5153 combo
- Potential to expand development into other cancer types
- Low capital investment until post MMB pivotal data
- Solid IP runway

Strategic Rationale for Adding a BET Inhibitor to Sierra's Portfolio

MF landscape is evolving with multiple combination studies ongoing

BET inhibition has shown initial proof-of-concept with disease-modifying potential

MMB could be the JAKi backbone of choice for BETi and other emerging MOAs with its favorable hematologic profile and potential benefits for myelosuppressed patients

Clinical validation of a MMB + BETi combination expands Sierra's opportunity

1. Potential for deeper and more durable responses and disease modification in MF
2. Protects and lengthens MMB's peak adoption if combination therapies become the mainstay of MF treatment; and
3. Pipeline expansion opportunities in other hematologic or solid tumor indications, through potential combos with SRA737, I/O, PARP and other MOAs

AZD5153: a Potent, Highly Selective & Differentiated BET Inhibitor

Selective inhibitor of the two BRD4 BET protein bromodomains (BD1, BD2)

- **Differentiated bivalent inhibitory activity** results in more potent and complete target inhibition relative to monovalent binders

Potent antiproliferative activity in heme cell-lines, typically with GI_{50} values of $\leq$100nM

Significant single agent anti-tumor activity in hematological xenograft models and in primary PDX models harboring BRD4 amplification

Potent modulation of clinically-relevant on-target biomarkers (e.g., MYC, HEXIM) corresponding to substantive TGI

Synergistic preclinical efficacy in combination with diverse agents

- Interestingly, profound synergy was observed between AZD5153 and the AZ ATRi, suggesting potential utility in combination with SRA737

Sources: Rhyasen et al, *Molecular Cancer Ther; 15 (11); 2563-74* and Rhyasen et al; *Plos ONE;* July 2018.

AZD5153 Clinical Observations

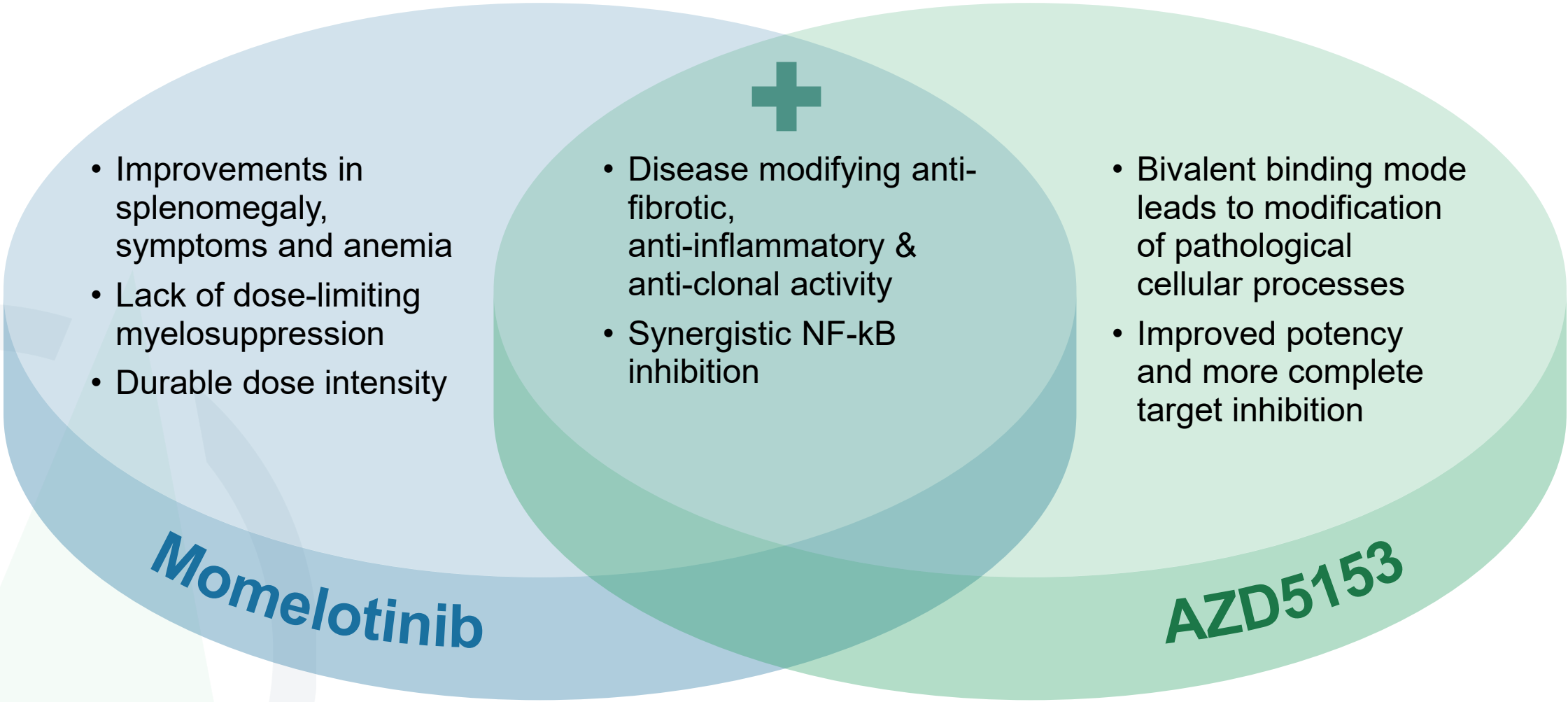
Active, well-tolerated, manageable safety as monotherapy and in combination with olaparib

- Has been dosed as monotherapy for >80 weeks and in combo with olaparib for >39 weeks
- Dose dependent exposure observed in the clinic
- Exposure-dependent modulation of PD biomarkers observed in peripheral blood samples from patients treated with AZD5153
- Expected correlation between exposure and platelet count decrease was observed
- Thrombocytopenia was manageable and reversible at doses above MEC
- Monotherapy overall appeared safe and tolerable with most common AEs being GI events, fatigue, thrombocytopenia, dysgeusia, dyspnea and anemia
  - Far majority were Grade 1-2

Source: Wang et al; *First-in-Human Study of AZD5153, a Small Molecule Inhibitor Of Bromodomain Protein 4 (BRD4), in Patients with Relapsed/Refractory (R/R) Malignant Solid Tumors and Lymphoma: Preliminary Data,* presented at ASCO 2019

Momelotinib + AZD5153 May Be a Powerful JAKi + BETi Combo

Potential Benefits Include:



Phase 2 MMB / AZD5153 Combo Study in MF – Initiation Planned for 1H 2022

Planned Phase 2 study will be designed to optimize dosing and provide proof-of-concept for Phase 3 trial design

Pharmacodynamic biomarker assessments will confirm target engagement and combination activity

Data from this trial will inform future development plans, including a potential registration-enabling Phase 3 study

This study will also support our hypothesis that momelotinib is an optimal combination agent in myelofibrosis