ACCELERATE Meeting on Menin Inhibitors

**Context:** Menin inhibitors were discussed at ACCELERATE international multi-stakeholder platform, Paediatric Strategy Forums on Acute Myeloid Leukaemia (April 2019)¹ and Epigenetic Modifiers² (January 2020), and the key opinion leaders on menin inhibitors believed it was very timely to have a meeting dedicated to the topic. Currently there are exciting therapeutic opportunities in this field, and this class of products could fulfil unmet needs for children with acute leukaemia. However, the number of patients eligible for trials of these medicinal products is very limited. The objective of the meeting was to discuss menin inhibitors, identify their potential role in treatment of children with acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML), develop a consensus between the relevant biopharmaceutical companies and academic paediatric oncologists, and determine how best to evaluate these assets in the context of a very limited target population.

**Meeting:** The meeting was held virtually on 6 June 2022 with 64 invited participants: 32 international paediatric oncology experts from Europe and the US; 28 representatives from six pharmaceutical companies (Biomea, Daiichi, Janssen, Kura, Sumitomo Pharma Oncology and Syndax); 2 patient advocates from Europe and the USA (representatives from Children’s Cancer Cause and Zoé4life); 1 representative from the Leukaemia Lymphoma Society, and the ACCELERATE Operations Coordinator. An overview of the molecular mechanisms of response to menin inhibitors and the role of menin inhibitors in leukaemia and relevant epidemiology were presented by academic experts. Details of six menin inhibitors (SNDX-5613 [Syndax Pharmaceuticals], Ziftomenib [Kura Oncology], JNJ-75276617 [Janssen], BMF-219 [Biomea Fusion], DS-1594 [Daiichi Sankyo], DSP-5336 [Sumitomo Pharma Oncology]) were presented by industry representatives. Four themes were discussed: i) Considerations for menin inhibitors; ii) Are five separate trials needed to determining efficacy across targeted leukaemias? iii) An effective strategy to evaluate menin inhibitors in a limited population; iv) How to move forward rapidly to front-line?

**Conclusions:** Amongst the conclusions, it was agreed that there is a clear, strong biological rationale, definitive pre-clinical data promising early clinical data that supports further evaluation of the activity of menin inhibitors in acute leukaemias. Menin inhibitors have the potential to address unmet needs in poor prognosis paediatric subtypes, including infant KMT2A-r ALL, high risk KMT2A-r AML and NUP98-r AML. Paediatric development of menin inhibitor-based strategies thus needs to be rapid. However, these are all rare populations and overall, one third of all patients with MLL KMT2A rearrangements are infants who have particularly unique challenges. As there are multiple products of the same class, a sequential approach is proposed. Menin inhibitors should move rapidly into front-line studies to be evaluated, especially infant leukaemia, as it is in this setting where there is the greatest unmet clinical need. A further meeting will be arranged in 18 months to review the landscape and facilitate decisions in the field when more clinical and translational research data are available from the adult and paediatric populations.