First-in-human phase 1-2A study of CB-103, an oral Protein-Protein Interaction Inhibitor targeting pan-NOTCH signaling in advanced solid tumors and blood malignancies

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CB-103 Phase 1-2A Clinical Study (CB-103-C-101)

NOTCH signaling is a key developmental pathway whose aberrant activation is recognized to play an oncogenic role in numerous human solid tumors and haematological malignancies. NOTCH signaling is inappropriately activated in genetic alterations, e.g. by mutations and/or chromosomal translocations, it becomes an oncogenic driver for NOTCH-dependent cancers, while upregulation of NOTCH receptors is linked to resistance to standard of care treatments (chemotherapy, radiotherapy, targeted therapies).

CB-103 is a new small molecule protein-protein interaction (PPI) inhibitor able to target NOTCH assembly within the cell nucleus leading to down-regulation of NOTCH target genes and inhibition of NOTCH signaling independently of NOTCH mechanism of activation. CB-103 has demonstrated efficacy and tolerability in different preclinical tumour models derived from various NOTCH-driven cancer indications and in blood from NOTCH-activated paediatric TALL leukemia pts.

METHODS

This first-in-human study (CB103-C-101) is a multicentre, open label, non-randomised, phase 1-2A study in adult patients with advanced or metastatic solid tumours and haematological malignancies of CB-103 administered once daily over 28-day treatment cycles. There are two parts in the study. Aim of phase 1 part with dose escalation is to determine the MTD/RP2D and phase 2A to determine preliminary safety and efficacy. On the start of the first dose, patients will be treated with escalating doses of CB-103 over the first 3 days (day 1, day 2, and day 3) and then will receive daily oral CB-103 dosing 103 dosing day 1.

Background:

Figure 8: CB103-C-101 Endpoints & Exploratory Analyses

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REFERENCES


CB-103 dosing day 1.

Figure 6: Developmental Clinical for CB-103 ongoing with first-in-human phase I/IIa study (First patient dosed on Dec 20th, 2017, 1st dose group completed)

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Figure 5: CB8103-C-101 Endpoints & Exploratory Analyses

ENDPOINTS

Table 1: Activity of CB-103 in cancer cell lines

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