RS-2024-RS-2024-00336018

Development of a selective Discoidin Domain Receptor 1 (DDR1) inhibitor with first-in-class novel targets in multiple KRAS G12X-mutant malignant lung and pancreatic cancers

CUREVERSE INC.

Disease Area	**Oncology & Cancer-associated fibrosis**
Product Type	**Small molecule inhibitor**
Indication	**Solid Tumor (KRAS variation)**
Target	**Discoidin Domain Receptor 1 (DDR1)**
Mechanism of Action	**DDR1 activates the PI3K-Akt, NF-κB, and Ras-Raf-ERK pathways. Specifically, NF-κB-mediated activation of the p62-NRF2 signaling pathway increases the proliferation of cancer cells by promoting mitochondrial biosynthesis. DDR1 selective inhibitors assist to fight cancer by inhibiting malignant fibrosis, which allows infiltration of immune T-cells by altering the alignment of extracellular matrix, which can increase the response ~~rate~~ of conventional anti-cancer drugs.**
Competitiveness	**First In Class** **-Drug efficacy against KRAS G12V, S mutations** **-Expandable to treat fibrosis such as CKD** **-Low side effect and good druglikeness** **-Potentially applicable to immune-oncology diseases**
Development Stage	**HIT**
Route of Administration	**Oral or IV Administration**

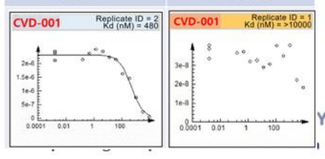
Key Data

Selective DDR1 Inhibitor (DDR2 over 80 times)

KINOMEscan™ active site-directed binding assay

1st

TARGET	CVD-001
Gene6 Symbol	Kd (nM)
DDR1	480
DDR2	>10000



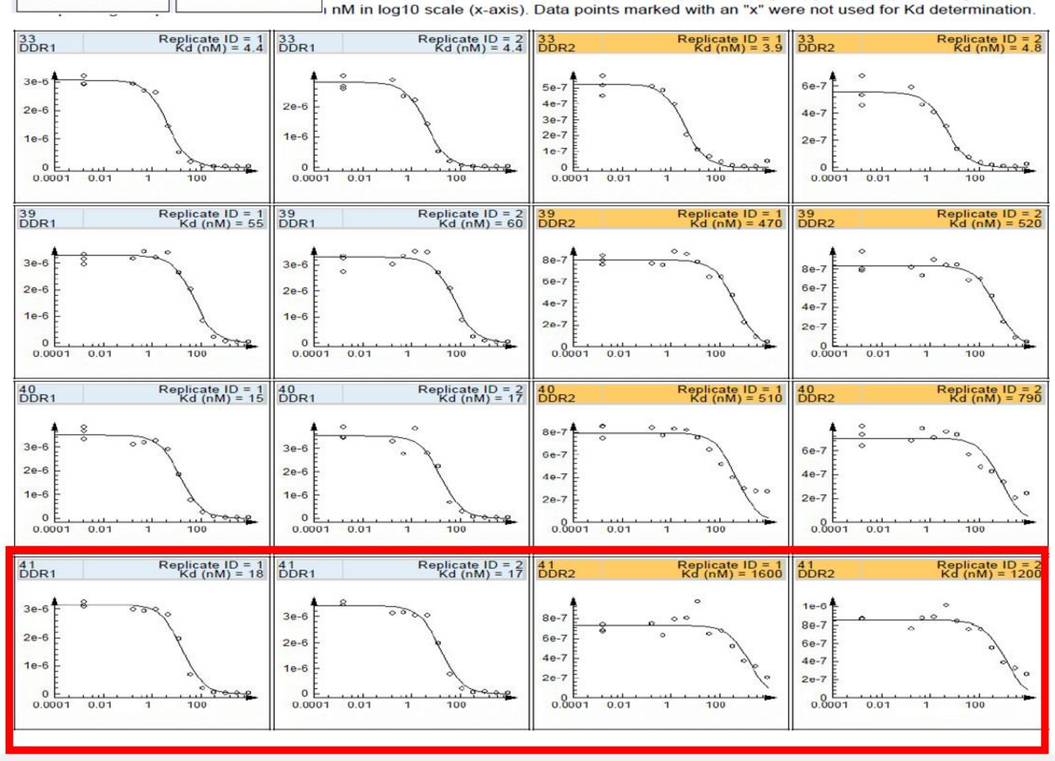
2nd **PZU701-01-s-00001 Study Results**

Table 1 - Matrix of Kds for PZU701-01-s-00001.

Target	33	39	40	41
Gene Symbol	Kd (nM)	Kd (nM)	Kd (nM)	Kd (nM)
DDR1	4.4	58	16	17
DDR2	4.3	490	650	1400

DDR1 17 nM
DDR2 1400 nM
Selectivity 80 times

-00001. The amount of kinase measured by qPCR (Signal; y-axis) is plotted against the nM in log10 scale (x-axis). Data points marked with an "x" were not used for Kd determination.



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