

## ► Asset Overview

|                          |   |
|--------------------------|---|
| <b>Product Type</b>      | Small Molecule  |
| <b>Indication</b>        | Oncology  |
| <b>Current Stage</b>     | Lead identification/optimization  |
| <b>Target (MoA)</b>      | Complex I NADH reductase (OXPHOS), Dihydroorotate dehydrogenase (DHODH) inhibition  |
| <b>Brief Description</b> | Many glycolysis-independent cancer cells require OXPHOS metabolic pathway for survival and are hypersensitive to inhibition of said pathway. OXPHOS mitochondrial metabolism also contributes to an immunosuppression in tumor microenvironment, whereas cytotoxic T cells are dependent on glycolysis, thus suggesting selective targeting of OXPHOS will be beneficial in cancer immunotherapy. |
| <b>Organization</b>      | Center for Drug Design and Discovery  |

## ► Differentiation

### Unmet Needs

- A subpopulation of several different types of cancer (glioblastomas, neuroblastomas, lung cancers, prostate cancers, chemoresistant AML) requires OXPHOS for survival (non-glycolytic cancer cell metabolism pathway)
- Inhibition of OXPHOS mitochondrial metabolism enhances anti tumor immunity

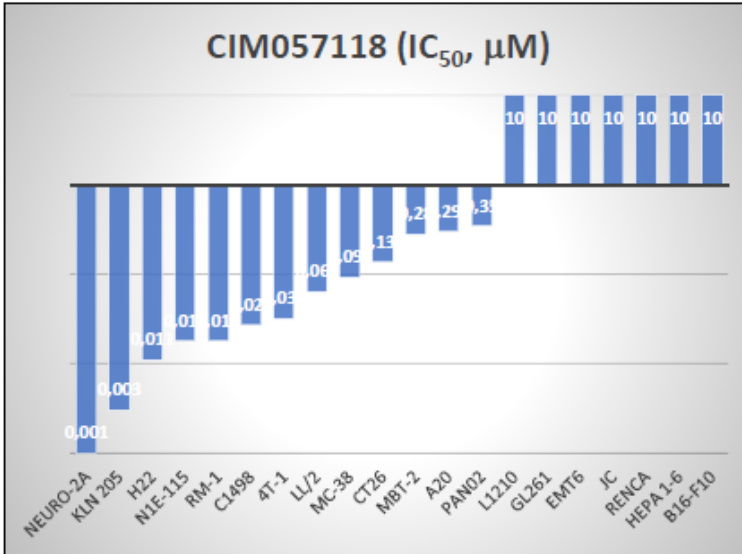
### Innovations

- Inhibitor compounds with good physiochemicals properties and a single digit nM potency for OXPHOS and DHODH
- Novel target that may elicit selective cancer cell killing effect
- May restore immune surveillance function in immunosuppressive tumor milieu, since OXPHOS metabolic pathway is essential for function of immunosuppressive cell subsets (M2 macrophage, Treg, MDSC), whereas cytotoxic T cells and other immune cells critical for cancer immunotherapy depends on glycolysis rather than OXPHOS as main metabolic pathway

# OXPHOS inhibitors/ DHODH inhibitors

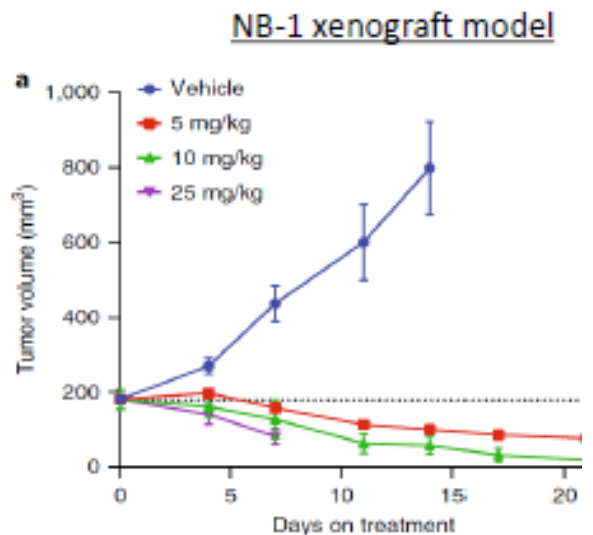
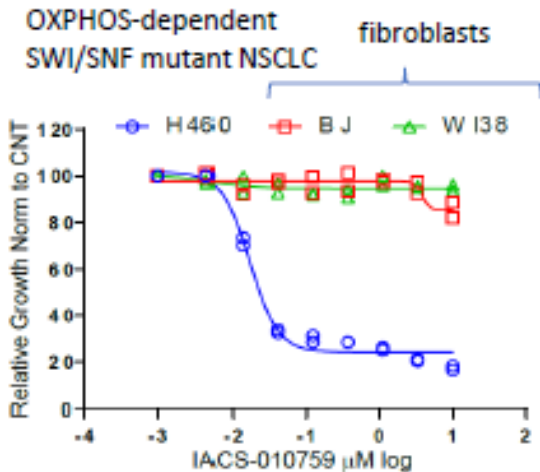
► Key Data

## Genetic modification schematics



| Cancer Type          | Cell Line | CIM057118 (IC <sub>50</sub> , μM) |
|----------------------|-----------|-----------------------------------|
| Neuroblastoma        | Neuro-2a  | 0,001                             |
| Lung Cancer          | KLN 205   | 0,003                             |
| Liver Cancer         | H22       | 0,011                             |
| Neuroblastoma        | N1E-115   | 0,018                             |
| Prostate Cancer      | RM-1      | 0,018                             |
| Leukemia             | C1498     | 0,027                             |
| Breast Cancer        | 4T-1      | 0,032                             |
| Lung Cancer          | LL/2      | 0,064                             |
| Colorectal Cancer    | MC-38     | 0,093                             |
| Colorectal Cancer    | CT26      | 0,137                             |
| Bladder Carcinoma    | MBT-2     | 0,28                              |
| Lymphoma             | A20       | 0,299                             |
| Pancreatic Cancer    | Pan02     | 0,35                              |
| Leukemia             | L1210     | 10                                |
| Neuroblastoma        | GL261     | 10                                |
| Breast Cancer        | EMT6      | 10                                |
| Breast Cancer        | JC        | 10                                |
| Renal adenocarcinoma | Renca     | 10                                |
| Liver Cancer         | Hepa 1-6  | 10                                |
| Melanoma             | B16-F10   | 10                                |

**OXPHOS inhibitors: cancer cell line sensitivity.** Sensitivity across cancer cell line panel reveals hyper sensitive mouse cancer cell lines under standard culture conditions



**OXPHOS inhibitors: Potent and cancer-specific anti tumor effect.**

**► Intellectual Property**

|                         |  |
|-------------------------|--|
| <b>Patent No.</b>       |  |
| <b>Application Date</b> |  |
| <b>Status</b>           |  |
| <b>Country</b>          |  |

**► Contact Information**

|                       |   |
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