



- **Epigenetic modifications** are a major driver of biological complexity and can have a role in the development of a variety of disease treatments.
- Epigenetics is an **emerging area** covering a broad range of mode of actions. However, only four drugs are currently approved and eleven agents are in early-stage trials.
- **Novel proprietary compounds** binding two epigenetic targets have been developed:
 - more effective than reference epigenetic compounds vs different cancer cell lines.
 - first-in-class dual reversible inhibitors of DNMT and HMT.
- **Indication:** cancer.

Opportunity and Competitive Landscape

- The fact that the epigenome is dynamic is of particular relevance to drug development, as it implies that specific disease-associated epigenetic states may be reversible with treatment.
- To date, the most investigated therapeutic area in terms of epigenetics is cancer.
- Beyond cancer, epigenetic factors have been implicated in inflammatory, autoimmune, metabolic, neurological and cardiovascular disorders.
- Four drugs with epigenetic mechanisms of action are currently approved. All of them are anticancer drugs and they are only focused on 2 modes of action (HDACs and DNMT-irreversible).
- Mostly, research is focused on developing novel HDAC inhibitors.

Application Scope

Cancer: a wide range of neoplastic diseases in where the epigenetics targets addressed are implied: from hematological malignancies, such as Acute leukemias and lymphomas, to solid tumors in liver, bladder and others.

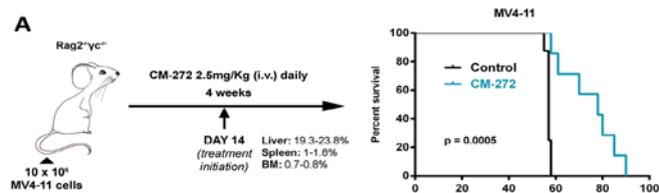
New agents

Small molecules hitting DNMT and HMT, IC₅₀ at low nM range. They are not SAM-competitive; in fact, selective vs 90 additional epigenetic targets MoA validated, through epigenetic marks, in cell lines and *in-vivo*. First-in-class reversible inhibitors.

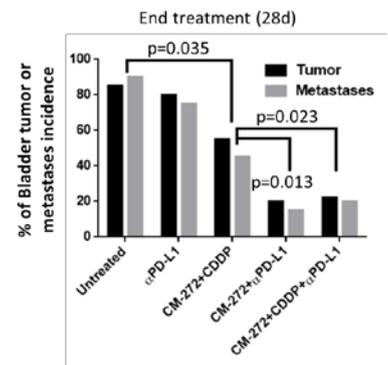
Proof of Concept

In vitro studies: G9a and DNMT1 inhibitory potencies (expressed as pIC₅₀) and the growth inhibitory potencies (expressed as pGI₅₀) for compounds CM-272, CM-579, selective G9a inhibitors (BIX-01294 and UNC-0638) and irreversible DNMT inhibitors (Azacitidine and Decitabine).

In vivo studies: PoC and efficacy studies using CM-272 in Acute Myeloid leukemia (A), Acute Lymphoblastic leukemia, Lymphoma, Hepatocarcinoma and Bladder Cancer.



Combination with Immunotherapy (CM-272+anti-PD-L1 reduce the Bladder cancer and metastases incidence by an endogenous antitumor immune response and immunogenic cell death (A) with the conversion of a cold immune-tumor into a hot tumor) **and with Anti-Apoptotic drugs** (CM-272 sensitizes cells of hematological neoplasia to BCL-2, BCL-XL or MCL-1 inhibitors and mitochondrial apoptosis).



Intellectual Property

Four independent patents filed: WO2015192981, WO201708507853, WO2017102677 and one unpublished.