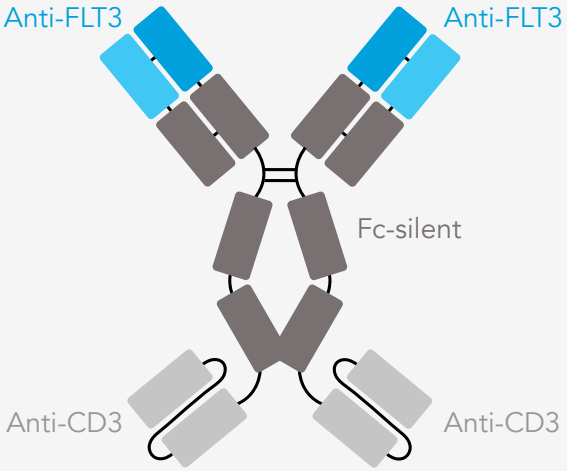
About CLN-049

CLN-049 is a novel T cell engaging bispecific antibody designed to simultaneously bind the extracellular domain of FTL3 on acute myeloid leukemia (AML) cells and the CD3 receptor subunit on T cells. AML is the most common form of acute leukemia in adults. Currently, the only curative therapy for AML is intensive chemotherapy with or without hematopoietic stem cell transplantation; however, only 6% of patients over 60 are eligible at diagnosis since the mean age is 68.[1,2]

CLN-049



ABOUT THE MOLECULE

CLN-049 offers promising therapeutic potential as FLT3 is expressed on leukemic stem cells, as well as blast cells, which may increase response durability.

WHERE IT'S BEING STUDIED

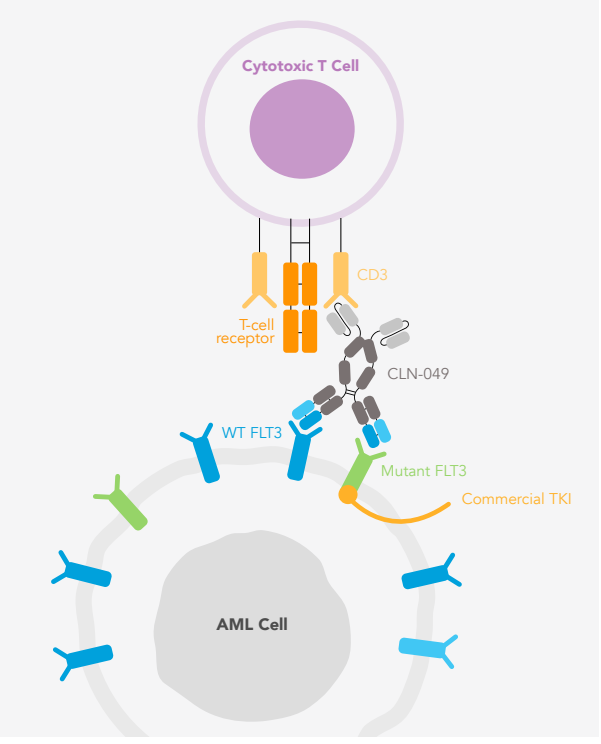
CLN-049 is currently being studied in a Phase 1 clinical trial in patients with relapsed/refractory AML and high-risk myelodysplastic syndrome.

HOW WE LICENSED IT

Cullinan Oncology acquired an exclusive license for CLN-049 from the German Cancer Research Center (DKFZ) and the University of Tubingen to develop the novel asset.

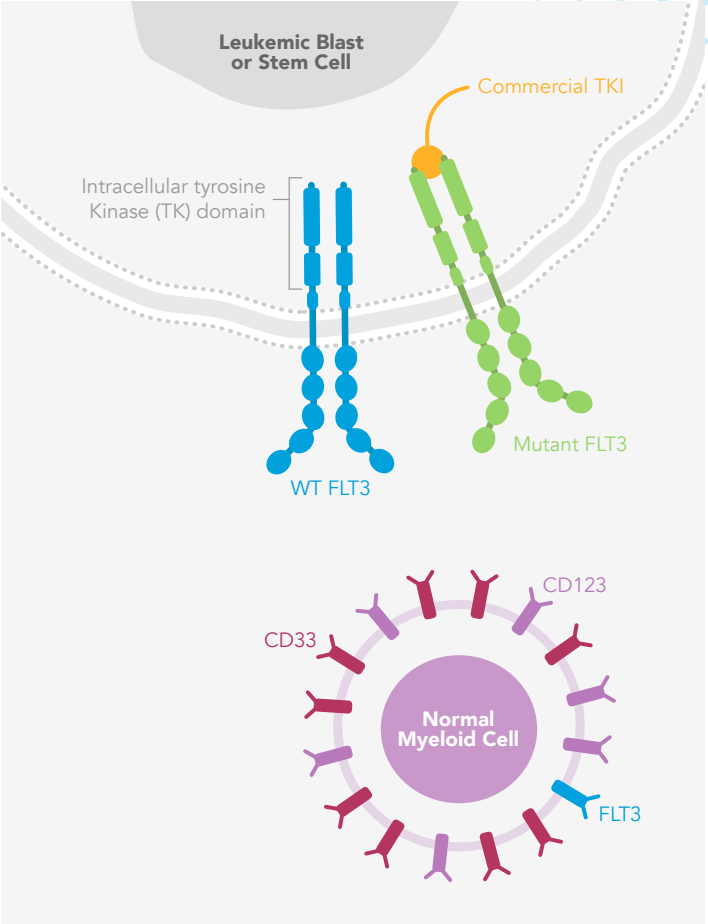
WHY TARGET FLT3 PROTEINS?

- FLT3 is expressed on AML cells in more than 80% of patients.
- FLT3 proteins play a key role in promoting leukemic cell proliferation and survival.
- Currently, the only available therapies targeting FLT3 are tyrosine kinase inhibitors (TKIs).
  - TKIs are effective in FLT3-mutant AML, which comprises 20-30% of all AML.[3,4]
  - Developing resistance to TKIs is common.[3,4]



CLN-049 TARGETS AND MECHANISM OF ACTION

- Pre-clinical models have shown that FLT3 is expressed on leukemic stem cells, including mutant and wild type forms, as well as blast cells, which may increase response durability.
- CLN-049 binds with high affinity to the extracellular domain of FLT3 on AML cells and the CD3 receptor subunit on T cells, redirecting the effector T cells toward cancer cells, facilitating T cell mediated cancer cell death.
- CLN-049 binds both mutant and wild type FLT3, allowing targeted action regardless of FLT3 mutational status.
- Due to limited expression on normal myeloid-derived cells, CLN-049 binding to FLT3 is expected to cause less cytokine release upon T cell activation than for high-abundance targets such as CD33 and CD123, which are frequently expressed on normal myeloid cells.
- CLN-049 was engineered to have two FLT3-binding Fab arms that promote higher avidity binding to FLT3 on AML cells, two CD3 binding single-chain Fv domains that are functionally monovalent to minimize non-specific T cell activation, and a non-functional Fc domain.



PRECLINICAL EVIDENCE AND CLN-049'S POTENTIAL

- CLN-049 eliminates patient-derived AML blasts in mouse models.
- CLN-049's ability to recognize both mutant and wild type FLT3 with high affinity offers the potential to treat AML regardless of FLT3 mutational status. TKIs, which target only mutant FLT3, can treat only 20-30% of AML cases.
  - CLN-049's potency is largely independent of FLT3 expression level or mutational status, allowing for consistent dosing based on efficacy and safety profile.
  - Both the FLT3 and CD3 binding domains are humanized to minimize the risk of immunogenicity.

REFERENCES

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