NB-007: Next-Generation Dual-Targeting FLT3/CSF1R Inhibitor

A breakthrough approach in hematologic oncology, simultaneously targeting the FLT3 and CSF1R pathways to address both tumor cells and the immunosuppressive tumor microenvironment. This dual mechanism offers a differentiated therapeutic strategy for acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS).

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NB-007: First-in-Class Dual FLT3/CSF1R Inhibitor

Program Overview

A first-in-class small molecule dual-targeting inhibitor of FLT3 and CSF1R for acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). This injectable therapeutic addresses a **$6B market opportunity** with **NMPA IND approval** in China and strong global patent protection beyond 2041 (PCT filed).

Dual Mechanism Advantage

Simultaneous inhibition of FLT3 (driving tumor cell proliferation) and CSF1R (modulating tumor-associated macrophages) creates a differentiated therapeutic approach that addresses both tumor cells and the immunosuppressive microenvironment.

Tumor Cells

FLT3 inhibition blocks malignant proliferation

Macrophages

CSF1R inhibition reprograms tumor microenvironment

Synergy

Combined action enhances anti-tumor efficacy

NB-007: Superior Single-Agent Activity and Safety

Dual-Pathway Innovation

Simultaneous inhibition of CSF1R and FLT3 pathways enables NB-007 to **act on macrophages and tumor cells concurrently**, improving the tumor microenvironment while directly suppressing malignant cell growth. This dual mechanism enhances anti-tumor effects beyond what either pathway inhibition could achieve alone.

High Selectivity

Better kinase selectivity profile than gilteritinib, reducing off-target effects and improving therapeutic window

Superior Single-Agent Activity

Outperforms mainstream drugs in AML/MDS when used as monotherapy, driven by dual mechanism

Avoids Combination Toxicity

Single dual-target agent eliminates DDI concerns and toxicity superposition from drug combinations

Delays Resistance

Dual targeting reduces likelihood of resistance development through single pathway mutations

Optimal Pharmacokinetic Profile

Exhibits a **long half-life meeting once-daily dosing requirements**, enhancing patient convenience and compliance. The extended PK profile maintains sustained target inhibition throughout the dosing interval, maximizing therapeutic benefit while minimizing pill burden in a population often managing multiple medications.

NB-007: First-in-Class FLT3/CSF1R Dual Inhibitor

Dual-Pathway Innovation

A breakthrough in targeted oncology therapy through simultaneous inhibition of CSF1R and FLT3 pathways. This dual-action mechanism modulates tumor-associated macrophages while directly targeting malignant cells, fundamentally reshaping the tumor microenvironment to enhance anti-tumor efficacy.

World's First FLT3/CSF1R Dual Inhibitor

FLT3/CSF1R dual-targeting inhibitor with differentiated mechanism of action.
Unique mechanism of action with no direct competitors in clinical development

Superior Safety Profile

Significantly wider therapeutic window compared to existing FLT3 inhibitors like gilteritinib

Once-Daily Dosing

Long half-life enables convenient QD administration, improving patient compliance

No Drug-Drug Interactions

No drug-drug interactions or additive toxicity from combination therapy. Eliminates DDI concerns and combination-related toxicities common with current therapies.

NB-007: Precision Targeting of FLT3/CSF1R

High Selectivity

Exceptional selectivity for its primary targets while showing minimal activity against off-target kinases. This precision targeting minimizes potential side effects and enhances the therapeutic window. Sub-nanomolar potency against FLT3 wild-type and clinically relevant mutations, with excellent selectivity over off-target kinases. This profile supports both efficacy and tolerability in clinical development.

Primary Targets (Sub-nanomolar IC50)

Enzyme	IC50 (nM)
FLT3 (Wild Type)	0.58
FLT3 (D835Y)	0.17
FLT3 (ITD)	0.5
CSF-1R	3.3
PDGFR-beta	16.3
CDK6/D1	18.7

Off-Target Selectivity

Enzyme	IC50 (nM)
C-kit	424.7
ROS1	605
ALK	966
ALK (F1174L)	>1000
PI3Kδ	1292
CDK7/H	>500

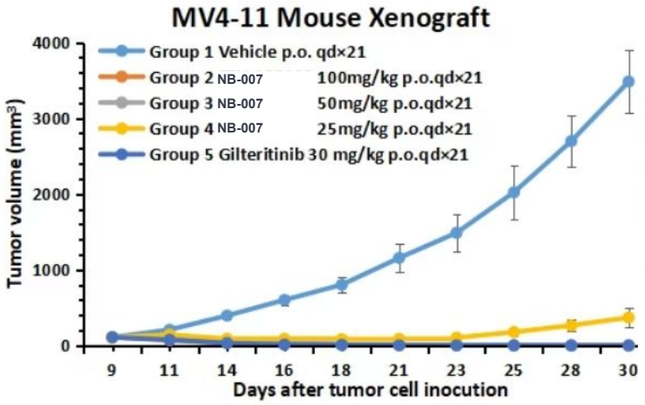
Key Advantage: >100-fold selectivity for FLT3/CSF1R over most off-target kinases, including critical safety-related kinases like C-kit and ALK. Critical kinases such as BTK, C-MER, MEK1, and mTOR showed no inhibition (IC50 >1000 nM). This selectivity profile supports a superior safety and tolerability profile. This exceptional selectivity profile minimizes potential off-target toxicities and supports a favorable therapeutic window.

NB-007: Robust Pre-Clinical Efficacy

Robust In Vivo Efficacy Across Models

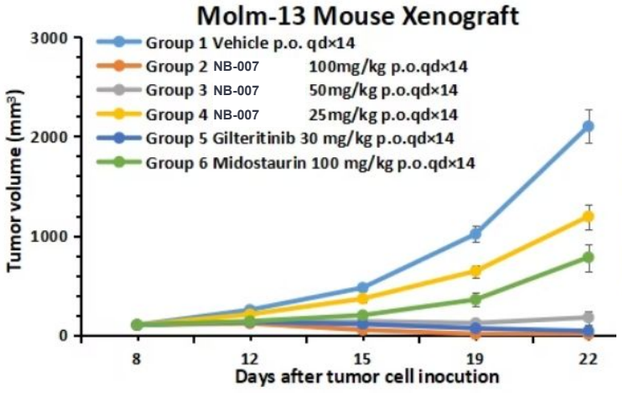
Strong anti-tumor activity across multiple xenograft models, achieving complete tumor regression in several studies. All models demonstrated statistically significant and dose-dependent efficacy. Consistent anti-tumor activity across different FLT3-mutant AML cell lines. These results validate the therapeutic potential of dual FLT3/CSF1R inhibition.

FLT3-ITD Model



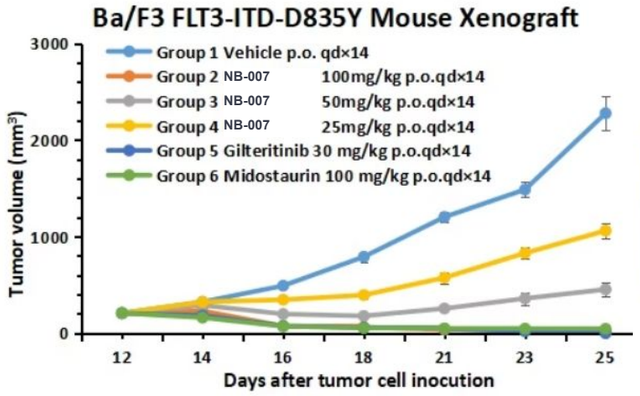
Near-complete tumor regression across all dose levels tested in the FLT3-ITD xenograft model. Highly significant tumor growth inhibition compared to vehicle control.

FLT3 Wild-Type Model



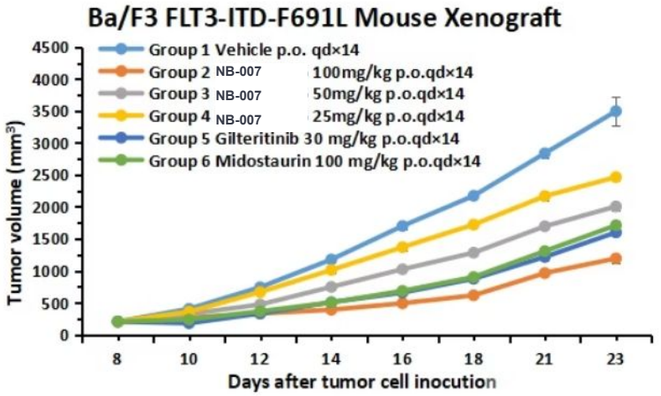
Dose-dependent efficacy with sustained tumor control.

FLT3 D835Y Model



Maintains potent activity against clinically relevant resistance mutation D835Y. Consistent activity across genetically diverse tumor models

Alternative Mutation Model



Broad efficacy across diverse genetic backgrounds supporting wide applicability. Reproducible efficacy supporting clinical translation.

NB-007: Best-in-Class Safety Profile

Exceptional safety profile and wide therapeutic window position NB-007 as a potentially best-in-class FLT3 inhibitor with reduced risk of dose-limiting toxicities and improved patient outcomes. Comprehensive toxicology studies demonstrate a substantially wider safety margin compared to gilteritinib, the current standard of care. The compound shows no concerning effects on cardiovascular, respiratory or central nervous systems at pharmacologically relevant exposures.

34x

Rat Safety Window

Safety window (12.33) versus gilteritinib (0.36) in rat toxicology studies

8.5x

Beagle Safety Window

Safety window (1.70) versus gilteritinib (0.2) in beagle toxicology studies

120

Rat STD10 (mg/kg)

Severely toxic dose in 10% of animals, demonstrating robust tolerability

Safety Pharmacology Profile

Assessment	Result
hERG Inhibition	IC50 = 5.13 µM (>8,800x selectivity)
CNS Effects	No adverse effects up to 600 mg/kg
Cardiovascular	No effects up to 150 mg/kg
Respiratory	No effects up to 150 mg/kg

Toxicology Summary

4-Week Repeat-Dose Studies

- Rat STD10: 120 mg/kg (>30x efficacious dose)
- Dog HNSTD: 15 mg/kg (>7x efficacious dose)
- Reversible findings in lymphoid tissues
- No unexpected or irreversible toxicities

Comparative Advantage: 34-61 fold wider safety margin compared to the approved FLT3 inhibitor gilteritinib, supporting potential for improved tolerability in patients.

Accelerating Innovation to Improve Patients' Lives

Navika Bio connects groundbreaking biotech innovation with global pharmaceutical partners to deliver transformative therapies to patients worldwide.

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Let's Connect

For more information about partnership opportunities and to join us on this exciting journey of bringing transformative therapies to patents worldwide, please reach out to:

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