NB-001: Dual-Target PIM/CDK Inhibitor for Hematologic Malignancies

A breakthrough in targeted therapeutics for acute myeloid leukemia and non-Hodgkin lymphoma. This innovative compound simultaneously inhibits PIM1/2/3 and CDK2/4/6 kinases, disrupting critical downstream signaling pathways that drive tumor cell differentiation and proliferation.

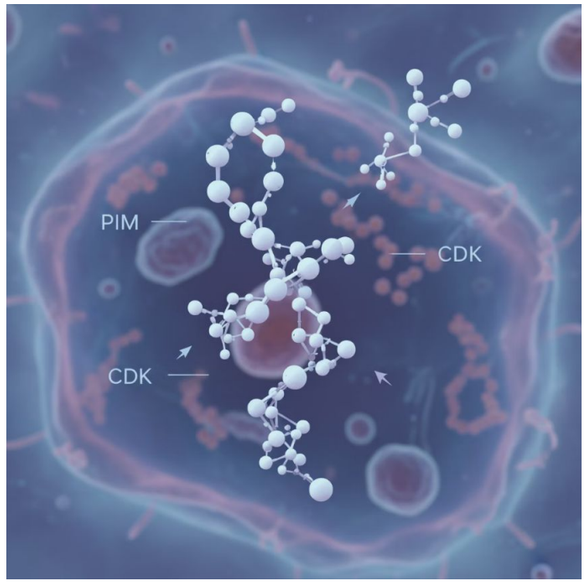
NAVIKA BIO

NB-001: First-in-Class Dual PIM and CDK Inhibitor

Program Overview

NB-001 represents a breakthrough in hematologic malignancies as the first dual inhibitor simultaneously targeting PIM1/2/3 and CDK2/4/6 kinases. This injectable small molecule addresses a **$15B market opportunity** in acute myeloid leukemia (AML) and non-Hodgkin lymphoma (NHL).

The program is currently advancing through Phase I clinical trials in both Australia and China, with **strong global patent protection extending beyond 2038** (PCT filed). This dual-action mechanism offers a differentiated approach to overcoming resistance mechanisms that limit current single-target therapies.



Key Attributes

- First-in-Class
- Injectable formulation
- Dual kinase inhibition
- Global clinical development

Dual Kinase Innovation

Targets PIM1/2/3 and CDK2/4/6 for a novel approach to overcome resistance.

Significant Market Potential

Addresses a $15B market in AML and NHL with a differentiated treatment.

Robust IP & Development

Strong global patent protection beyond 2038, advancing through Phase I trials.

NB-001: First-in-Class Dual PIM and CDK Inhibitor

Dual Pathway Inhibition

NB-001 simultaneously inhibits PIM1/2/3 and CDK2/4/6 kinases, disrupting downstream signaling pathways that drive tumor cell differentiation and proliferation. Pan-kinase PIM inhibition eliminates cross-compensation and reduces bypass resistance mechanisms.

Dose-Dependent Efficacy

In melanoma PDX models, NB-001 (ETH-155008) at 40mg/kg demonstrated superior tumor suppression compared to palbociclib at 100mg/kg, showcasing potent activity against CDK4/6 inhibitor-resistant strains with dose-dependent responses.

Enhanced Safety Profile

No drug-drug interactions or combination-related toxicity observed. Safety window equivalent to or better than gilteritinib and abemaciclib. Importantly, no QT interval prolongation detected, indicating superior cardiac safety compared to standard therapies.

Clinical validation is already emerging: **Complete response (CR) and partial response (PR) cases have been confirmed in both Australian and Chinese Phase I trials**, demonstrating early proof-of-concept in heavily pretreated patient populations.

Competitive Advantage: Genentech's PIM, AstraZeneca's CK2/PIM combination and Sanofi's PIM1/PIM2 programs all target single pathways and remain at preclinical stages, positioning NB-001 as the clinical leader in this therapeutic space.

NB-001: Competitive Advantages

Mechanism of Action

Pan-Kinase Inhibition

PIM1/2/3 inhibition abolishes cross-compensation and reduces bypass resistance, delivering superior therapeutic outcomes versus single-target approaches

CDK Resistance Solution

Active against CDK4/6 inhibitor-resistant strains, providing treatment options for previously resistant patient populations

Leading Global Progress

First-in-class positioning in PIM inhibitor track with strong patent protection extending beyond 2038 (PCT filed)

Safety Profile

- No drug-drug interaction (DDI) concerns
- No QT interval prolongation observed
- Superior cardiac safety profile
- Eliminates combination therapy toxicity risks

Clinical Progress

- Phase I trials active in Australia and China
- Complete response (CR) and partial response (PR) cases confirmed
- Strong efficacy signals in heavily pretreated patients

NB-001: Superior Safety Profile

Comprehensive Preclinical Assessment

NB-001 demonstrates a favorable safety profile across multiple preclinical evaluations, with no significant cardiovascular, respiratory, or autonomic nervous system effects observed. The compound shows minimal hERG inhibition (IC50 >10 μM), indicating low cardiac risk potential.

Safety Pharmacology Results

Study	Species	Dose Range	Outcome
hERG Effects	CHO Cell	0.04-10 μM	IC50 >10 μM
Autonomic Function	SD Rat	5.0-30.0 mg/kg	No effects
CV/Respiratory	Beagle	1.0-3.0 mg/kg	No effects

Competitive Safety Window

NB-001 demonstrates **superior safety margins** compared to approved therapies:

SD Rat: 1.4× (vs. Gilteritinib 0.36×)

Beagle: 0.2× (matching Gilteritinib, 10× better than Abemaciclib)

4-Week Repeat-Dose Toxicity Findings

In SD rats, the No Adverse Effect Level (NOAEL) was established at 5 mg/kg in females, with target organs including kidney, thymus, bone marrow, and testis. In beagles, the Highest Non-Severely Toxic Dose (HNSTD) was 2.0 mg/kg, with toxicity observed in gallbladder, testis, prostate, thymus, and sternal bone marrow, findings consistent with mechanism-based, reversible effects expected for this drug class.

NB-001: Australia Phase I: Clinical Proof of Concept

The Australian Phase I dose-escalation study enrolled nine heavily pretreated patients (3-4 prior lines of therapy) with relapsed/refractory (R/R) follicular lymphoma (FL), acute myeloid leukemia (AML), marginal zone lymphoma (MZL), and Waldenström macroglobulinemia (WM). The trial evaluated three dose cohorts: 10 mg, 20 mg, and 40 mg administered once daily in continuous 28-day cycles.

9

Patients Enrolled

From 12 screened subjects across 3 dose cohorts

0

DLT Events

No dose-limiting toxicities observed in 7 DLT-evaluable patients

1

Complete Response

CR achieved in FL patient at 10 mg dose (23 cycles)

1

Partial Response

PR observed in MZL patient at 40 mg dose (6 cycles)

Patient Demographics & Outcomes

Subject ID	Dose	Disease	Gender	Age	Prior Lines	Cycles	Response
1001-0001	10 mg	R/R FL	F	70	3	23	**CR**
1001-0002	20 mg	R/R FL	F	60	4	2	NA
1002-0001	20 mg	R/R AML	F	68	3	3	SD
1002-0003	20 mg	R/R AML	M	75	2	2	SD
1003-0004	40 mg	R/R MZL	M	69	4	6	**PR**
1003-0005	40 mg	R/R WM	M	61	3	5	SD
1005-0001	40 mg	R/R FL	M	56	3	3	PD

NB-001: Australia Phase I: Safety Analysis

The safety profile in the Australian cohort was generally manageable, with most adverse events (AEs) being Grade 1-2 in severity. Only one Grade 3 treatment-related adverse event (TRAE) was observed—a maculopapular torso rash in patient 1001-0002 receiving 20 mg, which was classified as a Serious Adverse Event (SAE) and Suspected Unexpected Serious Adverse Reaction (SUSAR) but did not meet DLT criteria.

Adverse Event Summary by Grade

Grade	Event Type	Count	Most Common
Grade 1	All AE	19	Nausea (4), Diarrhea (3)
Grade 1	TRAE	15	Diarrhea (3), Headache (2)
Grade 2	All AE	8	Various
Grade 2	TRAE	0	—
Grade 3	All AE	10	Various
Grade 3	TRAE	1	Rash (1)

Key Safety Observations

Grade 3 TRAE Detail: One patient (1001-0002) experienced a Grade 3 maculopapular rash at 20 mg dose. This event was managed successfully and did not result in discontinuation or dose modification that would classify it as dose-limiting.

- No Grade 4 or 5 events reported
- Gastrointestinal events (nausea, diarrhea) were most common but mild
- One SAE/SUSAR (Grade 3 rash) in 20 mg cohort
- No discontinuations due to toxicity

NB-001: China Phase I: Expanded AML Experience

The China Phase I trial enrolled 17 patients with relapsed/refractory AML across five dose cohorts (20 mg, 40 mg, 60 mg, 80 mg QD, and 40-50 mg BID), representing patients with 2-5 prior lines of therapy. This heavily pretreated population (median 3-4 prior regimens) provides critical safety and preliminary efficacy data in a challenging patient segment with limited therapeutic options.

01

Cohort 1: 20 mg QD

1 patient enrolled, evaluable for DLT. Progressive disease observed.

02

Cohort 2: 40 mg QD

6 patients enrolled, 1 DLT event. Stable disease achieved in select patients.

03

Cohort 3: 60 mg QD

3 patients enrolled, no DLT. Disease stabilization observed in 1 patient.

04

Cohort 4: 80 mg QD

3 patients enrolled, no DLT. Stable disease achieved in multiple patients.

05

Cohort 5: 40-50 mg BID

4 patients enrolled (3 at 40 mg, 1 ongoing at 50 mg). Disease stabilization observed.

Select Patient Outcomes

Subject	Dose	Gender	Age	Prior Lines	Cycles	Response
02008	80 mg	F	63	4	7	**SD**
02009	40 mg BID	F	52	3	1	PD
02013	50 mg BID	M	76	2	Ongoing	**SD**

Notably, patient 02008 achieved stable disease for 7 cycles at 80 mg QD, demonstrating sustained benefit in a patient with 4 prior treatment lines. Patient 02013 remains on treatment at 50 mg BID with stable disease, suggesting potential for durable disease control.

NB-001: China Phase I: Safety Profile Across Dose Escalation

The China Phase I study enrolled 19 screened patients with 16 ultimately enrolled across five dose cohorts. Safety data from 15 DLT-evaluable patients revealed one DLT event (Grade 3 rhabdomyolysis at 40 mg QD), five SAEs, and three SUSARs. The majority of treatment-related adverse events were hematologic (cytopenias) or gastrointestinal, consistent with the mechanism of action and baseline disease characteristics of heavily pretreated AML patients.

Overall Safety Summary

Cohort	Dose	Enrolled	DLT	SAE
1	20 mg	1	0	0
2	40 mg	6	1	3
3	60 mg	3	0	0
4	80 mg	3	0	2
5	40 mg BID	3	0	0

Most Common Treatment-Related Adverse Events

Nausea (Grade 1-2: 23 events; Grade 3: 2 events), vomiting (Grade 1-2: 25 events; Grade 3-4: 5 events), diarrhea (4-6 events per grade), neutropenia (Grades 1-4), thrombocytopenia (Grades 1-4), and anemia (Grades 1-2) were the predominant AEs. One Grade 3 rhabdomyolysis event in the 40 mg cohort was classified as a DLT, though this was an isolated occurrence.

Hematologic TRAEs by Grade

Grade 1
Anemia

Grade 2
Thrombocytopenia, neutropenia

Grade 3
Mild neutropenia

Grade 4
Severe neutropenia

Non-Hematologic TRAEs by Grade

Grade 1
Nausea

Grade 2
Vomiting, diarrhea

Grade 3
Vomiting, rhabdomyolysis

Grade 4
Vomiting

NB-001: Clinical Activity: Response Rates Across Indications

Combined data from Australian and Chinese Phase I trials demonstrates promising clinical activity in both AML and NHL patient populations. Twenty-four patients have been enrolled to date: 19 with relapsed/refractory AML and 5 with NHL subtypes. The NHL cohort achieved a 40% objective response rate (ORR) with 2 of 5 patients responding (1 CR, 1 PR), while disease control rate (DCR) reached 80%. In the heavily pretreated AML population, disease control was achieved in 53% of patients (10 of 19 with stable disease).

NHL Cohort (n=5)

ORR: 40% (2/5 patients)

- 1 Complete Response (CR)
- 1 Partial Response (PR)
- 2 Stable Disease (SD)

DCR: 80% (4/5 patients)

AML Cohort (n=19)

ORR: 0% (no CR/PR)

- 10 Stable Disease (SD)
- 8 Progressive Disease (PD)
- 1 Not Evaluable (NA)

DCR: 53% (10/19 patients)

Clinical Context: These response rates are particularly notable given that enrolled patients had received 2-5 prior lines of therapy and represent a heavily pretreated, refractory population with limited alternative treatment options. Disease stabilization in >50% of AML patients and meaningful responses in NHL patients support continued development.

Comparative Response Data by Disease Type

Disease	CR	PR	SD	PD	NA	Total	ORR / DCR
NHL	1	1	2	1	—	5	40% / 80%
AML	—	—	10	8	1	19	0% / 53%

NB-001: Response by Dose Level

Optimal Dose May Vary By Indication

Optimal therapeutic dose may vary by indication, with NHL patients potentially responding to lower doses while AML patients may require higher exposures. The favorable safety profile at 80 mg QD with 100% disease control supports further exploration of this dose level, while BID dosing regimens warrant continued investigation to optimize pharmacokinetic exposure and efficacy.

Efficacy Summary Across All Dose Levels

Dose (mg)	CR	PR	SD	PD	NA	Total	ORR	DCR
10	1	—	—	—	—	1	**100%**	**100%**
20	—	—	3	—	1	4	0%	**75%**
40	—	1	3	4	1	9	11%	44%
60	—	—	1	2	—	3	0%	33%
80	—	—	3	—	—	3	0%	**100%**
40 BID	—	—	1	2	—	3	0%	33%
50 BID	—	—	1	—	—	1	0%	**100%**

Identifying Optimal Therapeutic Window

Dose-response analysis across all enrolled patients reveals important trends for optimal dosing strategy. The 10 mg cohort demonstrated the highest response rate (100% ORR and DCR, n=1), achieving a complete response in an FL patient who remained on treatment for 23 cycles. The 20 mg cohort showed promising disease control (75% DCR) with 3 of 4 patients achieving stable disease or better. Higher dose cohorts (40-80 mg) demonstrated variable responses, with the 80 mg QD and 50 mg BID doses achieving 100% disease control rates in their limited patient populations.

Key Observations

- Lower doses (10-20 mg) show encouraging efficacy signals in NHL
- 40 mg cohort largest (n=9) with mixed responses
- 80 mg QD achieved 100% DCR (3/3 patients with SD)
- BID dosing (40-50 mg) under evaluation with ongoing patient

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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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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