BioNova Introduction

Pharma 烨辉医药 Jan 2024

I. Company Overview

Headquarters at Chamtime Plaza Shanghai

Two Veteran Founders of Track Records

Immunomedics

Hutchison Medi Pharma

abbvie

JAMA | Original Investigation

Effect of Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer
The FRESCO Randomized Clinical Trial

Jin Li, MD; Shukui Qin, MD; Rui-Hua Xu, MD, PhD; Lin Shen, MD, PhD; Jianming Xu, MD; Yuxian Bai, MD; Lei Yang, MD, PhD; Yanhong Deng, MD, PhD; Zhen-dong Chen, MD; Haijun Zhong, MD; Hongming Pan, MD, PhD; Weijian Guo, MD; Yongqian Shu, MD; Ying Yuan, MD, PhD; Jianfeng Zhou, MD; Nong Xu, MD; Tianshu Liu, MD; Dong Ma, MD; Changping Wu, MD; Ying Cheng, MD; Donghui Chen, MD; Wei Li, MD; Sanyuan Sun, MD; Zhuang Yu, MD; Peiguo Cao, MD; Haihui Chen, MD; Jiejun Wang, MD; Shubin Wang, MD; Hongbing Wang, MD; Songhua Fan, MD; Ye Hua, MD, MPH; Weiguo Su, PhD

ARTHRITIS & RHEUMATISM
Vol. 50, No. 5, May 2004, pp 1400–1411
DOI 10.1002/art.20217

Radiographic, Clinical, and Functional Outcomes of Treatment With Adalimumab (a Human Anti–Tumor Necrosis Factor Monoclonal Antibody) in Patients With Active Rheumatoid Arthritis Receiving Concomitant Methotrexate Therapy

A Randomized, Placebo-Controlled, 52-Week Trial

Edward C. Keystone,[1] Arthur F. Kavanaugh,[2] John T. Sharp,[3] Hyman Tannenbaum,[4] Ye Hua,[5] Leah S. Teoh,[5] Steven A. Fischkoff,[5] and Elliot K. Chartash[5]

BioNova History

Series A Dec.

Series B Aug.

Series B+ Nov.

2018

- BioNova Established

2019

- Nov.
  BN101: License deal signed with Kadmon

2020

- Jan.
  BN103& BN104: Discovery collaboration with PharmaResources
- Mar.
  BN102: License deal signed with Carna Bio
- Sep.
  BN101: IND cleared by CDE
- Dec.
  BN101: Phase 1 first subject dosed
- Dec.
  BN101: Received BTD

2021

- Feb.
  ADC co-development agreement with Ardeagen
- March.
  BN103: Stopped (early kill)
- May.
  BN101: Phase 2 FPI
- Oct.
  BN301: License deal signed with Sutro
- Nov.
  BN101: China NDA submitted
- Dec.
  BN102: IND filed

2022

- Jan.
  BN104: Best-in-class compound identified
- Feb.
  BN301: IND
- Apr.
  BN105: Initiated

2023

- Feb.
  BN102: Terminated license with Carna Bio
- Aug.
  BN101: NDA approved
- Aug.
  BN104: China IND
- Sep.
  BN104: US IND
- Oct.
  BN104: US FDA Fast Track Designation
- Oct.
  BN104: China FPI
- Dec.
  BN101: China right sold back to Sanofi

2024

Company Strengths and Vision

Execution

- Highly capable executive team with under-promise but over delivery mindset;
- Proven track records in BD, in-licensing with value creation and speedy clinical development;
- In-house cross-functional discovery team with efficient ongoing due diligence backed decisions for competitive advantage

Innovation

- Utilizing industrial best mastermind to architect differentiated in-house discovery and co-development pipeline
- Deep understanding in development and regulatory strategy to guide BioNova with timely development and high probability of success

Globalization

- Global team with insight to position promising targets with competitive advantage
- Assets with worldwide rights of out-licensing potentials
- Clear company growth plan to go from China to worldwide

BioNova is growing steadily with huge potential to become a top China biopharma with global footprint.

Vision - Growing into a Global Biotech

"Triple Jump" Strategy

04

- Clear company growth plan to **go from China to worldwide**.
- Long-term global innovation company and asset acquisition plans.

03

- "**Home grown**" novel target agents for global simultaneous development.
- Out-licensing opportunities for ex-China development and commercialization.

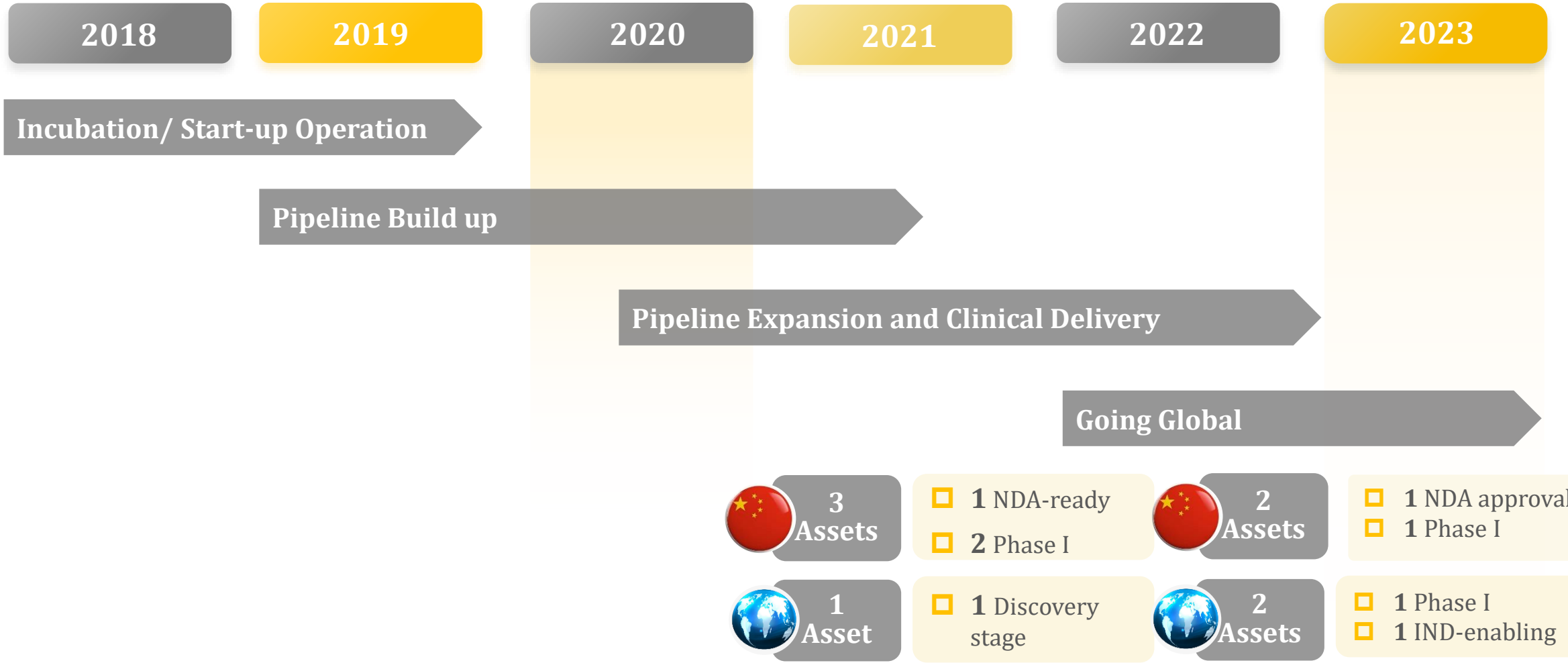
02

- Speedy move to cutting-edge technologies from partners' expertise and know-how.
- Innovative development strategy and regulatory pathways that add value to partners.

01

- "**Jump start**" with acquired assets targeting huge unmet medical needs but less "crowded."
- Carefully position discovery assets targeting proven biology and off to fast development potential.

Execution – Project Acceleration, Termination and Globalization



Value Creation: Belumosudil China Right Sold Back to Sanofi

Kadmon

Kadmon Establishes Strategic Partnership with BioNova to Develop and Commercialize KD025 for the Treatment of GVHD in China

NEW YORK November 7, 2019 – Kadmon Holdings, Inc. (NYSE: KDMN) today announced a strategic partnership with BioNova Pharmaceuticals Ltd. (BioNova) to form a joint venture to exclusively develop and commercialize KD025 for the treatment of graft-versus-host disease (GVHD) in the People's Republic of China.

Kadmon

U.S. FDA Grants Full Approval of REZUROCK(TM) (belumosudil) for the Treatment of Patients with Chronic Graft-Versus-Host Disease (cGVHD)

July 16, 2021

- REZUROCK is approved for the treatment of adult and pediatric patients 12 years and older with cGVHD after failure of at least two prior lines of systemic therapy -

Kadmon

Sanofi To Acquire Kadmon To Further Strengthen Growth of Transplant Business

September 8, 2021

SANOFI Kadmon

国家药品监督管理局

药品注册证书

受理号：JXHS2101080国　　证书编号：2023S01213

药品名称	药品通用名称：甲磺酸贝舒地尔片 英文名/拉丁名：Belumosudil Mesylate Tablets		
商品名称	中文：乐舒克 英文：----		
主要成份	甲磺酸贝舒地尔		
剂　　型	片剂	申请事项	药品注册(境外生产)
规　　格	0.2 g（按$C_{36}H_{32}N_6O_3$计）	注册分类	化学药品5.1类
药品注册标准编号	JX20230089	药品有效期	24个月
包装规格	30片/瓶	处方药/非处方药	处方药
审批结论	根据《中华人民共和国药品管理法》及有关规定，经审查，本品符合药品注册的有关要求，批准注册，发给药品注册证书。质量标准、说明书、标签及生产工艺照所附执行。药品生产企业应当符合药品生产质量管理规范要求方可生产销售。 严格执行上市后风险管理计划，按承诺完成中国青少年cGVHD人群的上市后研究，建议申请人进一步完善上市后研究方案以及临床试验风险控制计划，保证受试者安全。于首次药注期时提交临床试验总结报告，待完成KD025-213研究20例青少年cGVHD患者的随访分析后，及时将相关数据递交至药审中心。 待BN101-201研究完成后，及时递交临床试验总结报告。		
上市许可持有人	中文名称：---- 英文名称：Kadmon Pharmaceuticals, LLC 地　　址：55 Corporate Drive, Bridgewater, NJ 08807 United States of America		
生产企业	中文名称：---- 英文名称：UPM Pharmaceuticals, Inc. 地　　址：501 Fifth Street, Bristol, TN 37620 United States of America		
药品批准文号	国药准字HJ20230095	药品批准文号有效期	至2028年07月31日
附　　件	生产工艺信息表,质量标准,说明书,标签		
主　　送	烨辉医药科技（上海）有限公司		
抄　　送	中国食品药品检定研究院，国家药典委员会，国家药品监督管理局药品审评中心，国家药品监督管理局食品药品审核查验中心，国家药品监督管理局信息中心，国家药品监督管理局药品监督管理司。生产工艺信息表仅送注册申请人(主送单位)。		
备　　注	申请人应按照《药品标准物质原料申报备案办法》向其他批准标准物质原料以及有关物质的研究资料。		

药品注册专用章
2023年08月01日

国家药品监督管理局电子证照　https://zwfw.nmpa.gov.cn　2023-08-03 09:14:04:004

Innovation - In-house Discovery and Co-development Strategy

Fully utilize **BioNova knowledge and strength in hem/onc.** to build up in-house pipeline with synergistic potential for diseases with clear UMN;

Leverage innovative technologies from partners to maintain competitive advantage while reducing investments and risks.

In-house

- **"Home Grown" assets:**
  - Focusing on targets with clear mechanism and potential for quick registration;
  - Leveraging in-house expertise and deep understanding of the landscape;
  - Highly selective and cost-effective projects with clear criteria for early killing.

Co-development

- **Co-development** with master brains to own cutting-edge technologies:
  - Leveraging innovative technologies from global partners;
  - Cost-sharing approach to reduce investments and risks;
  - Maintaining decision power and options for more upside.

II. Product Pipeline

Pipeline Build-up Discipline

Clinically meaningful

- **Unmet medical need**
  - Disease areas where no standard care / effective therapy exists
- **High probability of development success**
  - No control or placebo control due to current SoC
- **Straightforward regulatory pathway**
  - Accelerated regulatory pathway with potential for conditional approval

Early signal for development decisions

- **Validated biological targets** with clinical evidence by drugs in the same class, or validated biologic targets with early clinical data
- **Early clinical data** in target population for go/no go decision

Competitive advantage

- **Less "crowded"** or with clear competitive advantage
- MoA or clinical development strategies for **product differentiations**

Cost-effective

- Lock up terms when **proof of mechanism or presence** is shown
- **PoC data** when commercial outlook can be justified

Current Pipeline

Product Candidate	Target	Indication	Discovery	IND Enabling	Phase 1	Phase 2	Phase 3	Commercial Rights
In-licensed pipeline								
BN301 (ADC)	CD74	NHL, AML, MM						China
In-house R&D pipeline								
BN104	Menin	AML, ALL						WW
BN105	PRMT5	Solid Tumors						WW

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BN104

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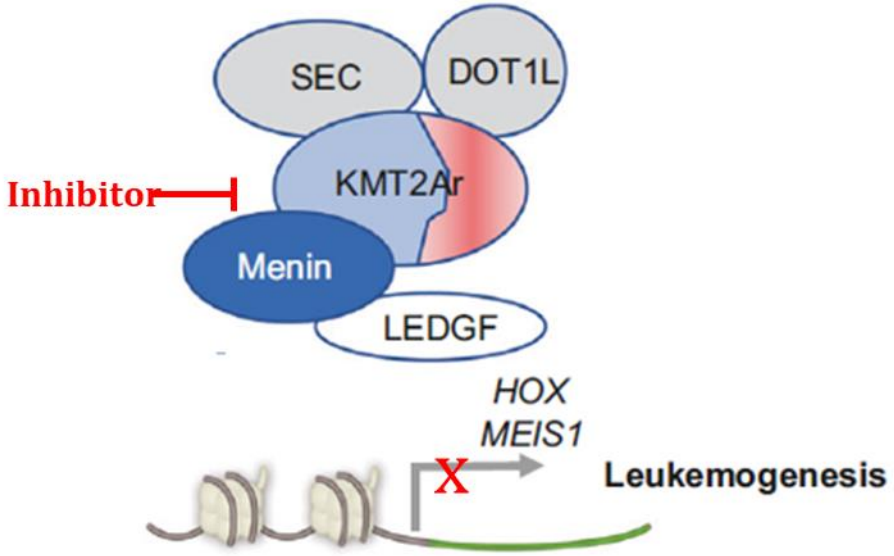
BN104 - Menin Fusion: A Validated Target for Both MLLr (KMT2Ar) and NPM1 Mutant

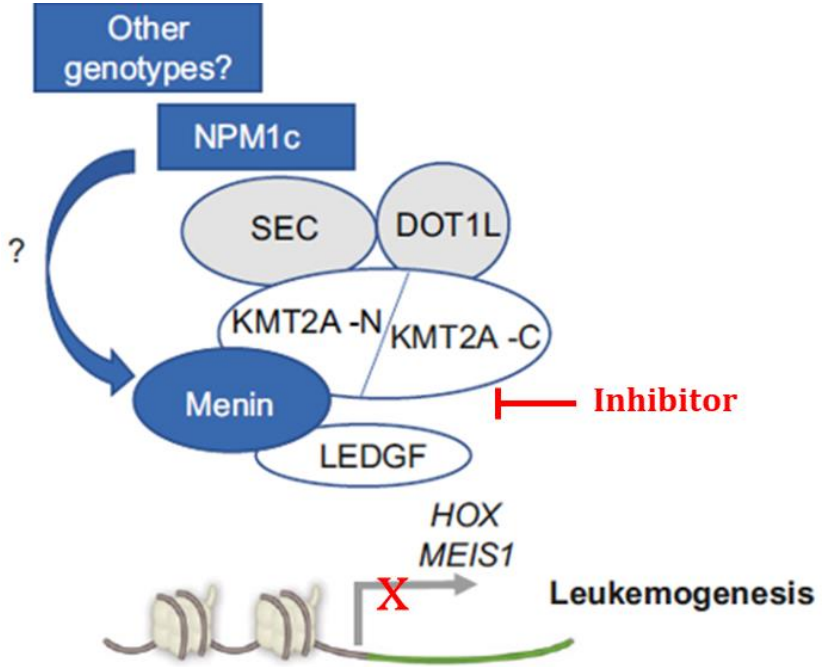
MLLr acute leukemias

- Annual global incidence 5,000-7,000
- 4-10% AML
- 10-15% ALL (80% of infant ALL)
- 15% therapy-related AML (70% for topo II)
- 5-year OS for adult MLLr <25%



NPM1c AML

- Annual global incidence ~20,000
- 20-30% AML
- 5-year OS for adult NPM1c 50%



Issa et al., Leukemia, 2021, 35, 2482–2495 ; Dohner, H. et al. Blood, 2017, 129(4), 24-447; Falini, B. et al. Blood, 2011, 117(4), 1109-1120;

BN104 – A Potential Best-in-Class Menin Inhibitor

Abstract #3943

Discovery of A Novel Menin-MLL Inhibitor for Potential Treatment of MLLr Leukemias and NPM1c AML

Taishan Hu[1*], Zhilin Deng[1], Honghai Li[2], Xiaochu Ma[2], Quanrong Shen[2], Lei Zhang[2], Peihua Sun[2], Ye Hua[1], and Bryan Huang[1*]
[1] BioNova Pharmaceuticals (Shanghai) Limited, Shanghai, China, [2]PharmaResources (Shanghai) Co., Ltd., Shanghai, China, *Corresponding authors:
taishan.hu@bionovapharma.com, bryan.huang@bionovapharma.com

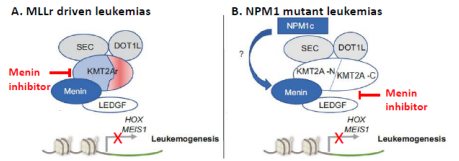
Abstract

Patients with MLL rearranged (MLLr) acute leukemias often have poor prognosis, and there is no targeted therapies available for this subtype of leukemias. The protein protein interaction (PPI) between MLLr and menin is critical for the pathogenesis of MLLr-driven leukemias. And it has been well demonstrated in both preclinic and clinic that blockade of this PPI could have therapeutic implications in the treatment of menin-MLL dependent leukemias.
Herein we report the discovery of BNM-1192, a small molecule menin inhibitor. BNM-1192 is a potent and highly selective menin inhibitor with optimized drug-like properties and showed excellent efficacy in MV4-11 xenograft mouse model. Furthermore, BNM-1192 has low risk in QTc prolongation given the fact it is an extremely weak hERG inhibitor with IC_{50} of greater than 100 μM. it also demonstrated favorable toxicological profile in preliminary tox studies .

Background

Rearrangement of the mixed lineage leukemia (MLL, also known as MLL1 or KMT2A) gene occurs in about 10% of acute leukemias, and is particularly prevalent in infant acute leukemias, accounting for up to ~70% of infant acute lymphocytic leukemia (ALL) cases. More than 80 partner genes are implicated in MLL fusions, and six main partner genes make up about 80% of cases, which include AF4, AF6, AF9, AF10, ENL and ELL. MLL fusion proteins enhance proliferation and block hematopoietic differentiation, ultimately driving the development of leukemia by dysregulation of the HOXA and MEIS1 genes. MLLr leukemia is one of the high-risk types of leukemia with aggressive nature, resistance to therapy, and high frequency of early relapse, and with a 5-year survival rate of only approximately 35%.

The interaction between menin and MLLr is critical to the pathogenesis of MLLr-driven leukemias. Recent studies also revealed the importance of the menin-MLL1 wild-type (wt) interaction in NPM1 mutant AML. And blocking the menin-MLL interaction has proved to be a viable therapeutic strategy for the treatment of MLLr associated acute leukemias and NMP1 mutant AML.



Adapted from Issa, G. C. et al., Leukemia, 2021, 35, 2482

BNM-1192 is a potent and selective menin inhibitor

Figure 1. left, Menin-MLL peptide cocrystal (PDB 4GQ6). Menin shown as ribbon in cyan, and MLL peptide as sticks in magenta. Right, docking pose of BNM-1192 binding to menin. BNM-1192 binds to the same menin pocket as MLL N-terminal peptide. And a hydrogen bond formed directly between small molecule and Glu363 of menin was revealed.

Table 1. Antiproliferative activities against leukemia cell lines.

	Cell lines	BNM-1192	SNDX-5613
IC_{50} (nM)	MV-4-11 (AF4 fusion)	3.5±1.2 (n=8)	9.2±3.0 (n=7)
	MOLM13 (AF9 fusion)	12	26
	OCI-AML3 (NPM1 mutant)	11	75
	HL-60 (MLL wild type)	>10000	~8000

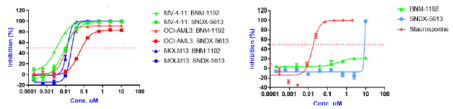


Figure 2. Dose response curve. Left, targeted cell lines; right, HL-60, control cell line.

- BNM-1192 is very potent against leukemia cell lines with MLL-fusion protein and NPM1 mutant.
- ~1000-fold selectivity over control cell line, HL-60, observed.

BNM-1192 leads to menin protein degradation

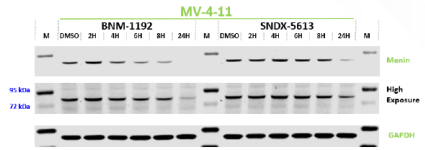


Figure 3. Western blot to determine menin protein. MV-4-11 cells were treated with BNM-1192 and SNDX-5613 at 10 μM for 2, 4, 6, 8, 24 hours, respectively, with DMSO as the control. Transfer: iBlot P0-9min; Sample: cell lysate; Total Protein: 30ug (BCA) 4-12% BT Gel & MOPS; M: Marker (Beyotime# P0069)

BNM-1192 demonstrated decent PK properties

Table 2. Cross-species PK

PK parameters	Mouse	Rat	Dog
CL (mL/min/kg)[a]	64	90	22
$t_{1/2}$ (h)[a]	1.6	2.4	3.9
Vss (L/kg)[a]	4.5	13	3.8
AUC_{0-24} (ng*h/mL)[b]	1272	272	6186
F (%)[b]	50	16 (175[c])	79

[a] iv 1mg/kg; [b] po 10 mg/kg; [c] po 100 mg/kg;

- Good to excellent bioavailability in mouse and dog; improved exposure at higher dose for rat.

BNM-1192 showed excellent efficacy in MV-4-11 xenograft mouse model

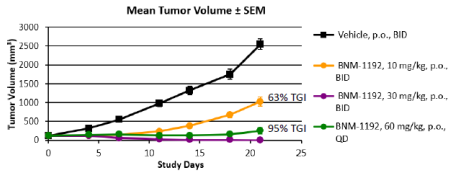


Figure 4. MV-4-11 xenograft mouse model. Mice were administered orally either vehicle or compound for 21 days dosed QD or BID as indicated.

Table 3. PK of mice with tumor burden

Dose (mg/kg)	C_{max} (ng/mL)	C_{8h} (ng/mL)	AUC_{0-24} (ng.hr/mL)
10	68	7.2	250
30	564	43	1680
60	1575	154	7166

- BNM-1192 showed dose-dependent efficacy
- BNM-1192 at 30 mg/kg BID resulted in tumor regression
- BNM-1192 at 60 mg/kg QD also showed good tumor inhibition (95%).
- Duration of coverage above IC_{50} (IC_{90}) seems more important than exposure for efficacy

BNM-1192 has low risk in QTc prolongation

Table 4. *In vitro* Early safety data

	BNM-1192	SNDX-5613
hERG (IC_{50}, μM)	>100	9.6
Mini Ames (TA98/TA100/TA1535/TA1537; WP2 uvrA (pKM 101)	Negative	ND

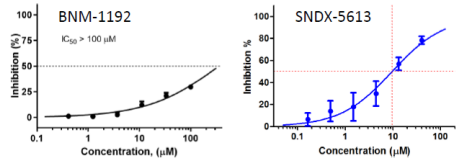


Figure 5. Concentration-dependent blockade of hERG channel. Left, BNM-1192; right, SNDX-5613.

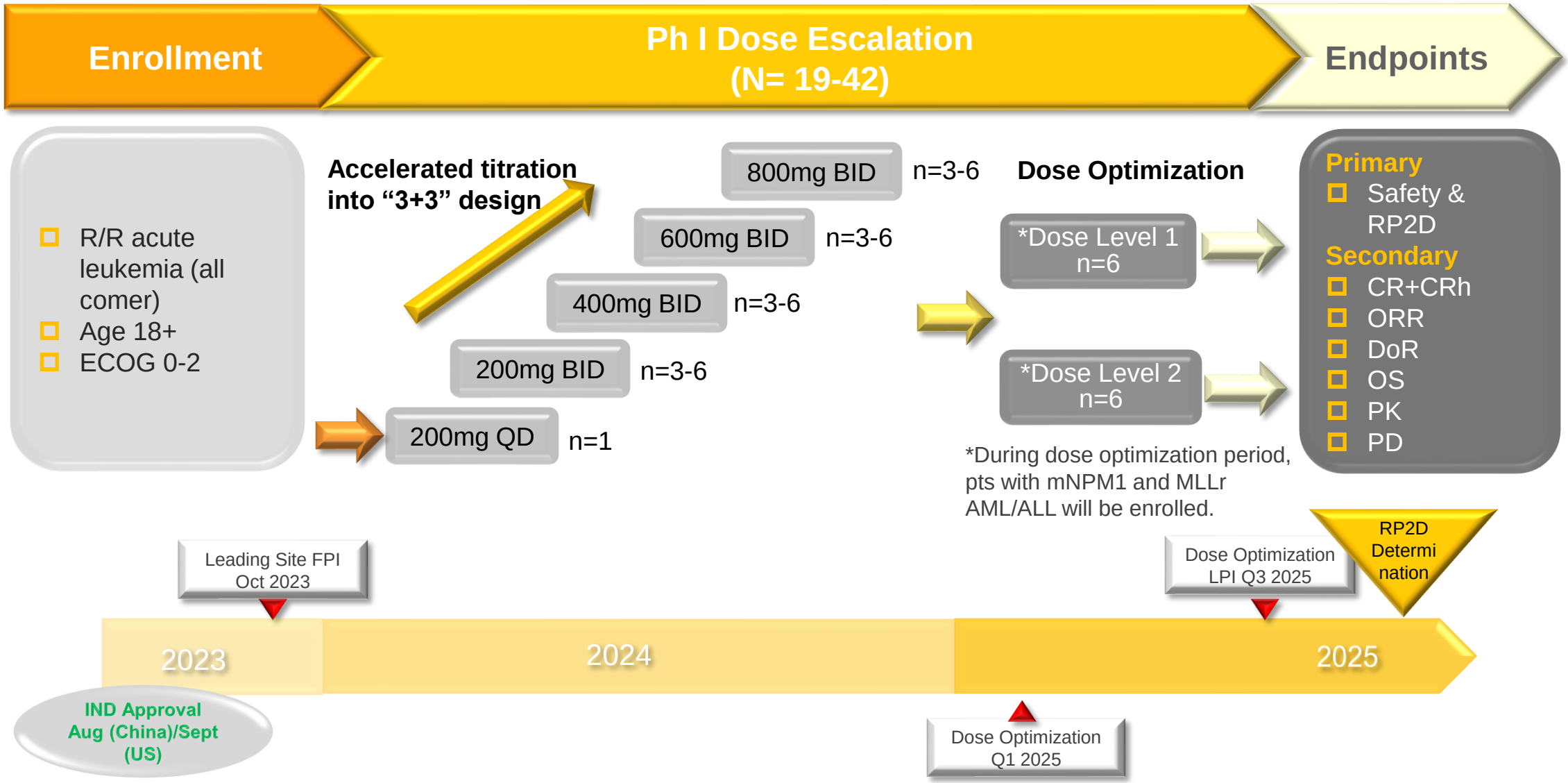
BNM-1192 showed favorable tox profile

- A 7-day preliminary tox studies in rat was done
- No significant findings
- The high dose, 1000 mg/kg, identified as the HNSTD
- >500-fold safety margin based on exposure (AUC)

Conclusions

- ☐ BNM-1192 is a low nanomolar menin inhibitor. As high as 1000-fold selectivity was observed for targeted cell lines over mechanistically irrelevant cell line.
- ☐ BNM-1192 resulted in tumor regression at 30 mg/kg, BID in MV-4-11 xenograft mouse model. And QD dosing is a promising alternative dosing regimen.
- ☐ BNM-1192 is an extremely weak hERG inhibitor, indicating very low potential in QTc prolongation.
- ☐ BNM-1192 demonstrated favorable profile in early safety and toxicology.
- ☐ IND-enabling studies of BNM-1192 is ongoing, and Phase 1 study is expected in early 2023.

BN104 China Phase 1 Dose Escalation Trial



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BN301

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BN301 - Potential First-in-Class ADC for Patients with NHL and MM

CD74 Expression in cancers

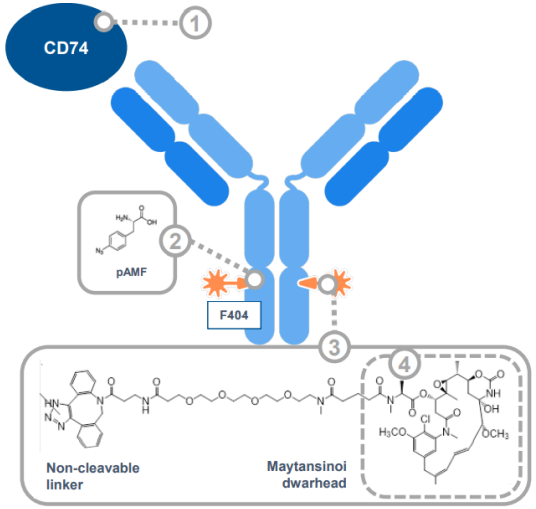
- CD74 is expressed in ~90% of B-cell cancers including myeloma and lymphoma
- CD74 also is expressed in nonhematopoietic cancers, such as gastric, renal, urinary bladder, non–small cell lung cancers, certain sarcomas, and glioblastoma

BN301:Potential First-in-Class CD74 Targeting ADC

- BN301/STRO-001 is a homogeneous antibody drug conjugate (ADC) with a drug-antibody ratio (DAR) of 2, targeting CD74:
  - CD74 is expressed in many hematological cancers and rapidly internalized
  - Conjugation through precisely positioned non-natural amino acids p-azidomethyl-L-phenylalanine, at positions F404 on the heavy chain
  - Comprises two non-cleavable linker-warheads that are **stable in circulation**
  - The active warhead, maytansinoid derivative, efficiently kills tumor cells following internalization of the ADC and was designed to **minimize bystander effects**

Frequent CD74 Expression in Multiple B-cell NHL Subtypes by IHC

	CD74 positive	%
B cell lymphoma – total samples	404/423	96
Follicular lymphoma	148/151	98
Grade 1 and 2	90/91	99
Grade 3 A and B	58/60	97
Diffuse large B-cell lymphoma	135/140	96
Extranodal marginal zone lymphoma	22/24	92
Splenic marginal zone lymphoma	4/5	80
Nodal marginal zone lymphoma	6/6	100
Mantle cell lymphoma	19/21	90
SLL/CLL	36/36	100
Lymphoplasmacytic lymphoma	5/5	100

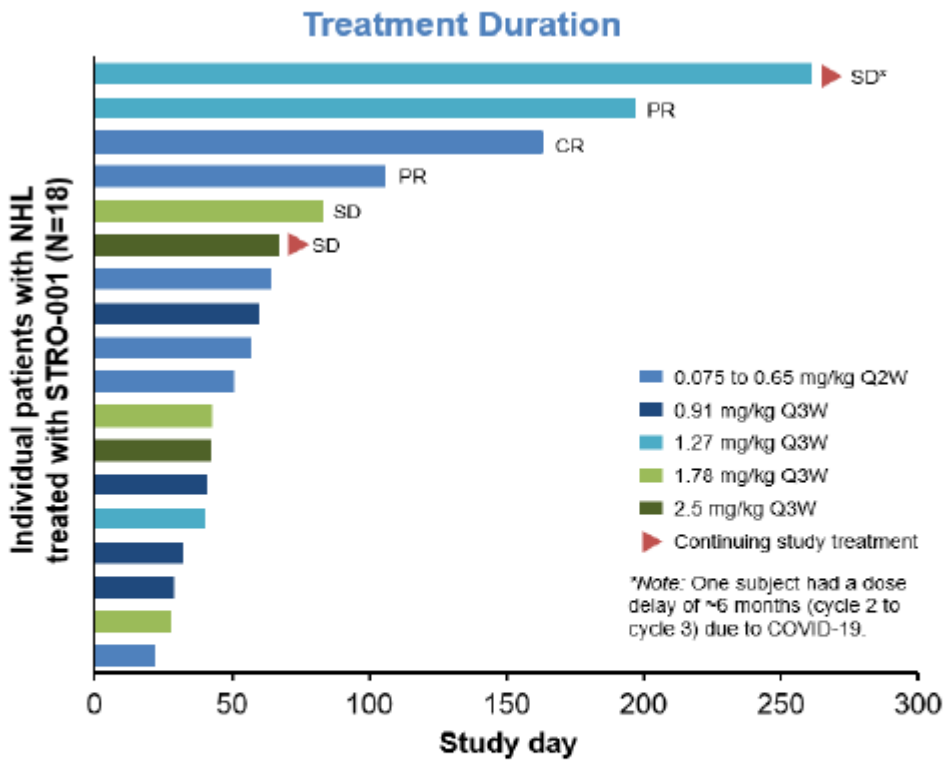


Competitive landscape

Owner	Immunomedics Gilead Sciences	Sutro Biopharma
Product	Milatuzumab	STRO-001
Status	Phase II	Phase I
Indication	GvHD, CLL, MM, NHL, SLE	Lymphomas, MM

3030 Preliminary Results of an Ongoing Phase 1 Dose Escalation Study of the Novel Anti-CD74 Antibody Drug Conjugate (ADC), STRO-001, in Patients with B-Cell Non-Hodgkin Lymphoma

626. Aggressive Lymphoma (Diffuse Large B-Cell and Other Aggressive B-Cell Non-Hodgkin Lymphomas)—Results from Prospective Clinical Trials *Poster Session III on Monday, December 7, 2020, 7:00 AM-3:00 PM PT*

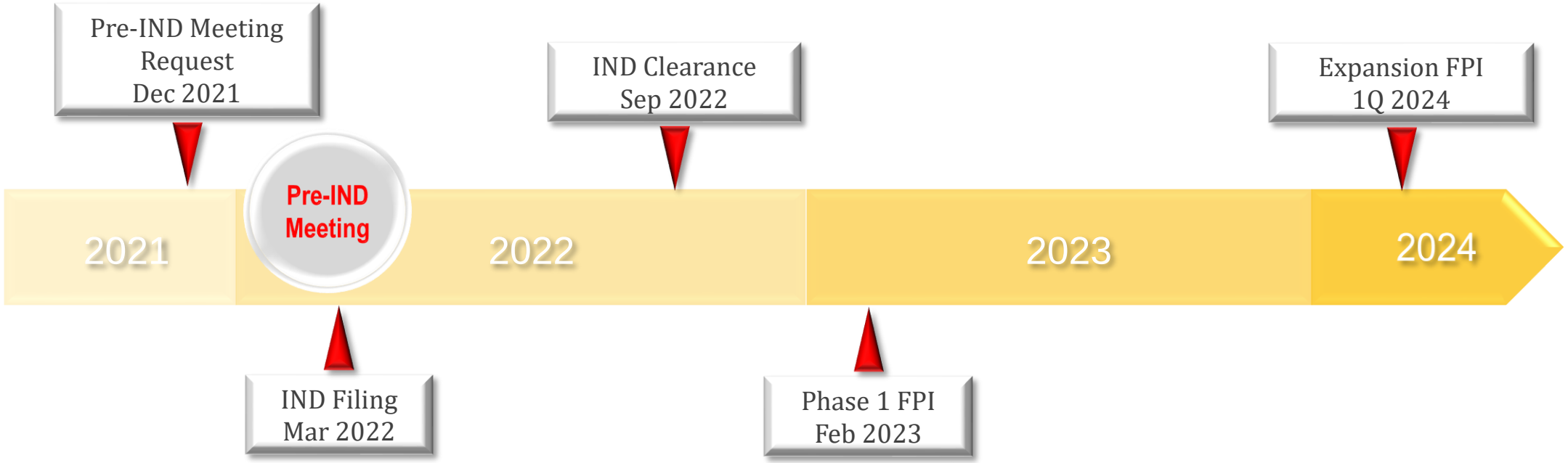


- STRO-001 was generally well tolerated, most AEs were Grade 1 & 2
- No ocular toxicity signals have been observed
- Median number of prior therapies is 4 (range 1-12)
- MTD has not been reached; next planned dose level is 3.5 mg/kg
- Preliminary anti-tumor activity has been observed in this heavily pre-treated patient population, including two DLBCL patients who had previously progressed after CAR-T

Dose level, mg/kg	Demographics and diagnosis	Prior Therapies	Best Response	Doses received	Duration of Treatment
0.075	82-year-old man with Stage III DLBCL, non-GC type diagnosed in 2015	- R-CHOP-R, - Rituximab/lenalidomide - Bendamustine/rituximab - Obinituzumab + gemcitabine + oxaliplatin	CR after 2 cycles (4 doses)	12	24 weeks (PD after 12 doses)
0.65	64-year old man diagnosed with double-hit Stage IV DLBCL in August 2017	- R-CHOP x 1 and EPOCH x 6 (2017) - RICE with IT prophylaxis (2017/2018) - Rituximab and XRT (2018) - Rituximab, gemcitabine + oxaliplatin with radiotherapy (2018) - Axicabtagene ciloleucel (CAR-T) (May 2018) - Rituximab and lenalidomide (Nov 2018)	PR at cycle 3	8	15 weeks (PD after 8 doses)
1.27	68-year old woman stage IV extranodal DLBCL, non-GC diagnosed in Feb 2018	- R-CHOP - RICE x 2 - DHAP x 2 - CAR-T (May 2019) - Lenalidomide (Nov 2019)	PR at cycle 3	10	27 weeks (PD at cycle 10)
1.27	51-year old woman, stage III marginal zone lymphoma diagnosed in May 2017	-Obinutuzumab	SD	10	45 Weeks Ongoing (Cycle 15)
1.78	36-year old man with stage IIIA follicular lymphoma diagnosed in June 2014	- Flt3L-vaccine immunotherapy - Rituximab - Pneumococcal conjugate vaccine immunotherapy - polyICLC (TLR-3 agonist) – immunotherapy - Pembrolizumab	SD	4	12 weeks (PD after Cycle 4)
2.50	74 year old man with stage IV follicular lymphoma	-Reituximab/fludarabine/Cytoxan -Ifosfamide/carboplatin, etoposide -Auto SCT	SD	8	24 weeks (PD after Cycle 8)

Shah et al., Blood ASH Online Journal 2020 (https://doi.org/10.1182/blood-2020-139829)

BN301 China Development Timeline



BioNova Company Highlights

- BioNova is a clinical-stage biotech company with **global vision and execution**.
- The company applies industry leading **innovative strategies** in every aspect of drug development.
- Extremely **capital efficient** with a laser focus on valuation-creation.

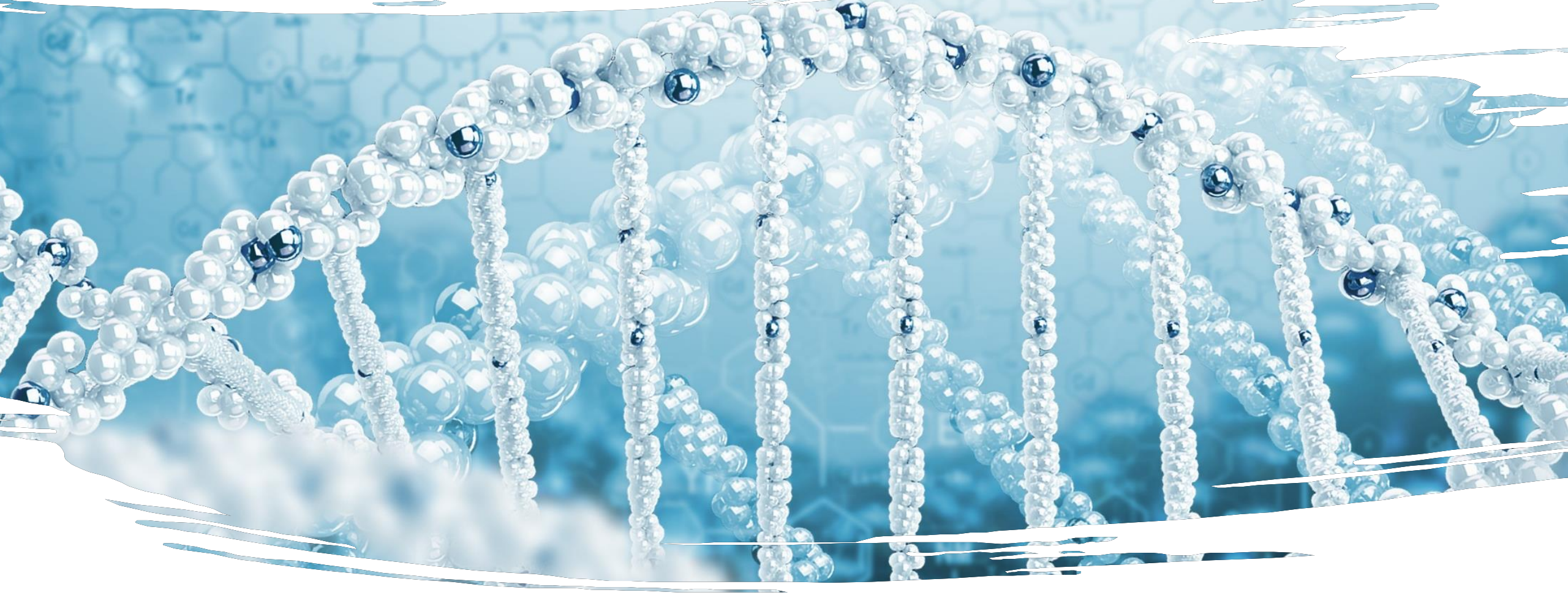
- **Experienced Founding Team** with deep understanding of development and regulatory strategy, as well as global insight to maximize the product value;
- **Proven Execution Excellence** in product development and successful track records in corporate management.

- **In-house Cross-functional Discovery Team** with highly selective and cost-effective principles and disciplines, supporting and driving a differentiated discovery and co-development strategy;
- **Innovative Pipelines** positioning products with competitive advantage in disease areas with high unmet clinical need and expedited regulatory pathway.

- Clear company growth plan to **go from China to worldwide;**
- **US Team Expansion in 2022** to strengthen drug discovery capability with a highly efficient US team;
- **Global Partnership** after clinical PoC to unlock the value of proprietary assets for global markets.

- **Strong Endorsement by Top Tier Life Science VC Funds**, supporting the robust expansion of the company.

Hillhouse Capital · 博远资本 BioTrack Capital · OrbiMed Healthcare Fund Management · Lilly Asia Ventures 礼来亚洲基金 · 泰福资本 TF Capital · 银杉泰资本 Rencent Capital · 榄联健康基金 YUNION Healthcare Ventures · 翰颐资本 HANNE CAPITAL · 金浦健康基金 Healthcare Capital · Med-Fine Capital 幂方资本 · MITSUI GLOBAL INVESTMENT



Thank You

BioNova Pharma 烨辉医药