BioNova Introduction

Pharma 烨辉医药 March 2022

I. Company Overview

BioNova Company History

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
- Throughout the year.
  Multiple licensing deals and fully owned programs expected

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.

Execution - Robust Pipeline Progress in 3 Years, with Promising Expected Milestones

2018 | 2019 | 2020 | 2021 | 2022 | 2023

Incubation/ Start-up operation

Pipeline Expansion

Clinical Delivery & Globalization

3 Assets

- **1** NDA-ready
- **2** Phase I

1 Asset

- **1** Discovery stage with WW rights

2020

Expected milestones by 2023

- **1** marketed product
- **2-3** Phase 2/registration trials
- **2-3** Phase 1 trials
- **Multiple** pre-clinical assets

2023

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.

Globalization - Overview and Development Plan

Growing into a Global Biopharma

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.

III. Product Pipeline

Pipeline Build-up Strategy

Clinically Meaningful

- **Unmet medical need**
  Disease areas where no standard care / effective therapy exists
- **High probability of development success**
  Surrogate endpoint with 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 early clinical data supporting MoA, or clinically validated targets with differentiated molecular features to become best-in-class
- **Early clinical data** in target population for go/no-go decision

Competitive Advantage

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

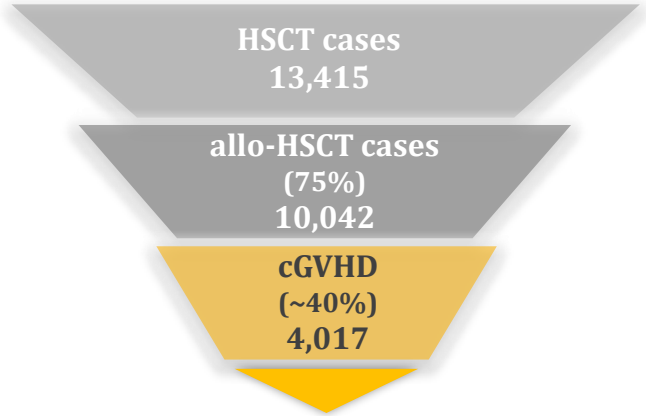
Current Pipeline

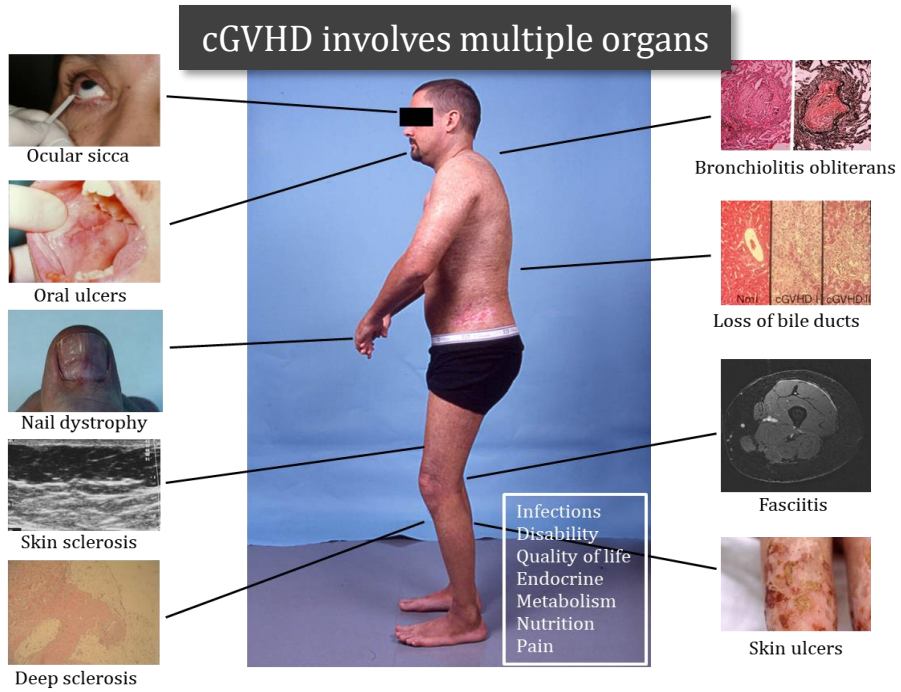
Product Candidate	Target	Indication	Discovery	IND Enabling	Phase 1	Phase 2	Phase 3	Commercial Rights
In-licensed pipeline								
BN101	ROCK2	cGVHD				NDA		China
BN102	BTK (reversible)	CLL/SLL, MCL, WM, MZL						China
BN301 (ADC)	CD74	NHL, AML, MM						China
In-house R&D pipeline								
BN104	Non disclosure	AML	PCC					WW

Chronic GVHD (cGVHD)

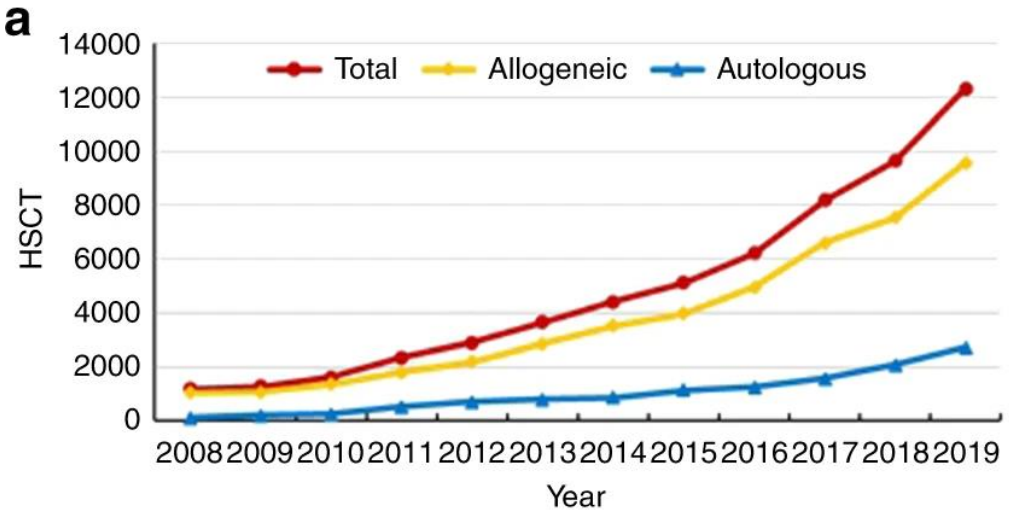
- **Graft-versus-host disease (GvHD)** is the common complication following allogenic hematopoietic stem cell transplantation (allo-HSCT) which is the most desirable therapy of curative potential for leukemia and lymphoma patients. It is a systemic disorder that occurs when the graft's immune cells recognize the host as foreign and attack the recipient's body cells, leading to inflammation and fibrosis in multiple tissues.
- **Chronic GVHD (cGVHD)** with a high incidence of 30%-70% in GvHD, is the major cause of late non-relapse death after HSCT. cGvHD may manifest simultaneously from acute GvHD (aGVHD), develop after the treatment of aGvHD, or may occur *de novo*. Classical cGvHD occurs 100 days after transplantation but may also overlap with aGvHD.

- **Estimated 2020 cGVHD incidence in China**





- **HSCT trend in China during 2008–2019**

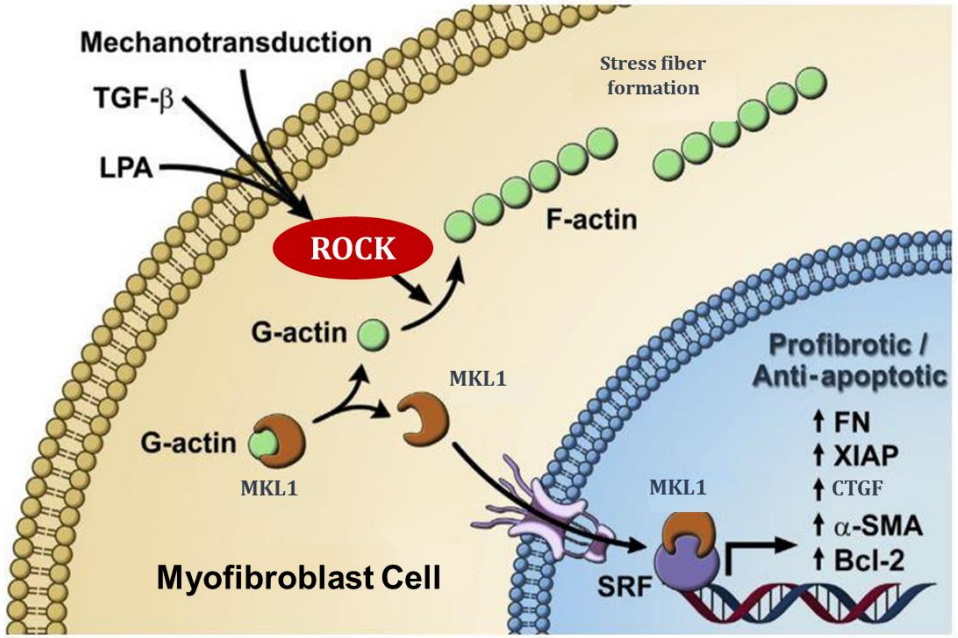


Hematopoietic stem cell transplantation activity in China 2019: a report from the Chinese Blood and Marrow Transplantation Registry Group

BN101: A FIC Selective ROCK2 Inhibitor for cGVHD

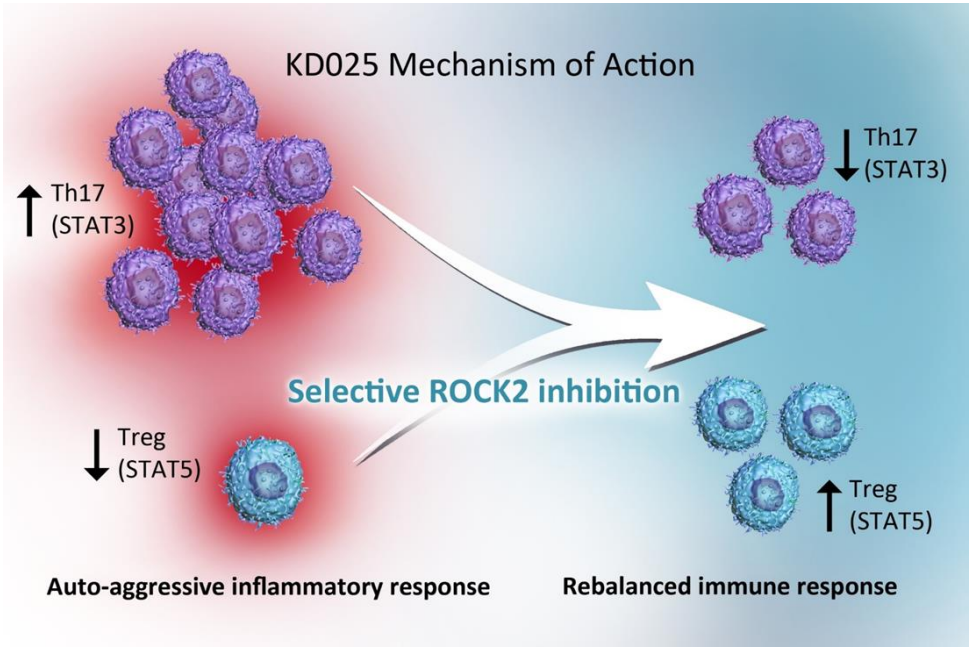
ROCK: an Intracellular Integrator of Pro-fibrotic Signal

- ROCK regulates multiple profibrotic processes, including myofibroblast activation
  - ROCK is downstream of major pro-fibrotic mediators
  - ROCK regulates fibroblast differentiation to myofibroblasts, a pathological cell type in fibrosis
  - ROCK mediates stress fiber formation
  - ROCK regulates transcription of pro-fibrotic genes



BN101/KD025: A FIC Selective ROCK2 Inhibitor

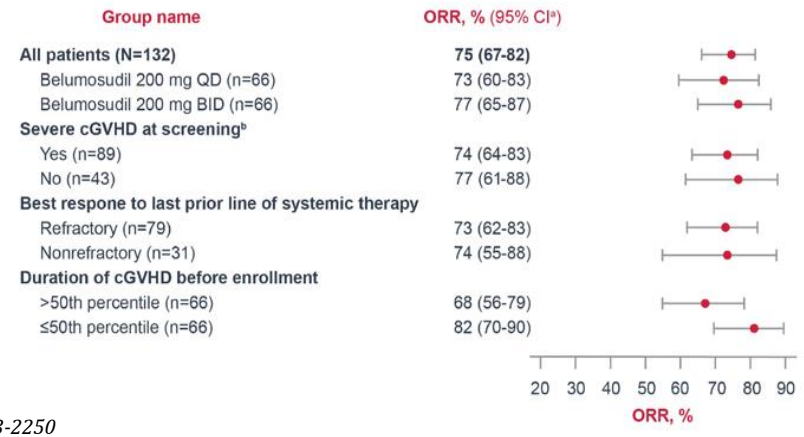
- ROCK2 inhibition downregulates pro-inflammatory Th17 responses and increases Treg function
  - Reduces STAT3 phosphorylation
  - Increases STAT5 phosphorylation
- ROCK2 inhibition re-establishes immune homeostasis

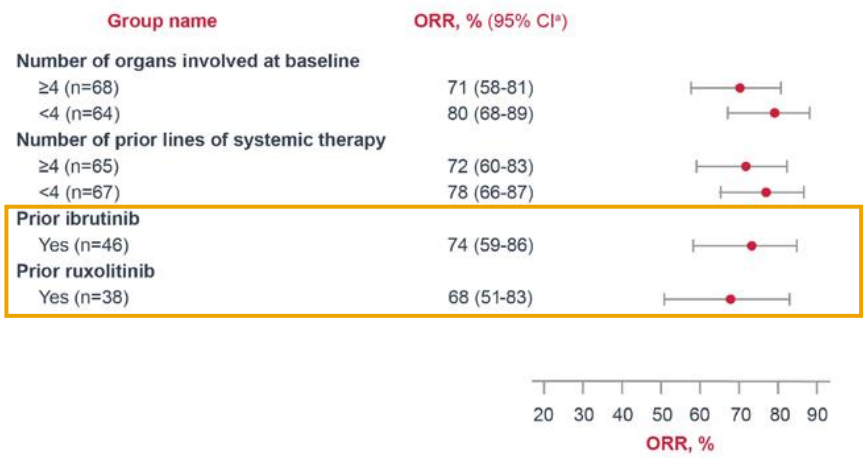


BN101: Superior Product Profile for cGVHD

		KD025[1]	Ibrutimib[2*]	Ruxolitinib[3*]
Dosing		QD	QD	BID
Indication		cGVHD 3L+	cGVHD 2L+	aGVHD 2L+
Efficacy (ORR/CR)		73%	67%	76.4%
Key Patient Characteristics	Median prior line	3	2	< 2 lines
	>=4 organ involved	50%	7% (72% <= 2)	NA
	Moderate/severe cGVHD	27%/70%	52%/40%	40.6%/58.8%
Serious AEs (Gr 3/4 >=5%)	Infection	8%	36% (1 grade 5)	19.4%
	Anemia	0%	2%	12.7%
	Thrombocytopenia	0%	0%	15.2%
	Neutropenia	0%	0%	8.5%
	Hypertension	6%	0%	4.8%
	Atrial fibrillation		2%	

High response rate of BN101
regardless of prior treatment with ibrutinib or ruxolitinib





1. *ASH 2020*
2. *Miklos D. et al. BLOOD, 23 November 2017: 130(21): 2243-2250*
3. *Robert Z. et al. NEJM, 15 July 2021: 228-238*

* *Not approved for cGVHD in China*

BN101 Global Development Timeline

2015

- cGVHD IND in US

2017

- 5 Oct, Orphan Drug Designation for cGVHD

2018

- 16 Oct, FDA Breakthrough Therapy Designation

2020

- 9 Sep, IND approval in China
- 30 Sep, Rolling submission of cGVHD NDA to FDA
  - 30 Nov, NDA submission completed
- 26 Nov, Ph 1 trial in China
- 18 Dec, CDE Breakthrough Therapy Designation

2021

- Feb, China Ph1 completed
- Apr, BN101-201 clinical trial
- 16 Jul, FDA approval in US
- China NDA filed in Nov 2021

BN104 - A Potential Best-in-Class X Inhibitor (target not disclosed)

A Validated Target with High UMN

- **A novel validated target for ALL and AML mutants:**
  - Annual global incidence >5,000 in ALL mutant.
  - Annual global incidence ~20,000 in AML mutant.
  - 5-year overall survival for adults < 50%.

Advantageous Competitiveness

- **Favorable Physicochemical Properties:**
  - BN104 is smaller in size, and less greasy than the two leading clinical compounds;
  - BN104 is a weak basic compound, whereas the two clinical compounds whose structure could partially result in the adverse effects observed in nonclinical or clinical studies.
- **High Selectivity, Acceptable DMPK Properties, and Low DDI, hERG risk**
  - Selectively targeting the targeted leukemic cells;
  - Metabolically much more stable in human than the leading clinical compounds;
  - Much weaker inhibitory activity on hERG than the leading clinical compounds, potentially avoiding the hERG-related QTc prolongation in human.

Current Development Status

- Further profiling of BN104 is ongoing, and IND application is expected in Q1 2023;
- PCT application in November 2021.

BN102 - Resistance to Covalent BTK Inhibitors Creates a New High Unmet Medical Need

B-cell Malignancies

- **B-cell malignancies** include chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and B-cell non-Hodgkin's lymphoma (NHL), such as diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), follicular lymphoma (FL), marginal zone lymphoma (MZL) and lymphoplasmacytic lymphoma/Wahrenheit's macroglobulinemia (LPL/WM)
- In 2021, CLL and NHL together accounted for 5.4% of all new cancer cases in the United States and 4.1% of all cancer deaths.[1, 2]
- GLOBOCAN data shows that in 2020 there will be 92,834 new cases of NHL in China, accounting for 2.0% of all new tumor cases, and an increasing trend year by year, with 54,351 deaths, accounting for 1.8% of all tumor deaths.[3]
- In China, B-cell NHL accounts for approximately 75% of all NHL.

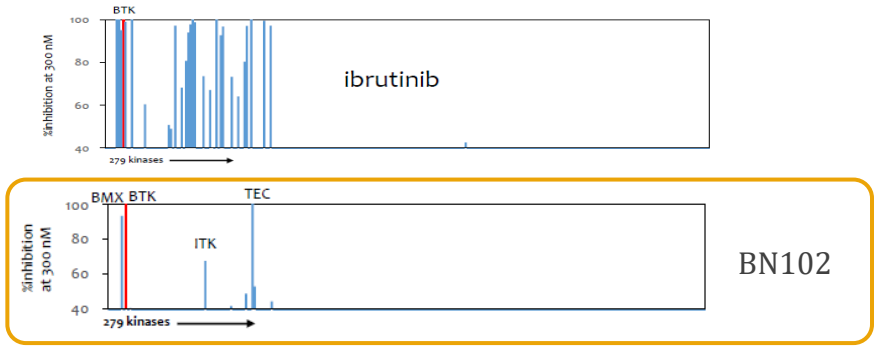
Reversible BTK Inhibitors

- **BTK (Bruton's Tyrosine Kinase)** plays a key role in B cell antigen receptor (BCR) signal transduction
  - BCR signal transduction is essential for the survival and proliferation of leukemia cells in many B-cell malignancies
- **Current therapeutics:** Covalent BTK inhibitors such as ibrutinib have been approved for the treatment of CLL/SLL, MCL, MZL and WM
  - 2020 ibrutinib global sales exceeded 10 billion USD. However, no treatment exists once patients progress on covalent BTK inhibitors
- **Next-generation, reversible BTK** inhibitors have demonstrated very promising efficacy in patients progressed on covalent BTK inhibitors. [4]

1. https://seer.cancer.gov/statfacts/html/nhl.html
2. https://seer.cancer.gov/statfacts/html/clyl.html
3. https://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf
4. ASH 2021

BN102 - A Highly Selective, Potent Reversible BTK Inhibitor

High kinase selectivity

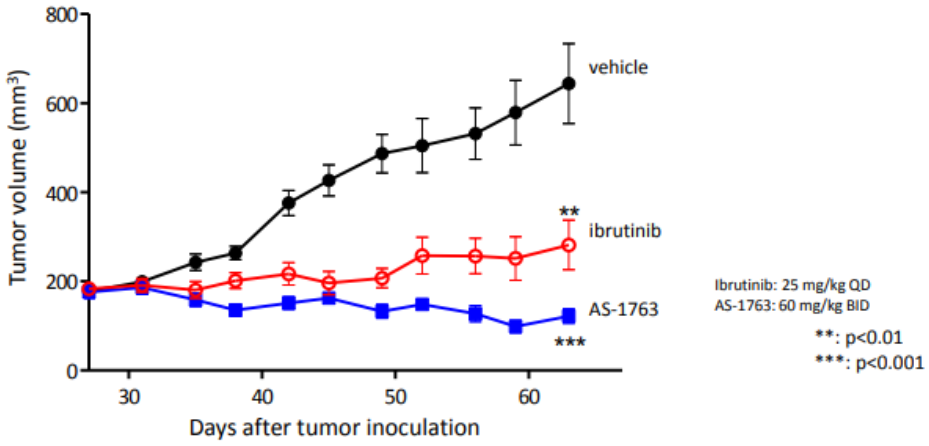


In vitro pharmacological activities of BN102

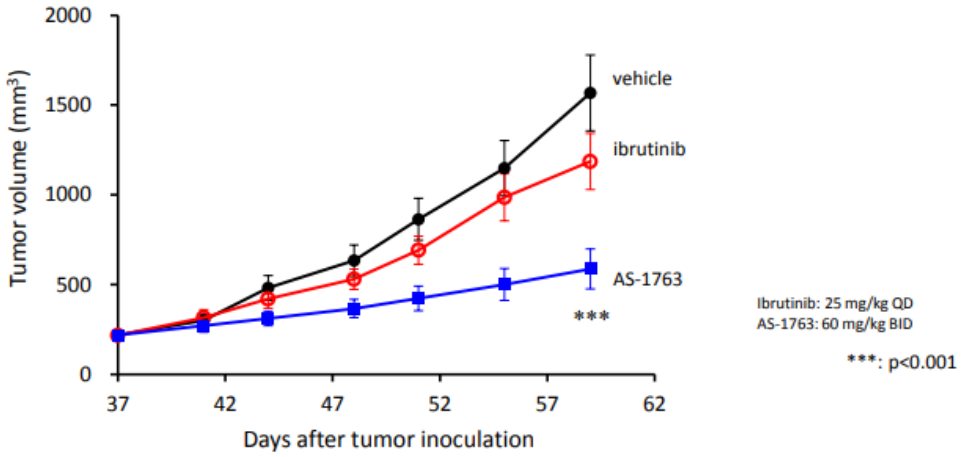
	IC50(nM)	
	BN102	ibrutinib
Autophosphorylation BTK (Ramos)	1.4	1.1
CD69 activation (Human whole blood)	11	8.1
Cancer cell growth (OCI-Ly10 cells)	1.8	0.75
Cancer cell growth (OCI-Ly10 [BTK C481S] cells)	20	1030
Normal cell growth (HEL299 cells)	6370	6870

50-fold strong activity

In vivo antitumor effects of BN102 on human B-cell non-Hodgkin lymphoma cell line, OCI-LY10 tumor xenograft mouse model (n=8-10)



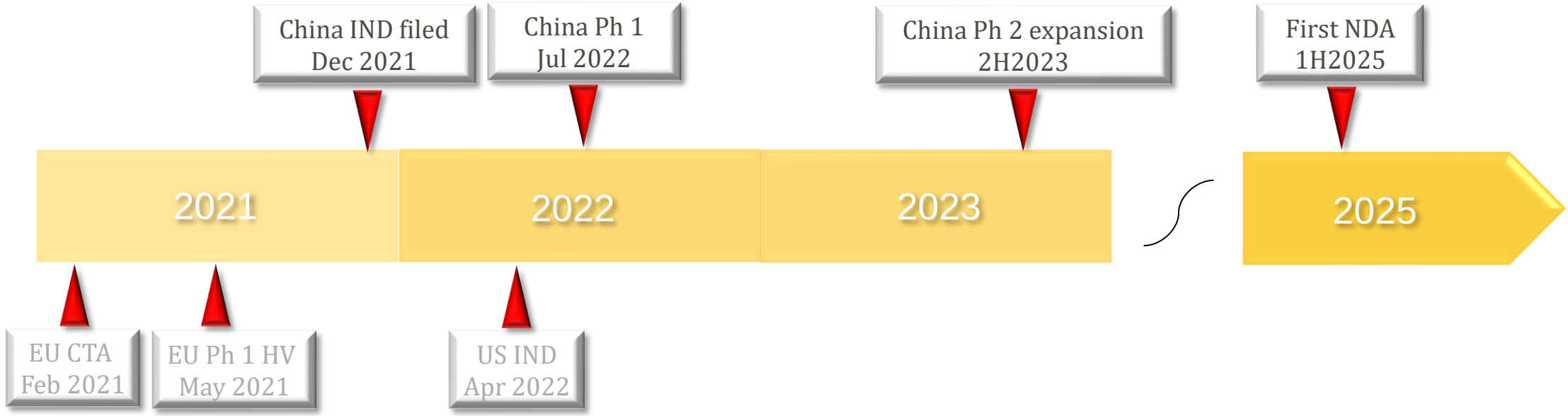
In vivo antitumor effects of BN102 on ibrutinib-resistant BTK^{C481S} knock-in OCI-LY10 tumor xenograft mouse model (n=11)



Ramos: human Burkitt lymphoma cell line
OCI-Ly10: human B-cell non-Hodgkin lymphoma cell line
OCI-Ly10 [BTK C481S]: BTK[C481S] knock-in OCI-Ly10 cells
HEL299: human embryo lung cell line

J Med Chem. 2021 Oct 14;64(19):14129-14141.

BN102 China Development Timeline



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

CD74 Expression in cancers

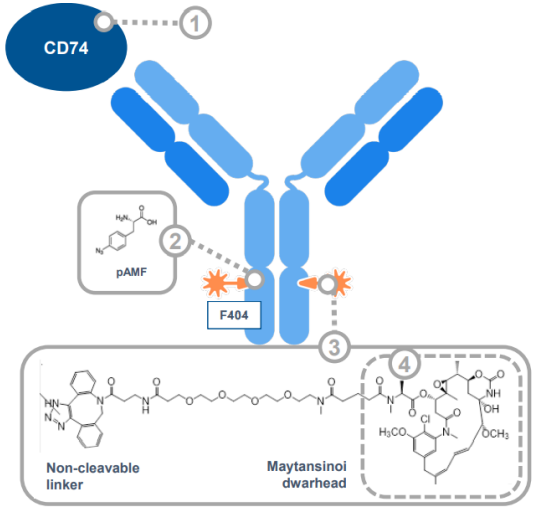
- CD74 is expressed in ~90% of B-cell cancers including myeloma and lymphoma
- CD74 also is expressed in nonhematopoietic cancers, such as gastric, renal, urinary bladder, non–small cell lung cancers, certain sarcomas, and glioblastoma

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

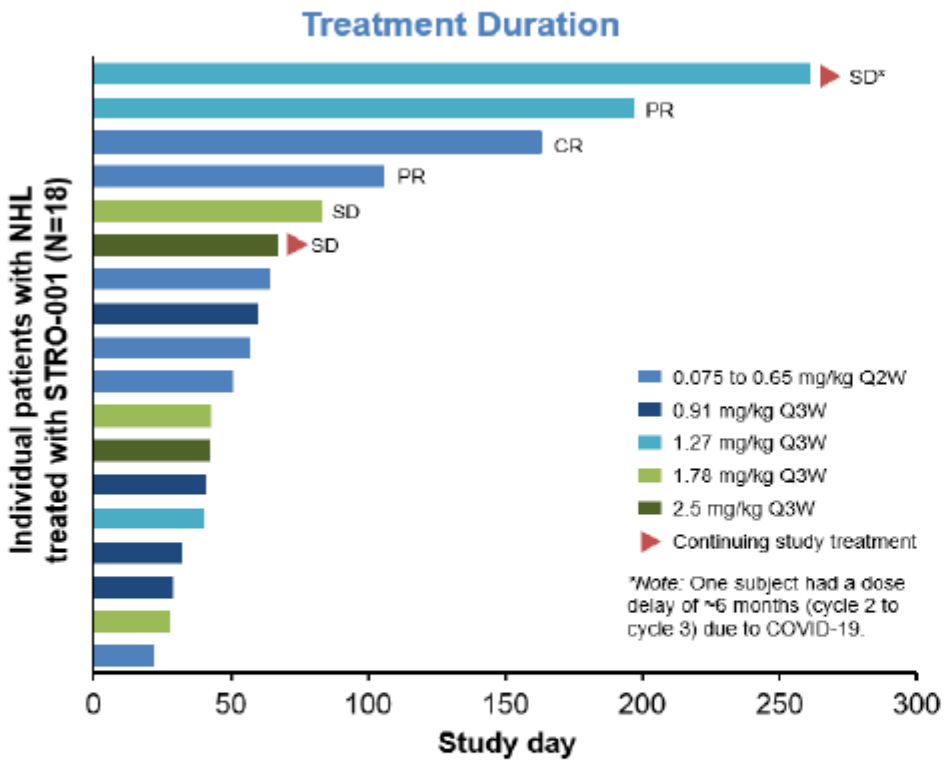


Competitive landscape

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*

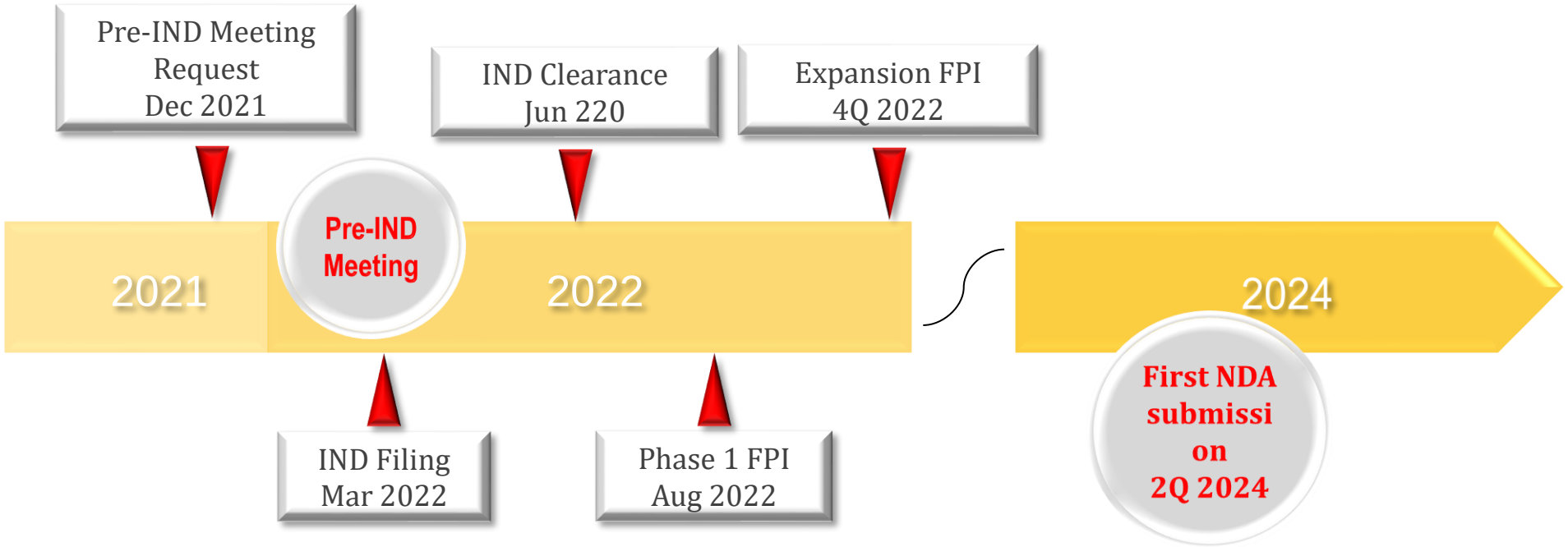


- STRO-001 was generally well tolerated, most AEs were Grade 1 & 2
- No ocular toxicity signals have been observed
- Median number of prior therapies is 4 (range 1-12)
- MTD has not been reached; next planned dose level is 3.5 mg/kg
- Preliminary anti-tumor activity has been observed in this heavily 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 biopharmaceutical 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.

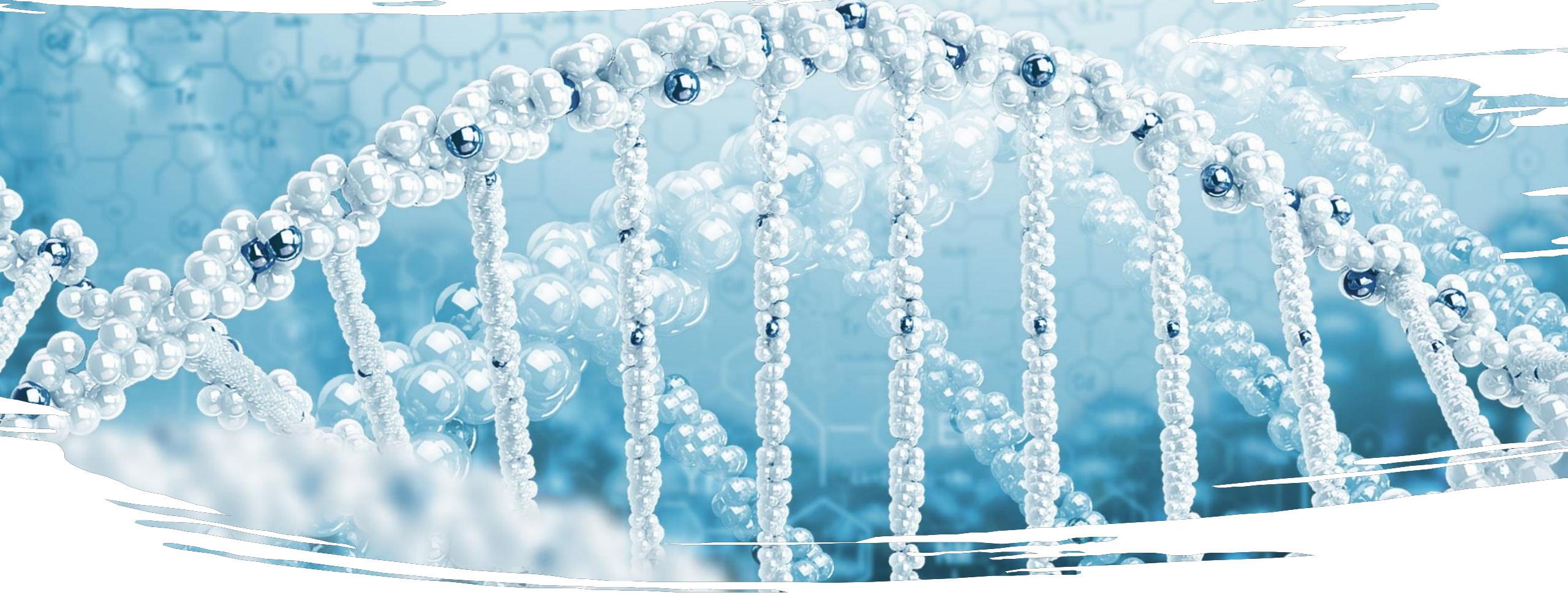
- **Experienced Founding Team** with deep understanding of development and regulatory strategy, as well as global insight to maximize the product value;
- **Proven Execution Excellence** in product development and successful track records in corporate management.

- **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.
  (Current pipeline including 1 NMPA NDA asset, 2 phase 1 assets and 1 discovery-stage assets with global rights)

- Clear company growth plan to **go from China to worldwide;**
- **US Expansion in 2022** to bring products to value inflection point with a highly efficient US development team;
- **Global Partner** 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 · 楹联健康基金 YUNION Healthcare Ventures · 翰颐资本 HANNE CAPITAL · 金浦健康基金 GP Healthcare Capital · Med-Fine Capital 幂方资本 · MITSUI GLOBAL INVESTMENT



Thank You

November 2021

BioNova Pharma 烨辉医药