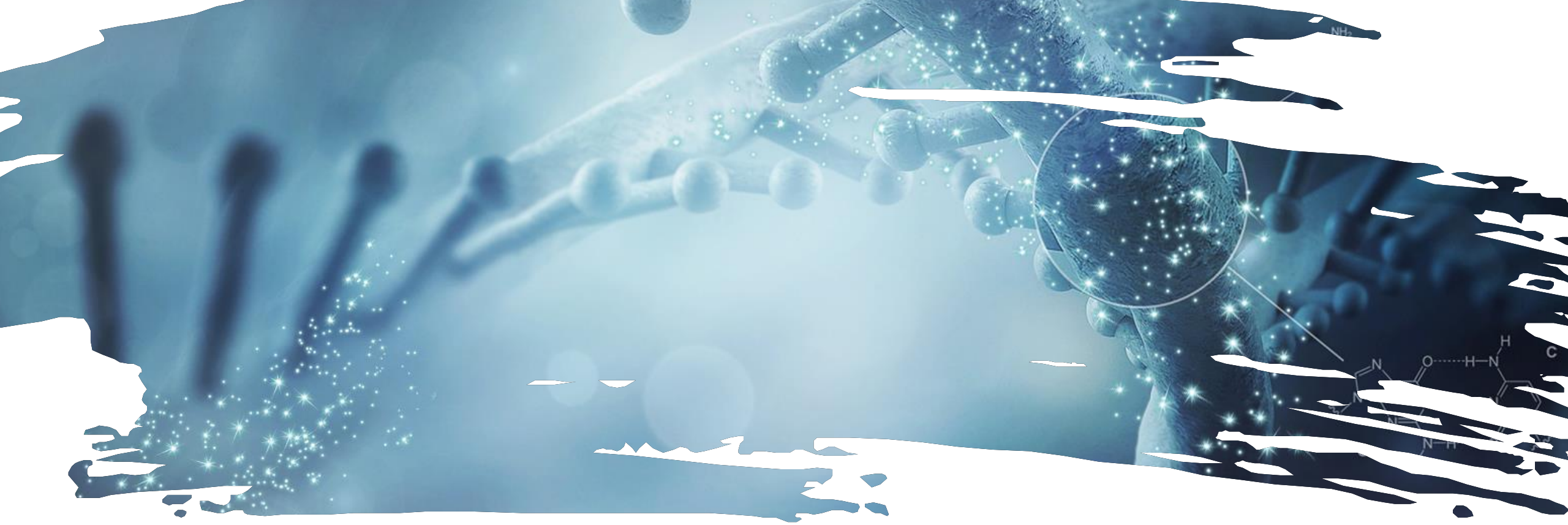
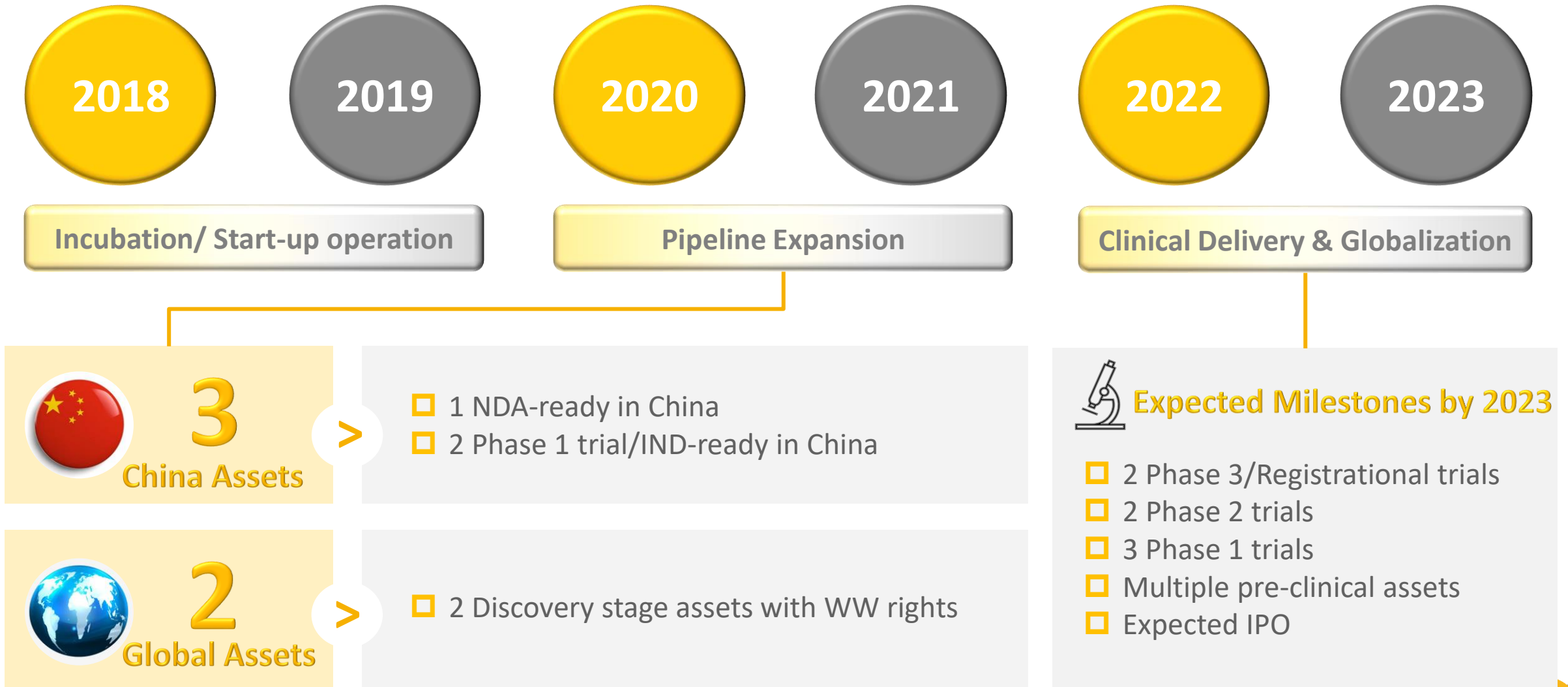


BIONOVA Introduction
Pharma 焯辉医药 October 2021



Company Overview

BioNova – An Innovative Biopharmaceutical Company



BioNova Is Supported by Top Tier Life Science VC Funds

2018/12



2020/08



2020/11



BioNova's Seasoned Development Leadership Team (1/2)

□ Ye Hua, MD, MPH, Founder, Chairman and CEO, *ad interim* CMO



- Over 20 years of experience in clinical development and regulatory submissions in Pharma/Biotech industry
- Contributed multiple blockbuster brands global regulatory approval, including Humira, Reclast/Zometa, Revlimid and Pomalyst in USA, EU and China



□ Bryan Huang, Ph.D., MBA, Co-founder, CFO and Chief Strategy Officer



- Over 20 years of solid experience in the pharmaceutical industry and healthcare investment banking
- Former Head of Business Development and Strategy at Immunomedics and former lead of business development search, valuation and portfolio strategy at Celgene



□ Taishan Hu, Ph.D., SVP & Head of Drug Discovery (Small Molecule)



- Over 20 years' career in medical chemistry and drug discovery with 30 peer-reviewed articles published and over 30 patents authored, respectively
- Former Site Head of SH Institute of Drug Discovery, Zhejiang Hisun where he built up a multi-disciplinary drug discovery team and successfully delivered several preclinical drug candidates



□ Yu Wang, TA Head, Hematology Clinical Development



- Hematologist by training and 7 years practicing medicine up to attending physician
- Physician scientist for new drug development in hematology
- Former Medical Director at FUSUNKite, leading CAR-T program



BioNova's Seasoned Development Leadership Team(2/2)

□ Bo Cui, Head of Regulatory Affairs



- Over 10 years' experience in domestic pharmaceutical industry
- Successfully led and contributed to several IND and NDA submissions and achieved approvals for domestic and imported new drugs, including biologics and small molecule drugs



□ Fang Liu, PhD, Director of Translational Development / Biomarker



- Over 15 years experience in translational development and biomarker research
- Extensive knowledge and experience in oncology biomarkers / CDx and CAR-T



□ Xiaorui Wang, PhD, Director of Project Management



- Over 10 years experience in industry and academia with stronger leadership skills
- Well-rounded experience in regulatory, clinical operations and research



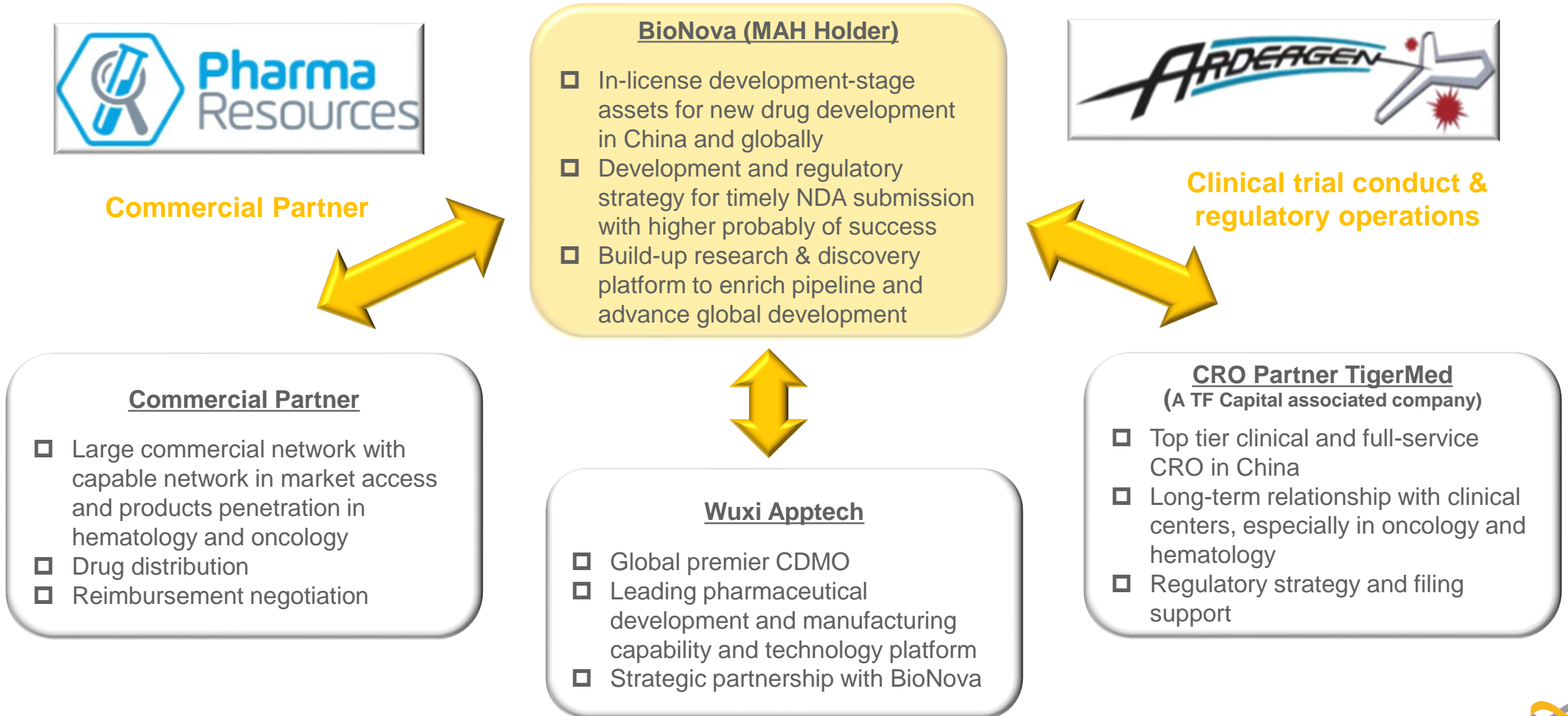
□ Peng Wang, CMC Director

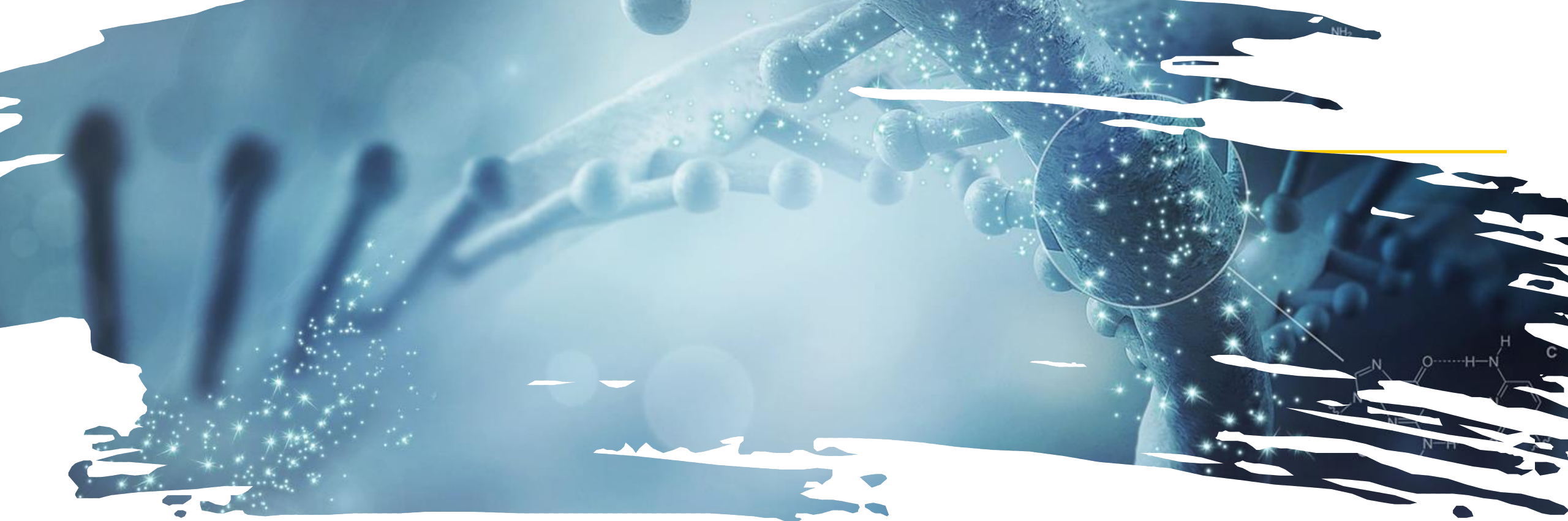


- More than 15 years' experience in CMC research and development,
- Having led more than a dozen drugs to go through different research stages (IND-NDA)



Efficient VIC Operating Model



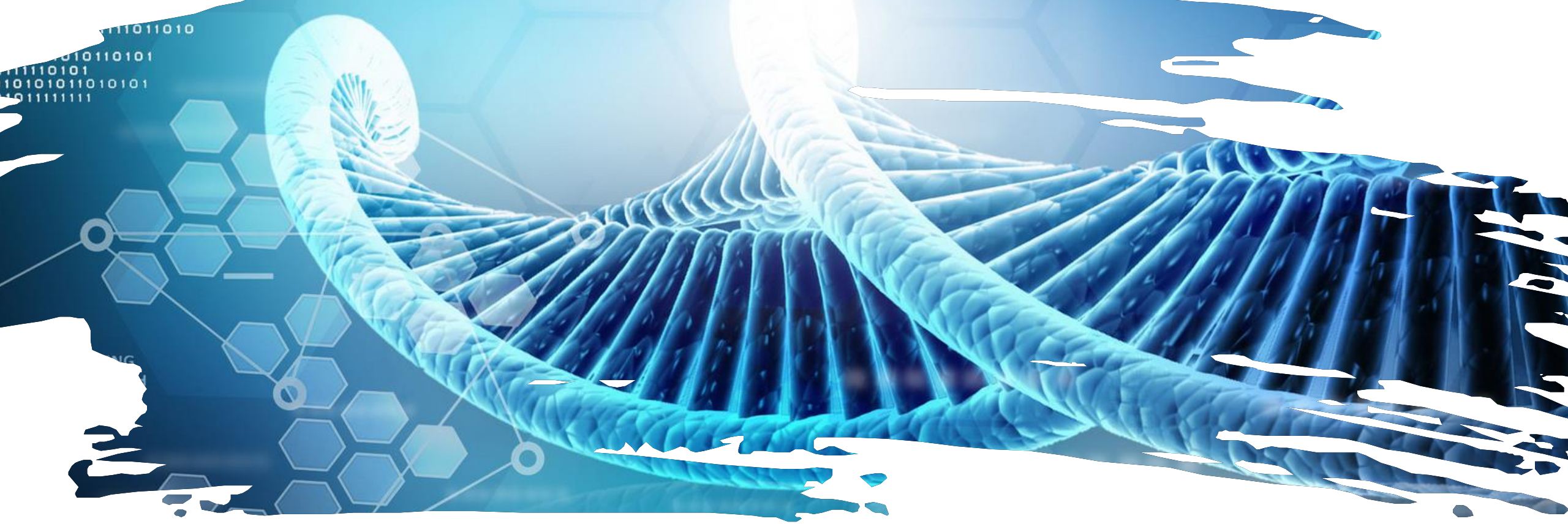


Product Pipeline

Current Pipeline

Product Candidate	Target	Indication	Discovery	IND Enabling	Phase 1	Phase 2	Phase 3	Commercial Rights
BN101	ROCK2	cGVHD						China
BN102	BTK (reversible)	CLL/SLL, MCL, WM, MZL						China
BN301 (ADC)	CD74	NHL, MM, AML						China
BN104	Undisclosed	Hematologic malignancies						WW





BN101

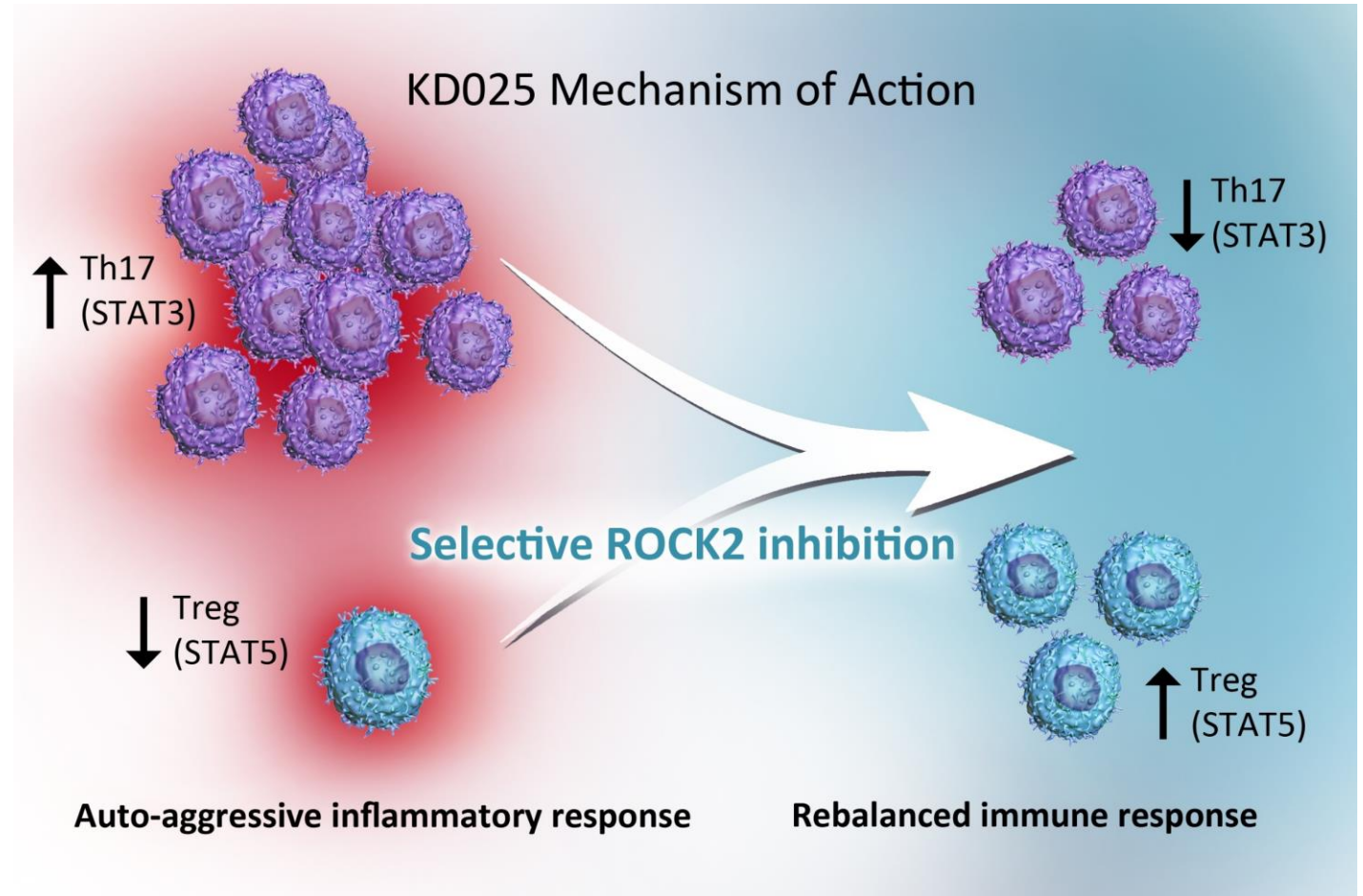
FDA and NMPA Breakthrough Therapy Designation for cGVHD

BN101 / KD025 – A selective ROCK2 Inhibitor

ROCK2 inhibition downregulates pro-inflammatory Th17 responses and increases Treg function

- Reduces STAT3 phosphorylation
- Increases STAT5 phosphorylation

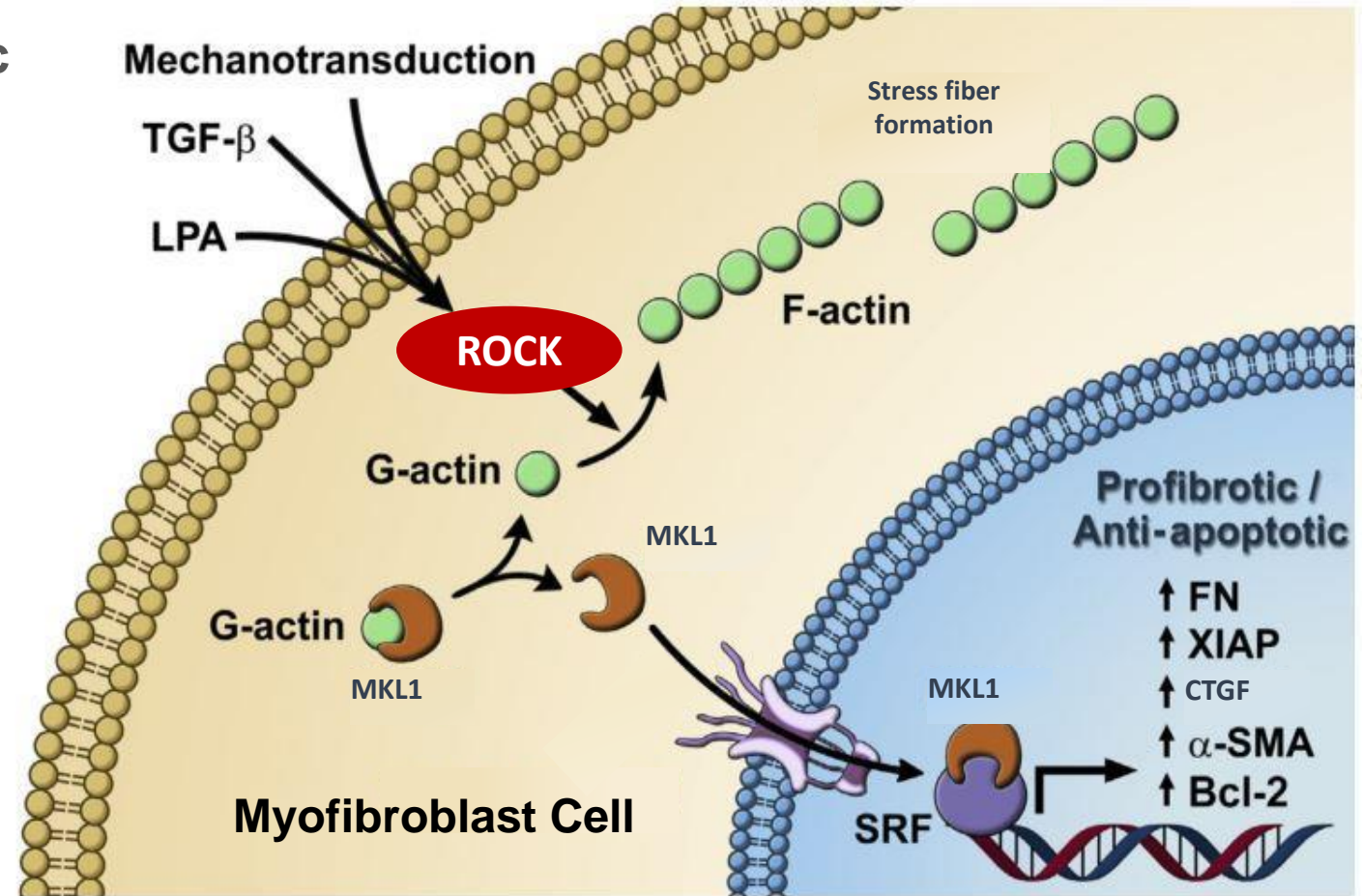
ROCK2 inhibition re-establishes immune homeostasis



ROCK is 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



Spectrum of Manifestations in Chronic GVHD



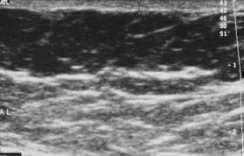
Ocular sicca



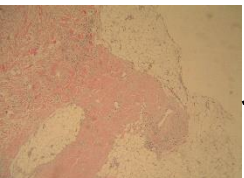
Oral ulcers



Nail dystrophy



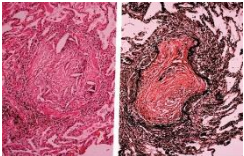
Skin sclerosis



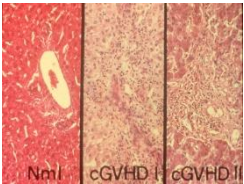
Deep sclerosis



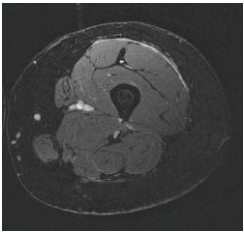
Infections
 Disability
 Quality of life
 Endocrine
 Metabolism
 Nutrition
 Pain



Bronchiolitis obliterans



Loss of bile ducts

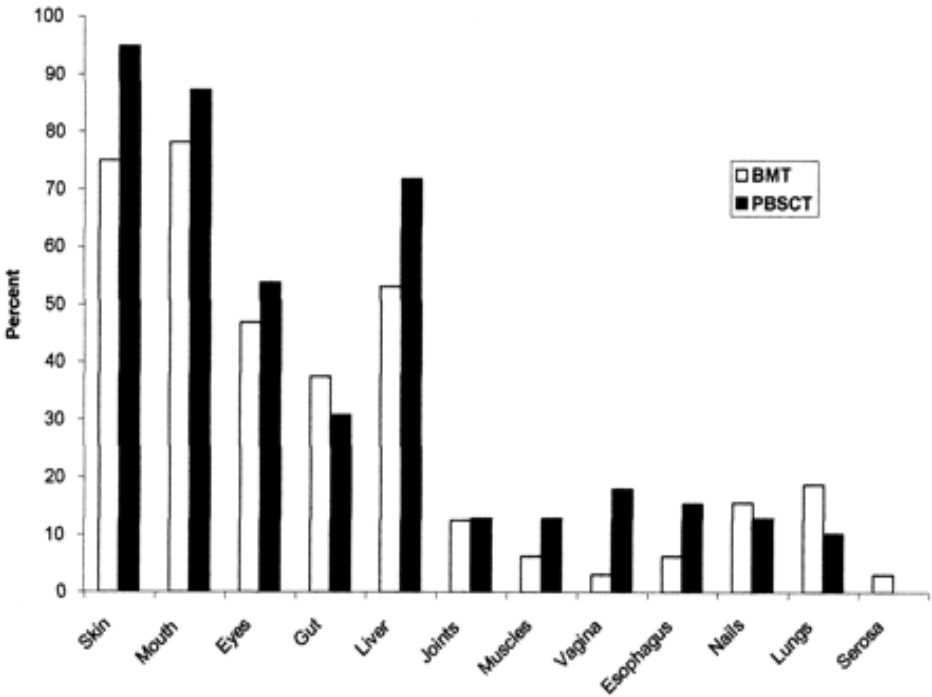


Fasciitis



Skin ulcers

cGVHD involves multiple organs



Belumosudil/BN101 Global Development for cGVHD



5 Oct, Orphan Drug Designation for cGVHD

- 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

2015

cGVHD IND in US

2017

2018

16 Oct, FDA Breakthrough Therapy Designation

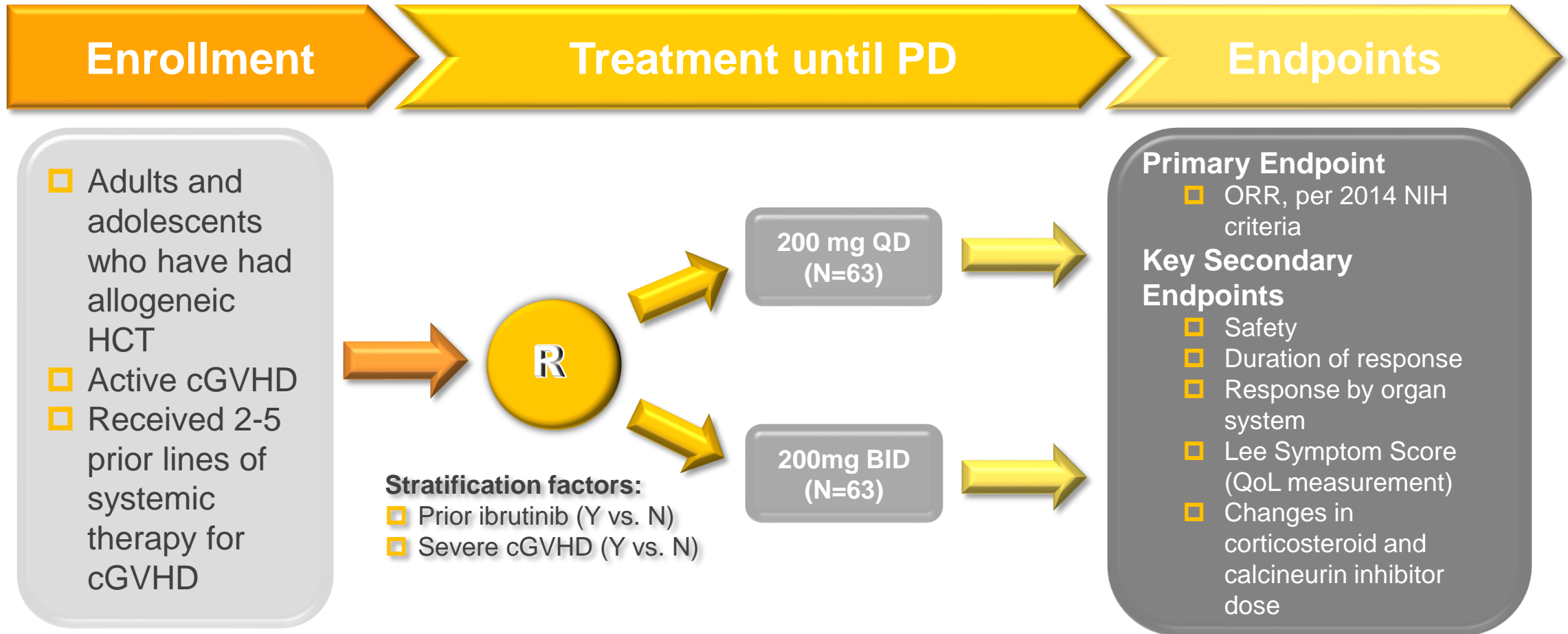
2020

2021

- Feb, China Ph1 completed
- Apr, BN101-201 clinical trial
- 16 Jul, FDA approval in US
- Expecting NDA filing by Dec

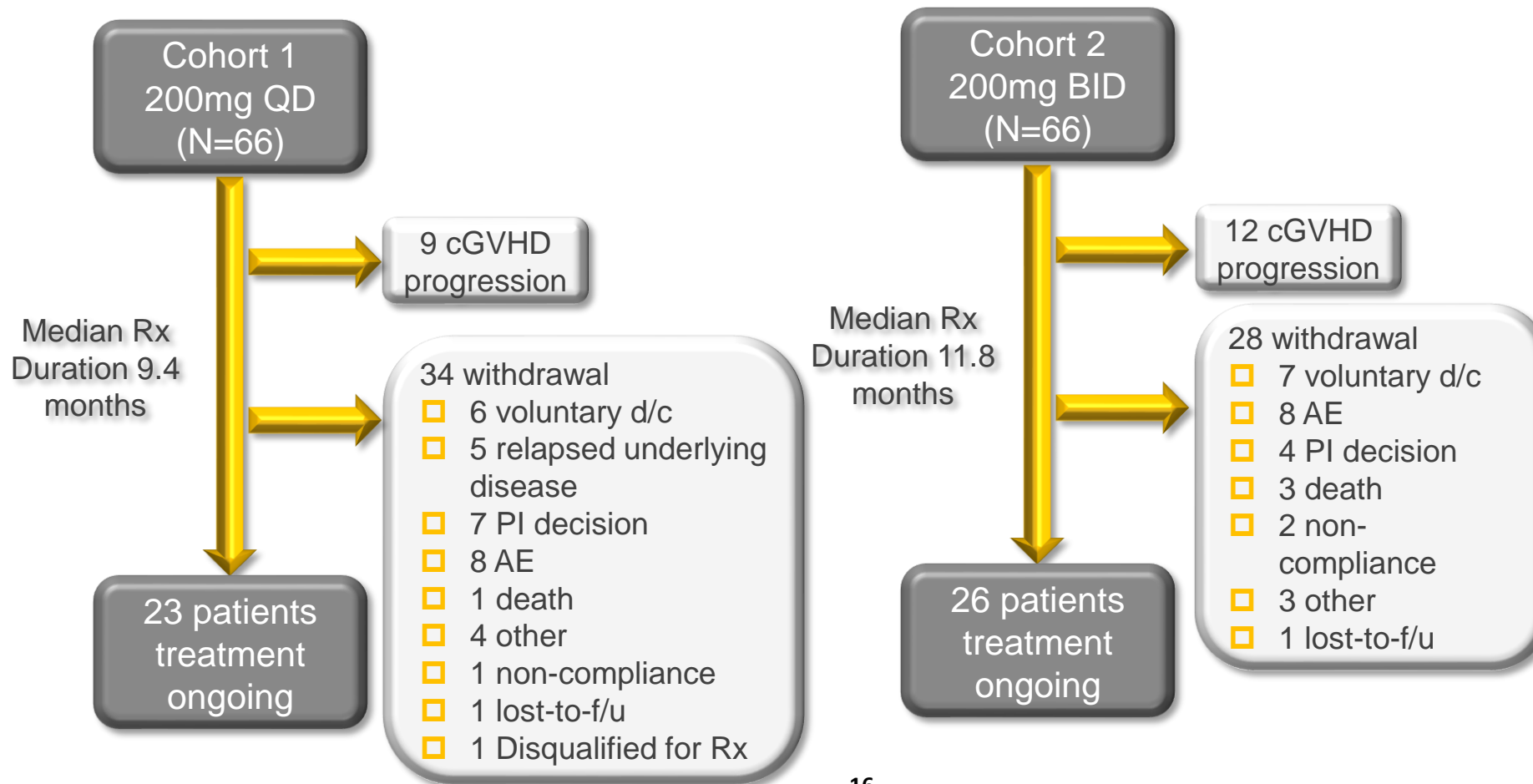


ROCKstar (KD025-213) Registration Trial for cGVHD



ROCKstar (KD025-213) Patient Disposition

- All data as of 19Aug2020
- Median follow up time: 13.6 months
- Median duration of treatment: 10.4 months

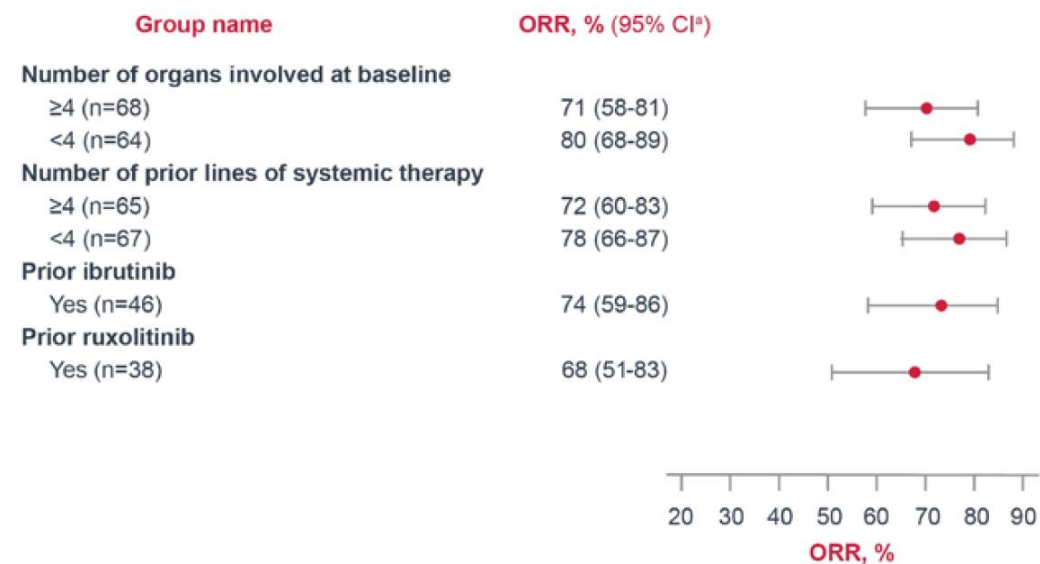
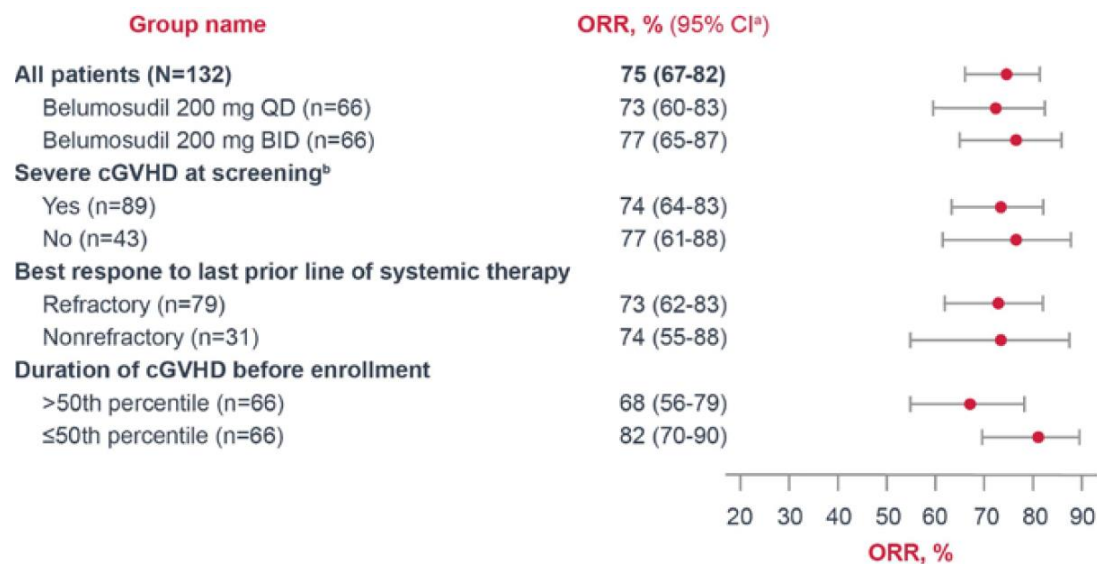


ROCKstar (KD025-213) Results - Primary Analyses

(Data as of August 2020, ASH Data)

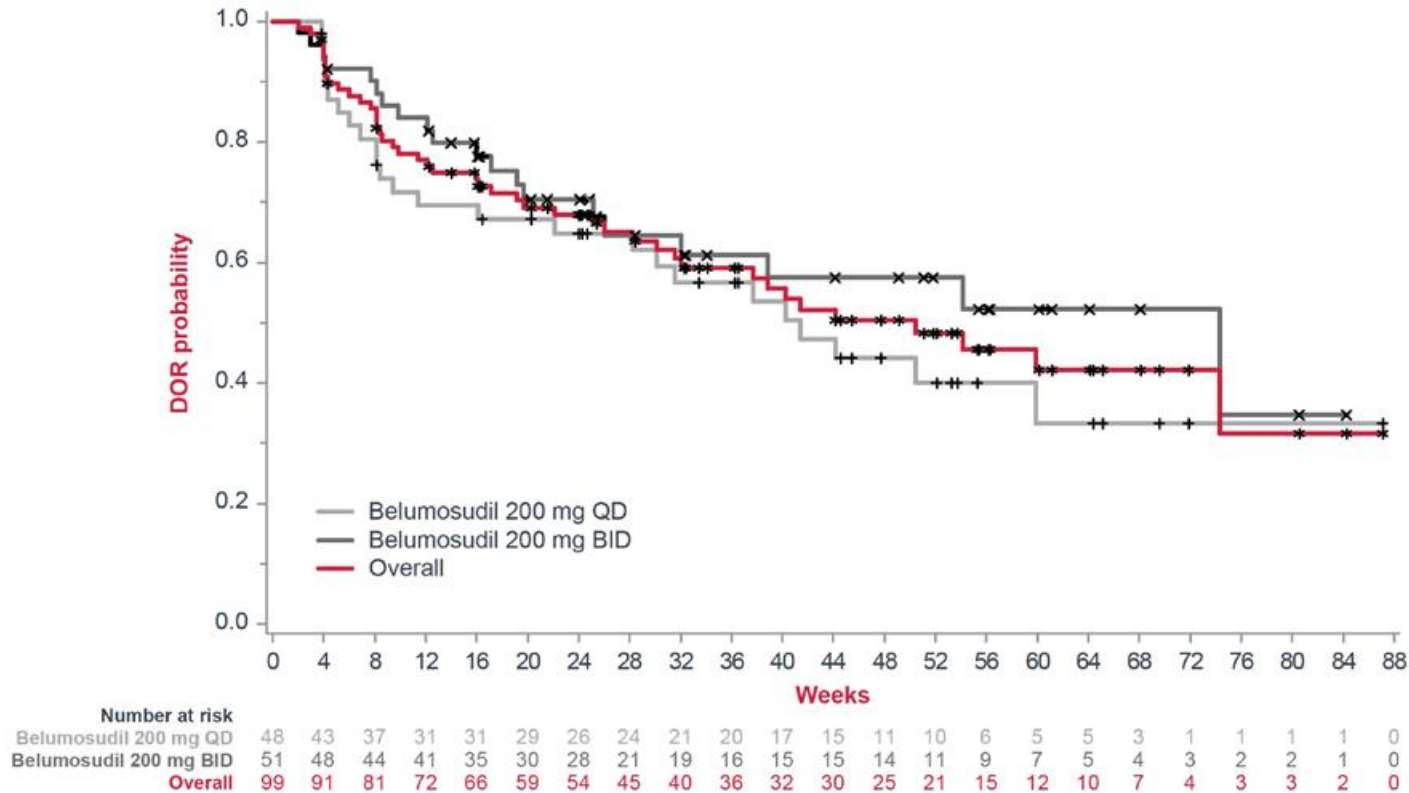
Belumosudil	N	ORR	95% CI
200 mg QD	66	73%	(60, 83)
200 mg BID	66	77%	(65, 87)

- KD025 achieved **clinically and statistically significant ORR** in both arms
- Complete responses have observed in **all affected organ/ system**
- Seven patients achieved overall **CR**
- Consistent ORRs across all key subgroups



The ROCKstar Study: Duration of Response

Kaplan-Meier plot of DOR



Overall, 44% of patients have remained on belumosudil therapy for >1 years.

The median DOR was **50 weeks**, and 60% of responders maintained responses for ≥ 20 weeks.



ROCKstar (KD025-213) Safety and Tolerability

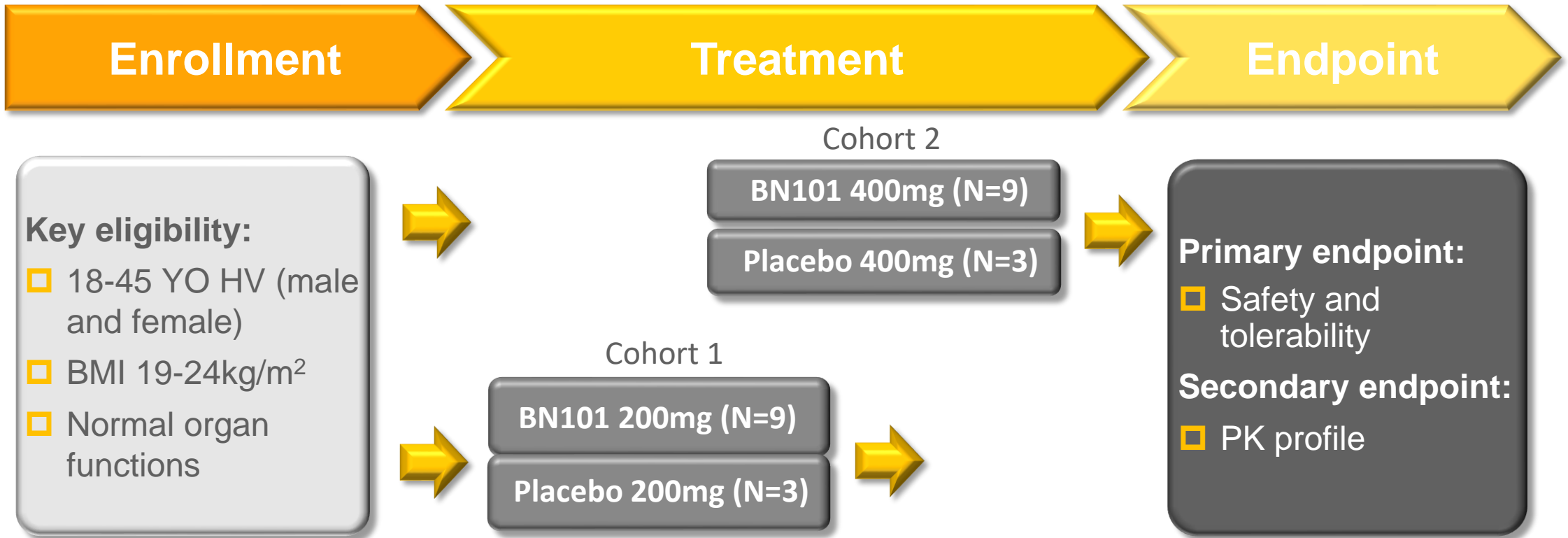
Safety Overview	Cohort 1 200 mg QD (N=66) n (%)	Cohort 2 200 mg BID (N=66) n (%)	Overall (N=132) n (%)
Median months of treatment	9.4	11.8	10.4
Any Adverse Event (AE)	65 (99)	66 (100)	131 (99)
Grade 3/4 AE	37 (56)	34 (52)	71 (54)
SAE	27 (41)	23 (35)	50 (38)
Drug related AE			
Any related AE	49 (74)	40 (61)	89 (67)
Related SAE	5 (8)	2 (3)	7 (5)
On study death ¹	4 (6)	4 (6)	8 (6)

¹ KD025 QD: aspiration pneumonia; hemoptysis; MODS/septic shock; relapse
 KD025 BID: cardiac arrest (2); infection; respiratory failure

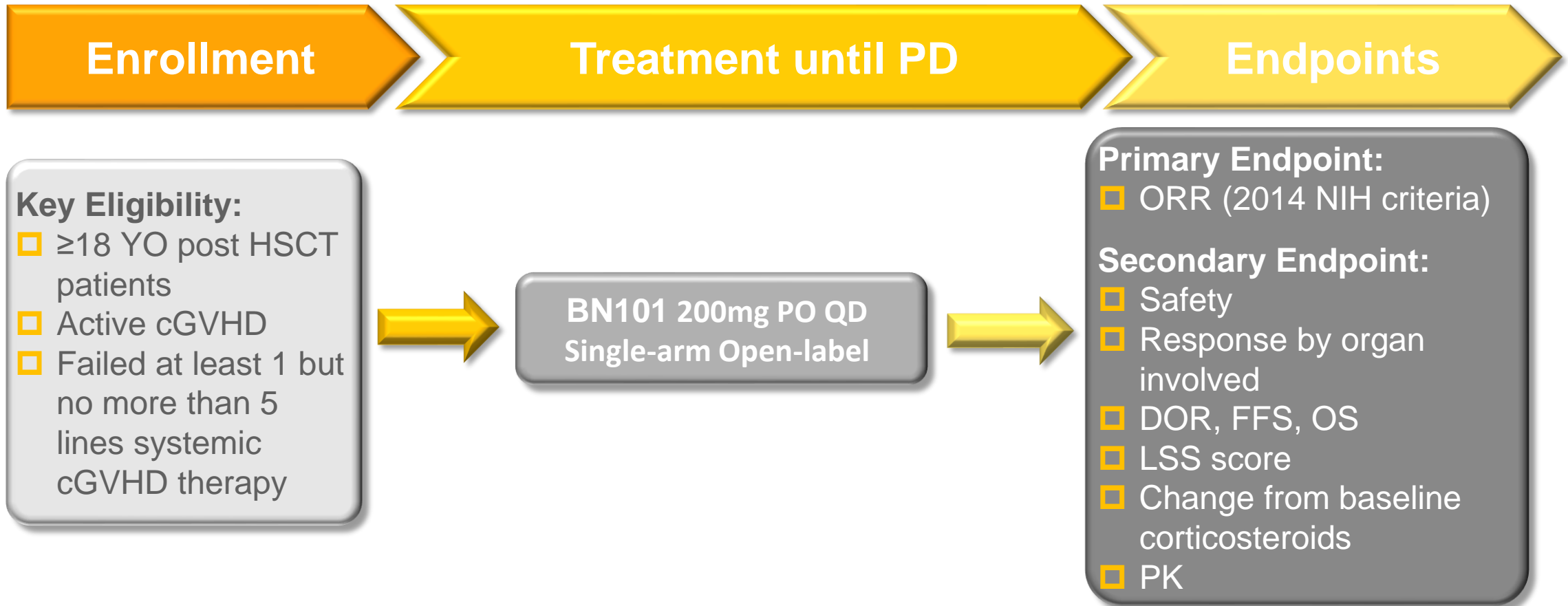
Commonly reported AE	Cohort 1 200 mg QD (N=66) n (%)	Cohort 2 200 mg BID (N=66) n (%)	Overall (N=132) n (%)
All Grade AE (≥20%)			
Fatigue	30 (46)	20 (30)	50 (38)
Diarrhea	23 (35)	21 (32)	44 (33)
Nausea	23 (35)	18 (27)	41 (31)
Cough	20 (30)	17 (26)	37 (28)
Upper respiratory tract infection	17 (26)	18 (27)	35 (27)
Dyspnea	21 (32)	12 (18)	33 (25)
Headache	13 (20)	18 (27)	31 (24)
Liver-related AE	12 (18)	19 (29)	31 (24)
Peripheral edema	17 (26)	13 (20)	30 (46)
Vomiting	18 (27)	10 (15)	28 (21)
Muscle spasms	13 (20)	13 (20)	26 (20)
≥ Grade 3 (≥ 3%)			
Pneumonia	6 (9)	4 (6)	10 (8)
Hypertension	4 (6)	4 (6)	8 (6)
Hyperglycemia	3 (5)	3 (5)	6 (5)



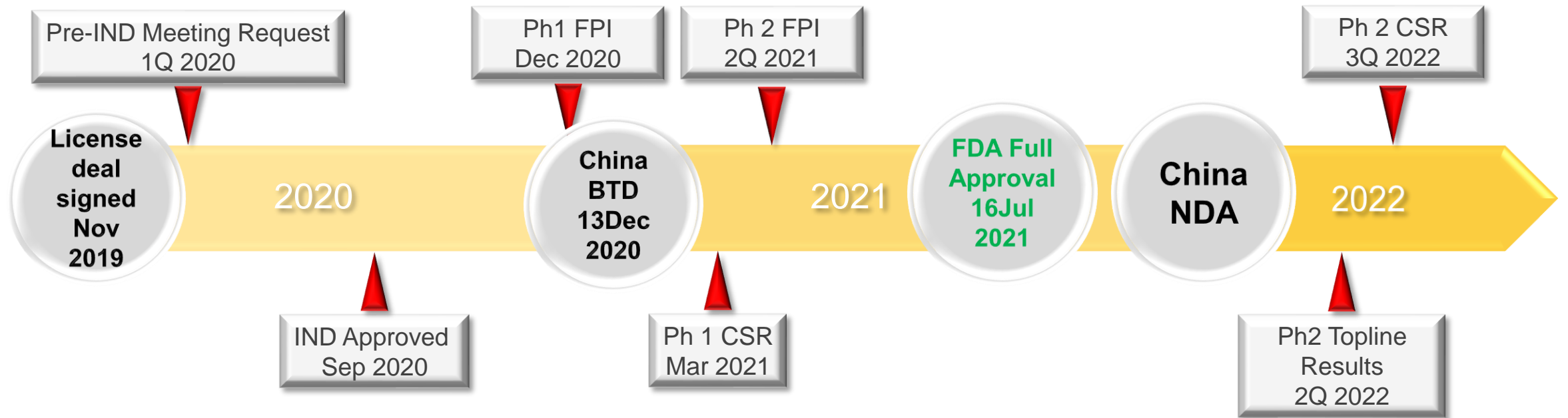
Belumosudil China Phase 1 Healthy Volunteers' Trial (Completed)

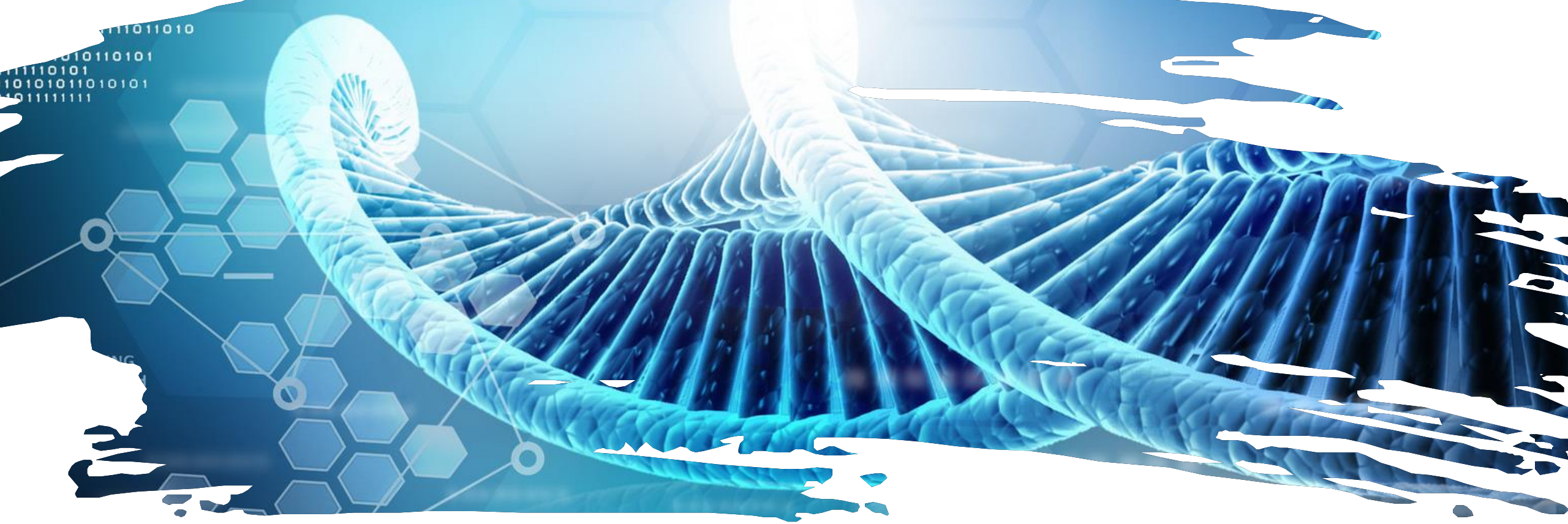


Belumosudil China Ph II cGVHD Trial (Ongoing)



Belumosudil Development Timeline in China





BN102

A highly selective, potent reversible BTK inhibitor

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.

1. <https://seer.cancer.gov/statfacts/html/nhl.html>

2. <https://seer.cancer.gov/statfacts/html/clyl.html>

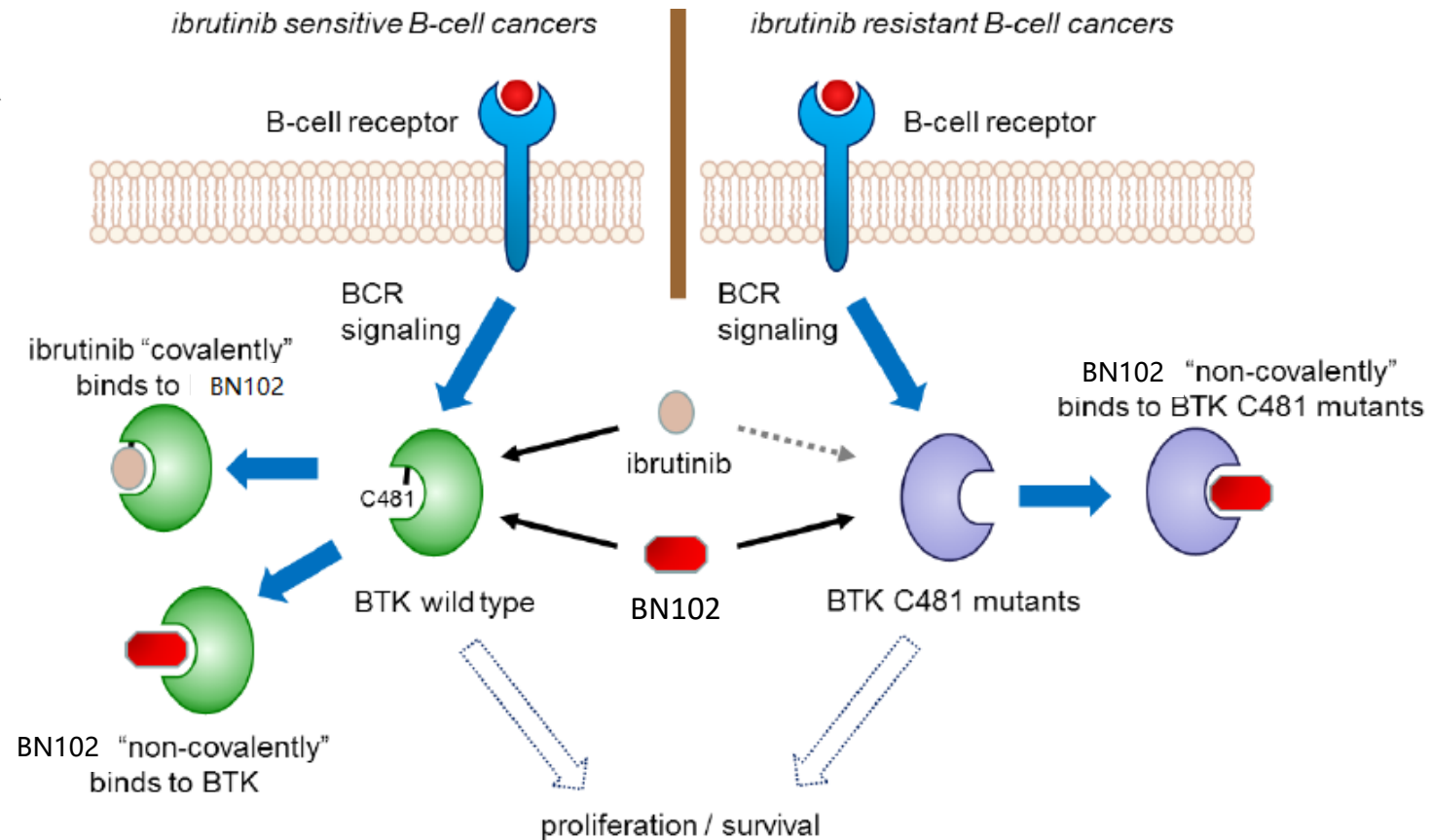
3. <https://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf>



MoA of BTK Inhibitors and Acquired Resistance

□ **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
- 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



□ Ibrutinib irreversibly binds to Cys481 of BTK, and the main resistance mechanism is believed to be through the C481S mutation, that is, the mutation of cysteine to serine



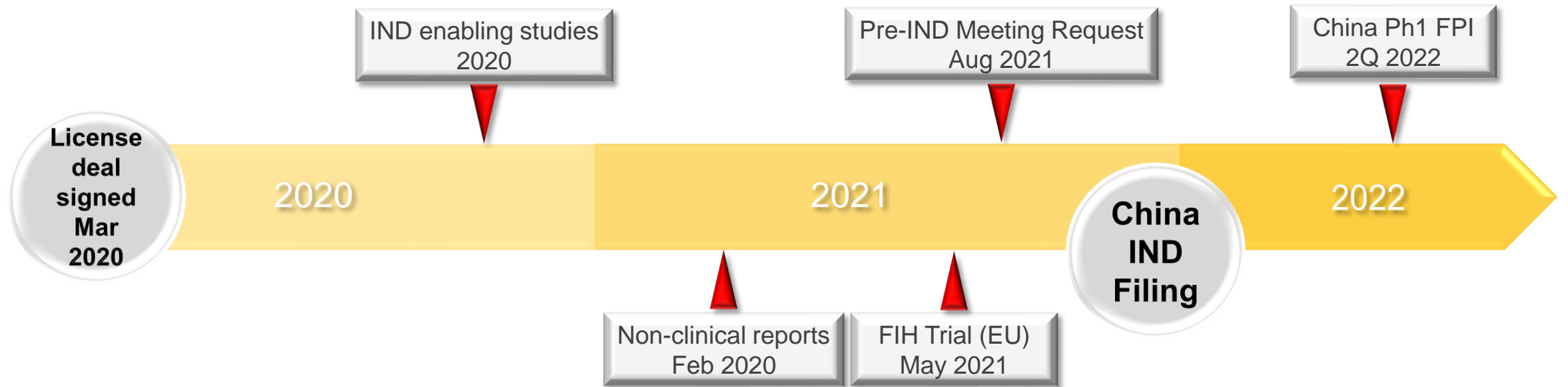
BN102 China Phase 1/2 Trial Objectives

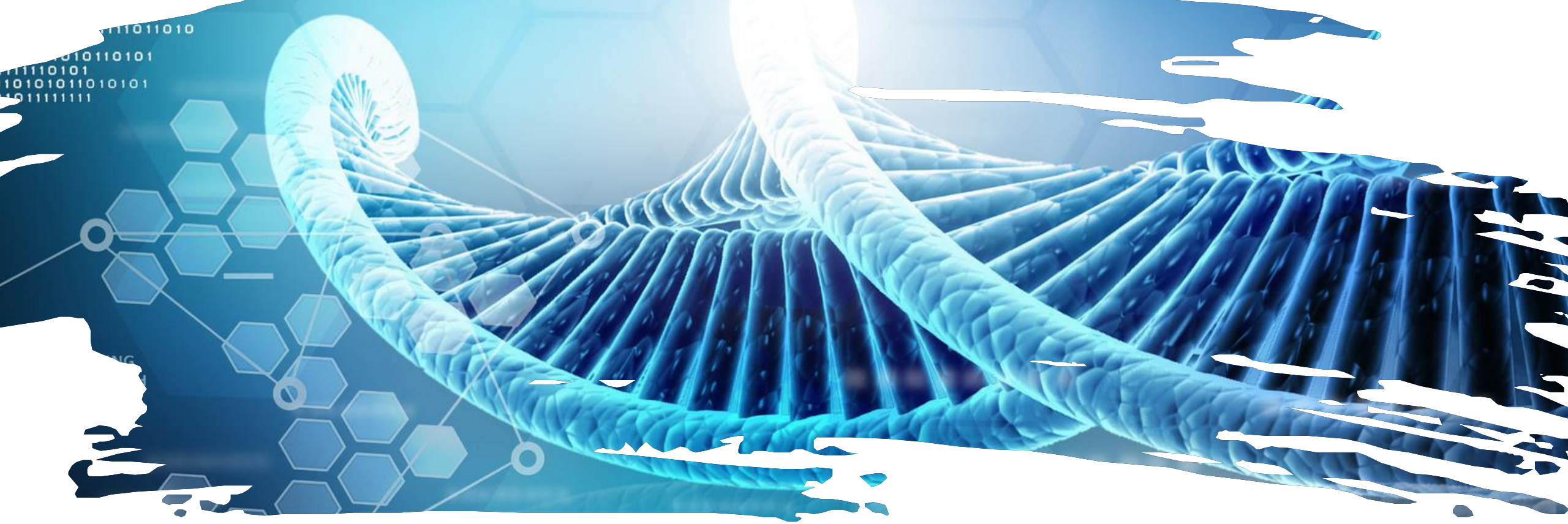
- To evaluate the safety and efficacy of BN102 in treated patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and B-cell non-Hodgkin's lymphoma (NHL) in a multicenter phase I/II clinical trial research

	Ph I	Ph II
Primary	<ul style="list-style-type: none"> Determine the MTD and RP2D of BN102 in patients with hematologic malignancies 	<ul style="list-style-type: none"> To evaluate the efficacy of BN102 in CLL/SLL or B-cell NHL patients who have failed prior therapies
Secondary	<ul style="list-style-type: none"> To evaluate the safety and tolerability of BN102 To evaluate the BN102 pharmacokinetic (PK) profile Preliminary evaluation of BN102 efficacy in CLL/SLL and or B-cell NHL patients who have failed prior therapies 	<ul style="list-style-type: none"> To evaluate other efficacy parameters of BN102 in patients with CLL/SLL and B-cell NHL who have failed or cannot tolerate previous standard treatments, including DOR, PFS, and OS To evaluate the safety profile of BN102 To evaluate BN102 PK profile in CLL/SLL and B-cell NHL patients
Exploratory	<ul style="list-style-type: none"> To evaluate the efficacy and pharmacodynamic (PD) characteristics of BN102 in patients with CLL/SLL and different subtypes of B cell NHL 	



BN102 Development Timeline in China

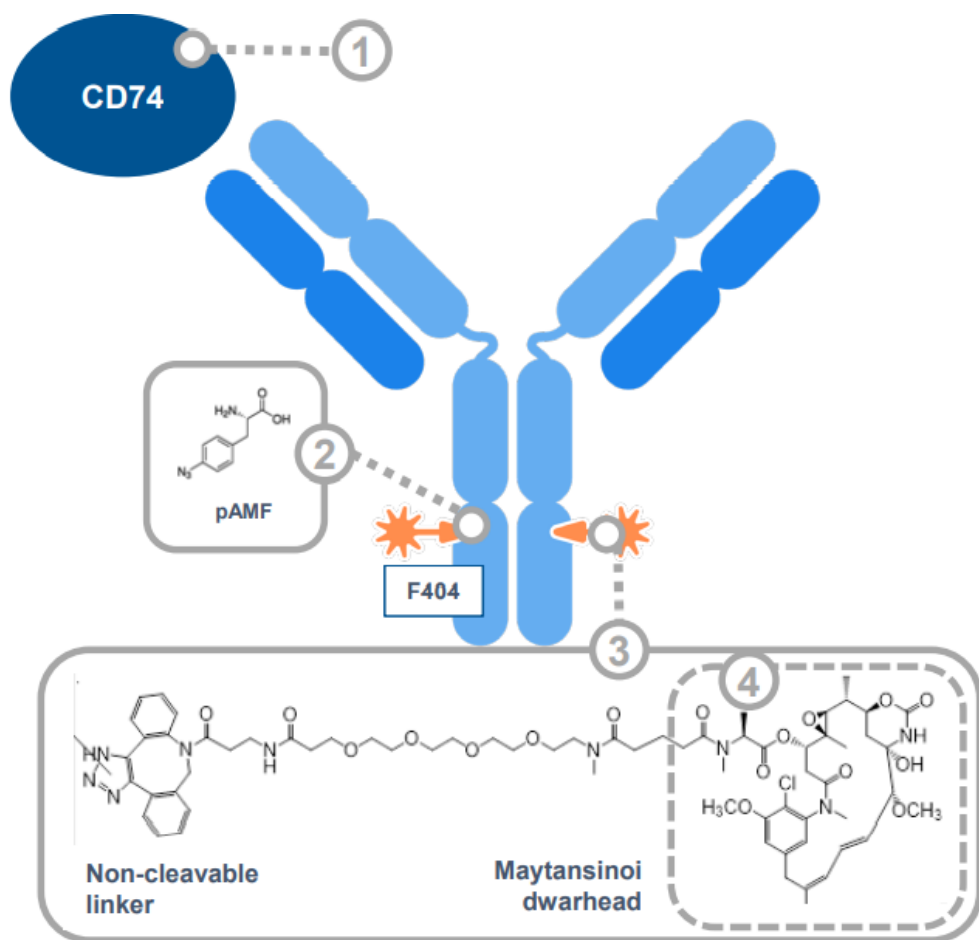




BN301

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

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

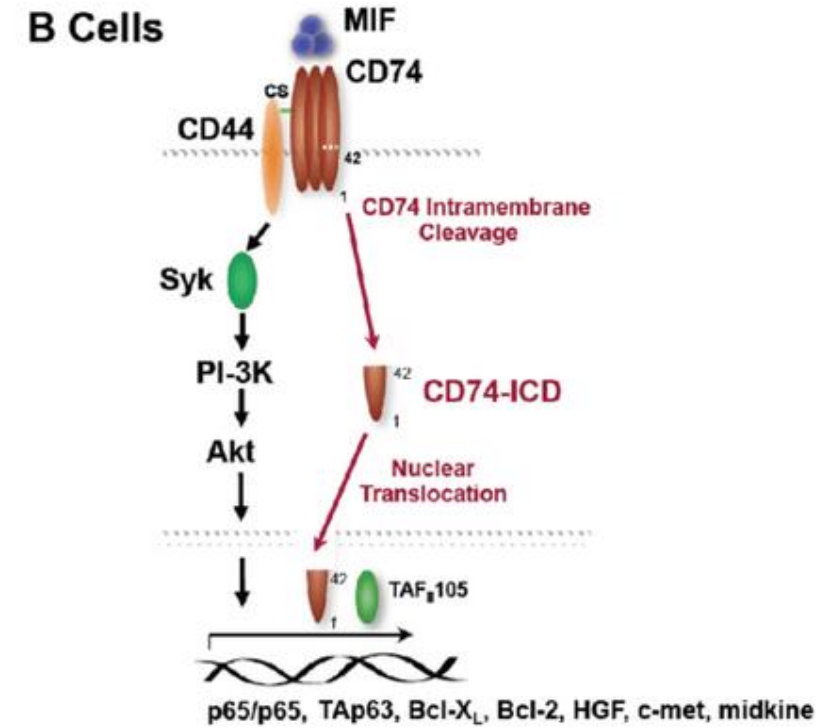
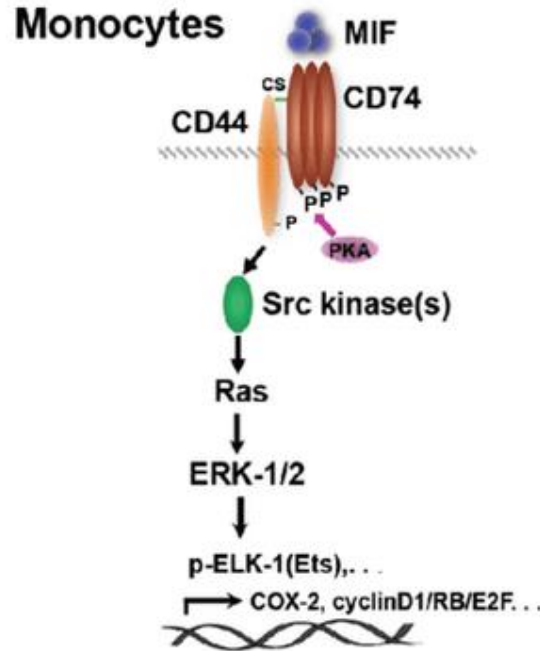


- BN301/STRO-001 is a homogeneous **antibody drug conjugate (ADC)** with a drug-antibody ratio (DAR) of 2, targeting **CD74**:
 - CD74 is expressed in many hematological cancers and rapidly internalized
 - Conjugation through precisely positioned non-natural amino acids p-azidomethyl-L-phenylalanine, 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**

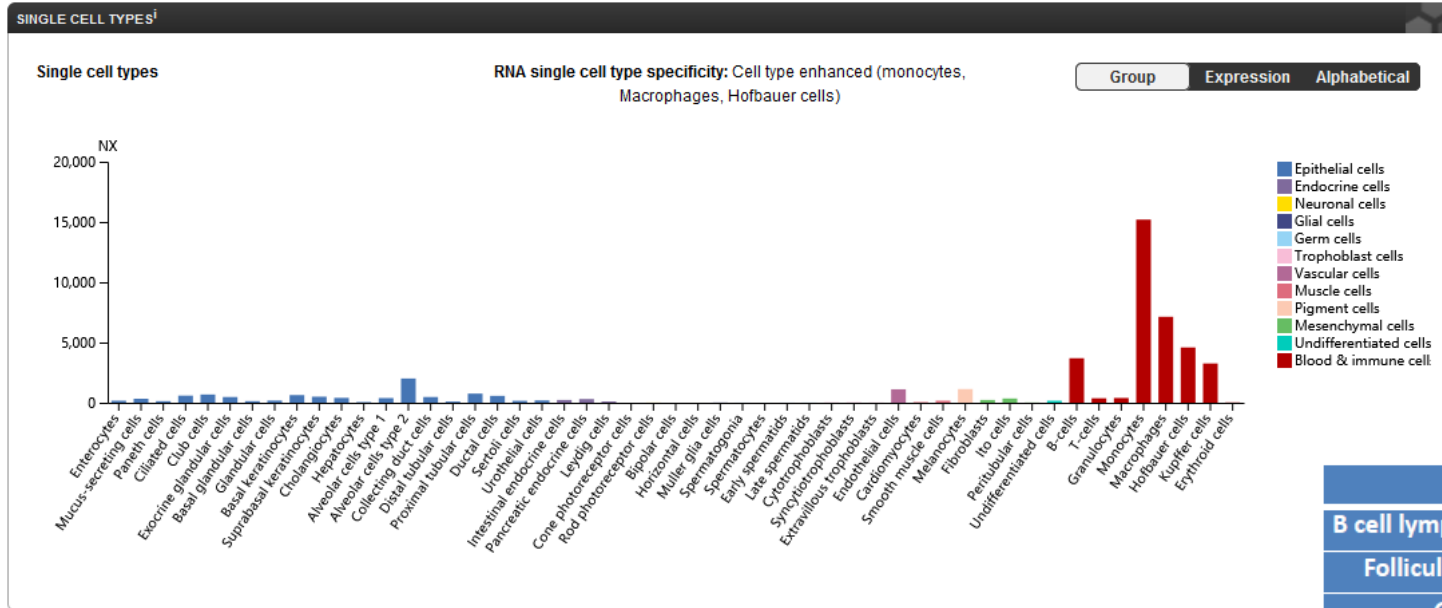


CD74 Signaling Pathway

- CD74 is a type II transmembrane glycoprotein that functions as a MHC class II chaperone and as a high affinity receptor for the pro-inflammatory cytokine macrophage migration inhibitory factor (MIF)
- Upon binding to MIF, the CD74-intracellular domain translocate to the nucleus where it acts in conjunction with NF- κ B pathway members to induce B-cell proliferation and survival
- In normal human tissues, CD74 is expressed on HLA class II-positive cells, including B-cells, monocytes, macrophages and dendritic cells



CD74 Expression



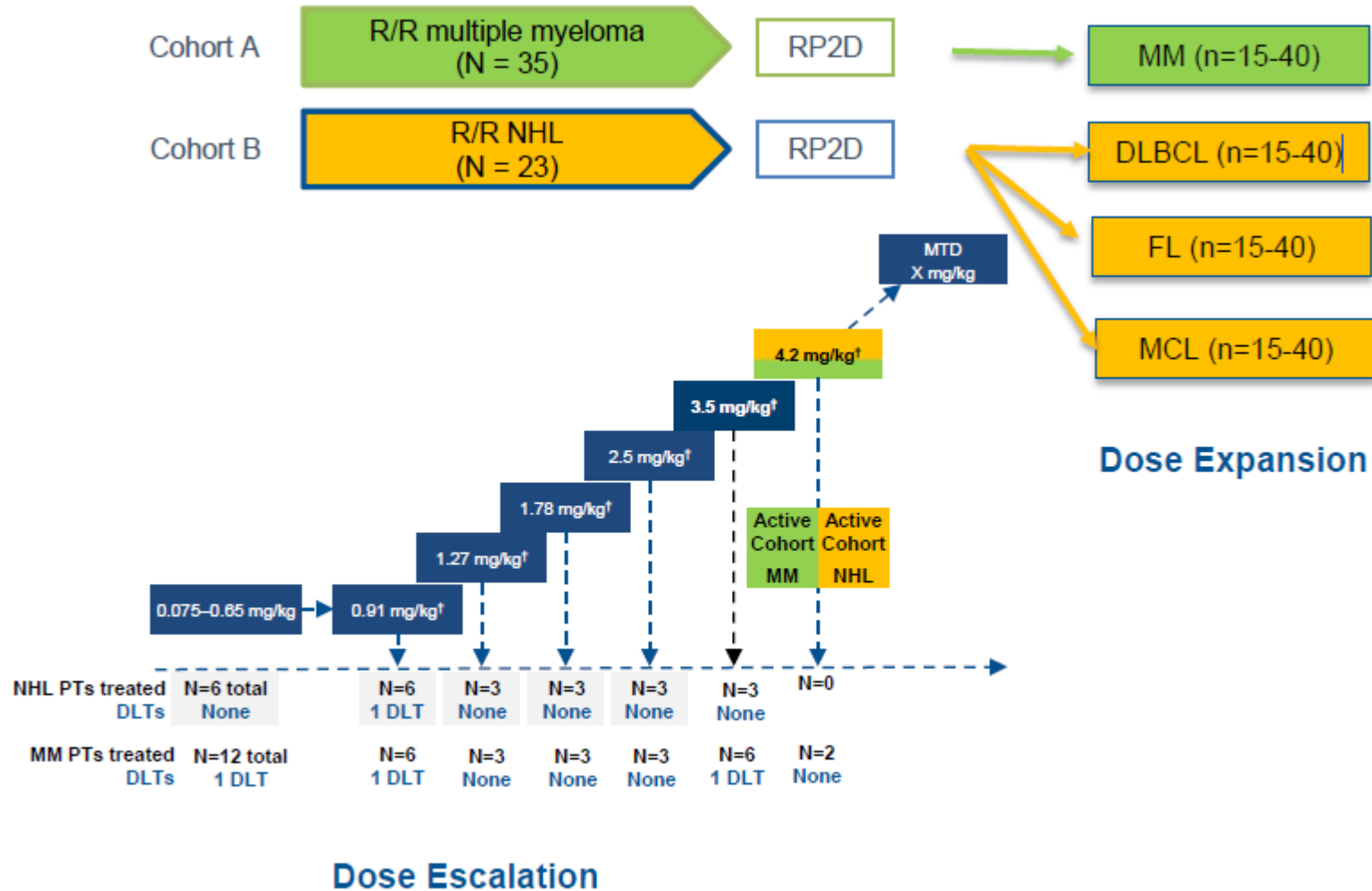
Frequent CD74 Expression in Multiple B-cell NHL Subtypes by IHC

	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

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



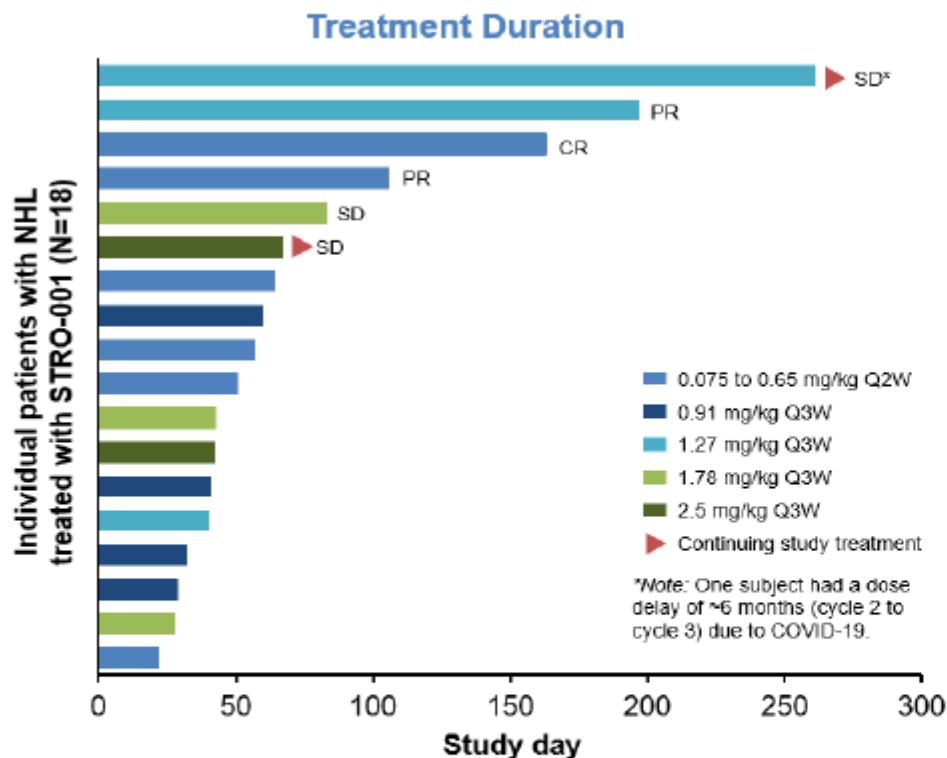
STRO-001-BCM1 Dose Escalation Study Design and Status





3030 Preliminary Results of an Ongoing Phase I 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*



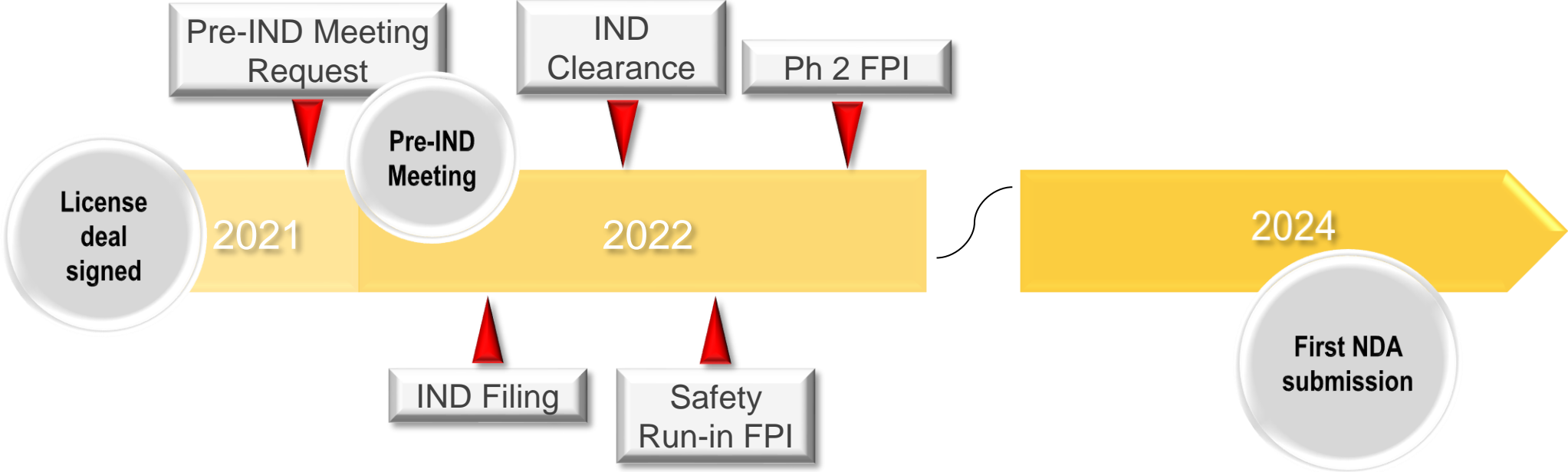
- STRO-001 was generally well tolerated, most AEs were Grade 1 & 2
- No ocular toxicity signals have been observed
- Median number of prior therapies is 4 (range 1-12)
- MTD has not been reached; next planned dose level is 3.5 mg/kg
- Preliminary anti-tumor activity has been observed in this heavily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



STRO-001 Development Timeline in China



Company Highlights



Seasoned development team with track records in new drug development and strategic transactions

- ❑ Average > 20 years in global pharma and biotech companies and led multiple drug registrations
- ❑ In-depth understanding in unmet medical needs, SoC and regulatory policies
- ❑ Extensive KOL and hospital networks across Chinese medical society
- ❑ Value creation by selected assets of high probability of success as well as of commercial value

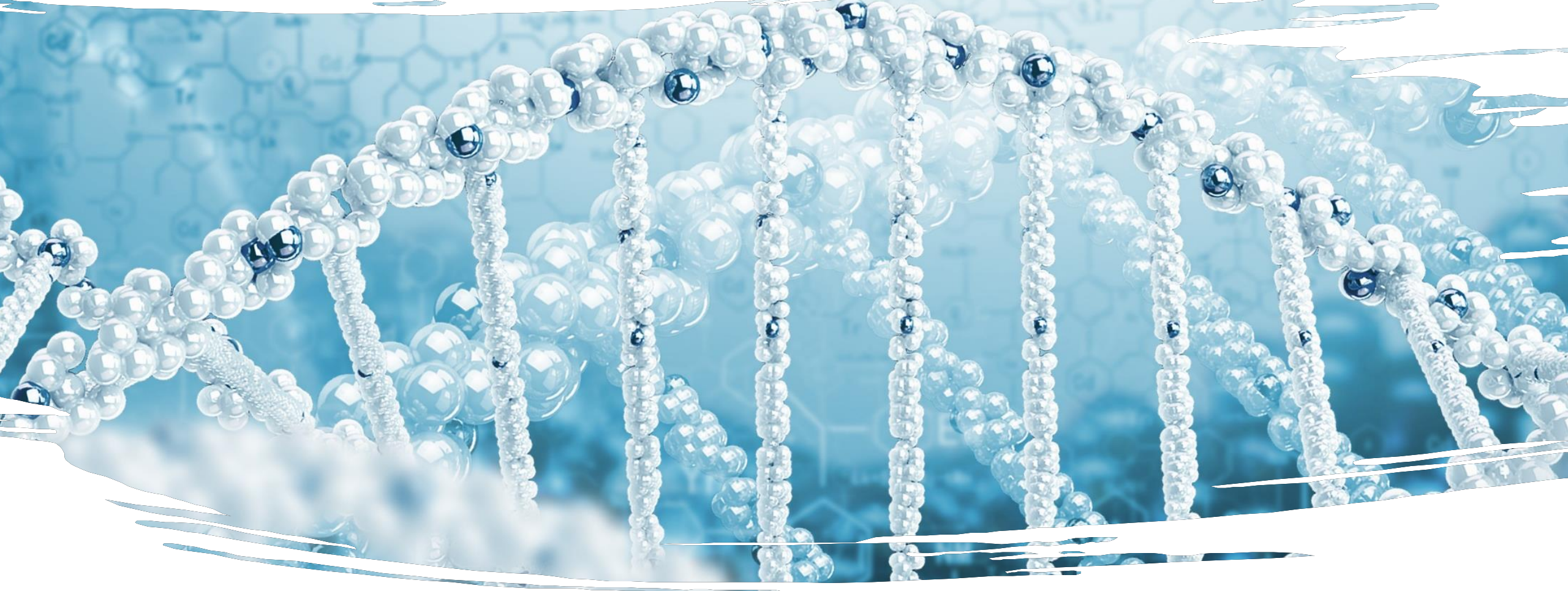
Extensive collaborations to supplement discovery, CMC and commercial

- ❑ Top-tier CDMO and CRO for high quality discovery and development
- ❑ Competitive advantage in selected target therapies
- ❑ Broad network and collaborations from investors' eco-system

Premier biotech in China for Global

- ❑ Near-term license-in clinical-stage assets to build up pipeline and company infrastructure
- ❑ Mid-term balanced income to spending financial outlook with ability of China commercialization
- ❑ Long-term international presence for novel targets global development and commercialization





Thank You