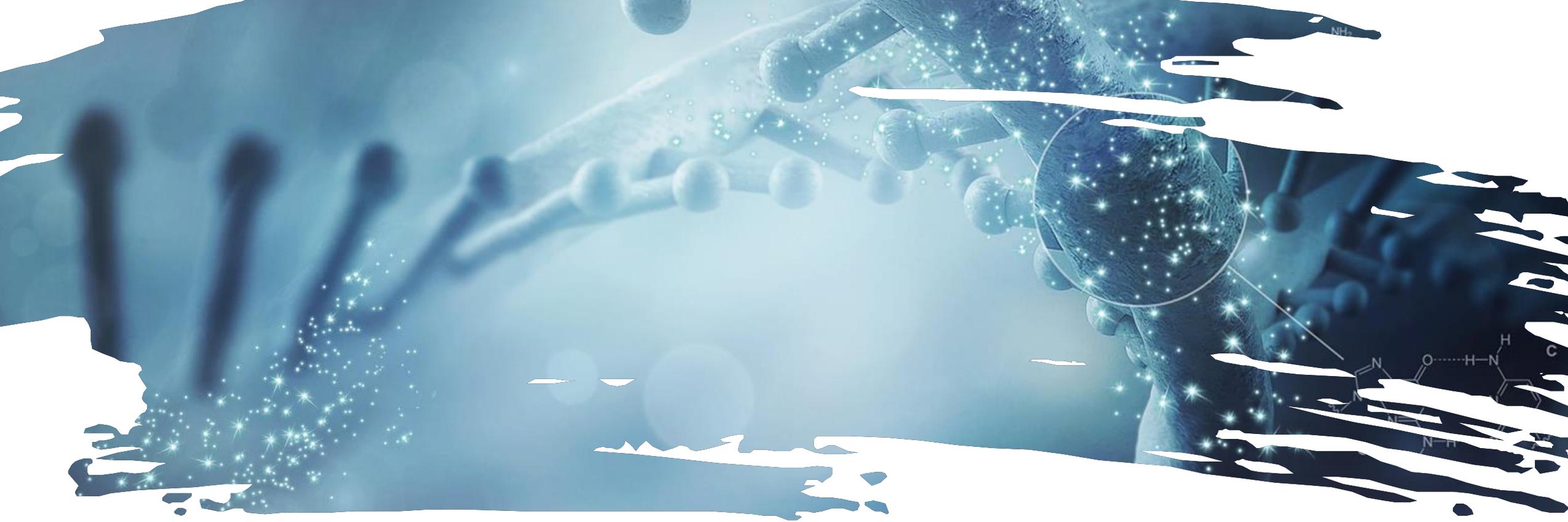


**BIONOVA** Introduction  
Pharma 焯辉医药 March 2021



# Company Overview

# Company Profile

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## □ Seasoned management team with track records in drug development and strategic transactions

- Average > 20 years in global pharma and biotech companies and led multiple drug registrations
- In depth understanding of unmet medical needs and regulatory policies in China
- Extensive KOL and hospital networks across Chinese medical society

## □ Extensive commercial coverage and market access in China with commercial partners

- > 2,000 sales force covering the tier 1-5 cities in China
- Strong ties with the largest pharmacy chains in China
- Strong government affairs capability with capable market access at both state and province level

## □ Strong financial support by top tier life science VC funds

- Company is funded by premier VC funds, including Hillhouse, TF capital, Lilly Asia Ventures and BioTrack Capital

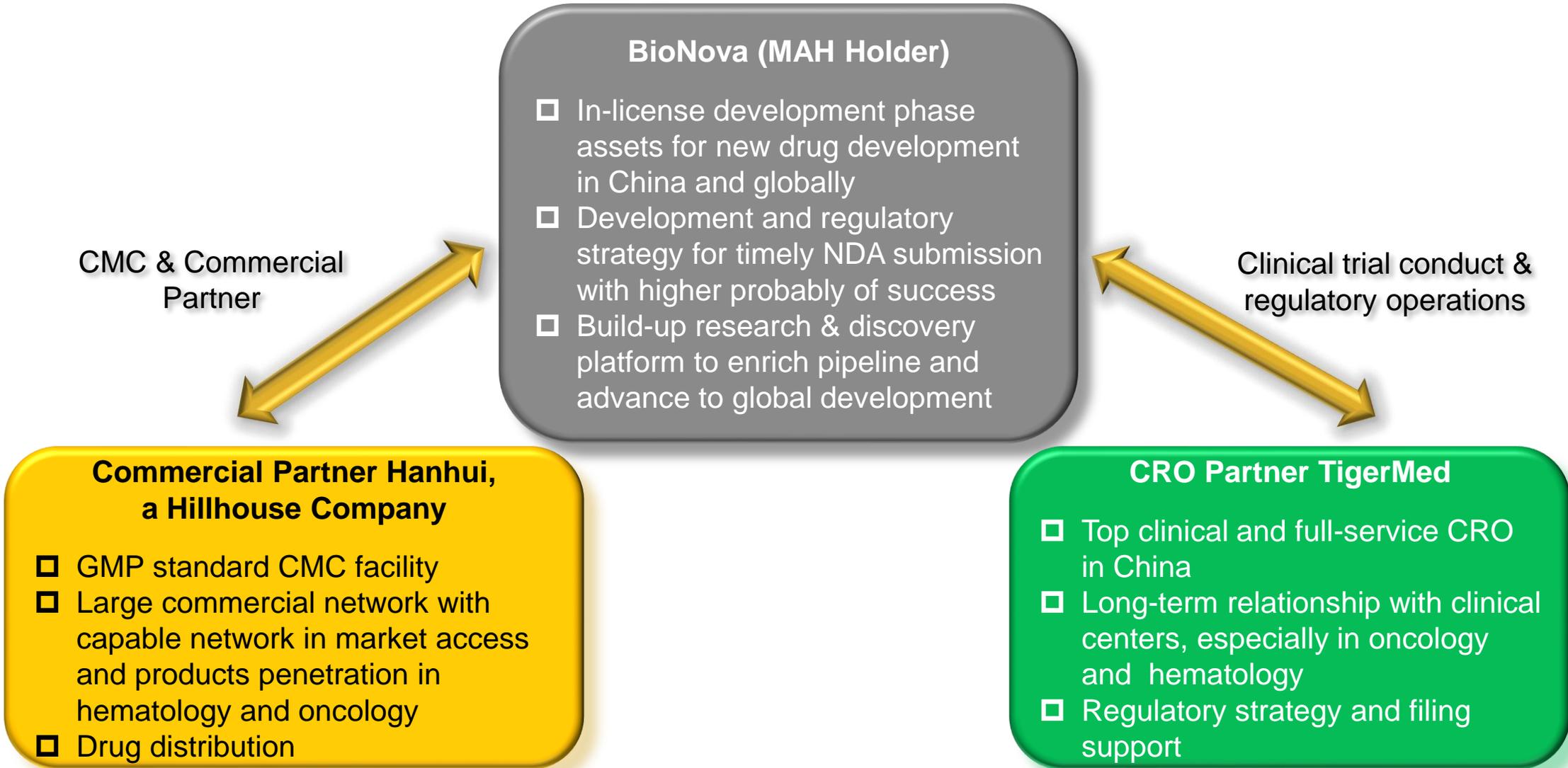


# Current Pipeline (as of June 2020)

Product Candidate	Target	Indication	Discovery	IND Enabling	Phase 1	Phase 2	Phase 3	Commercial Rights
BN101/ KD025	ROCK2	cGVHD, aGVHD					China	
BN102	BTK (reversible)	CLL/SLL, MCL, WM, MZL						China
BN103	Undisclosed	Hematology						Global
BN104	Undisclosed	Hematology						Global



# Efficient VIC Operating Model





# Management with Track Record

# Seasoned Management Team

## □ Ye Hua, MD, MPH, Chairman and CEO

- Over 20 years of experience in clinical development and regulatory submissions in global 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, CFO and Chief Strategy Officer

- Over 20 years of experience in pharmaceutical industry and healthcare investment banking
- Recently 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 Shanghai 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 research physician for new drug development in hematology
- Former Medical Director at FusonKite, leading CAR-T program

## □ Wenwu Huang, Head of Regulatory Affairs

- Over 15 years' experience in domestic pharmaceutical industry
- Former Deputy GM of Shanghai Shyndec Pharmaceutical Co. Ltd R&D center

## □ 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).



# Track Record

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 Der Zhen-dong Chen, MD; Haijun Zhong, MD; Hongming Pan, MD, PhD; Weijian Guo, MD; Yongqian Shu, MD; Ying Yuan, MD, PhD; Jianfeng Z Nong Xu, MD; Tianshu Liu, MD; Dong Ma, MD; Changping Wu, MD; Ying Cheng, MD; Donghui Chen, MD; Wei Li, MD; Sanyuan Sun, MD; Z Peiguo Cao, MD; Haihui Chen, MD; Jiejun Wang, MD; Shubin Wang, MD; Hongbing Wang, MD; Songhua Fan, MD; **Ye Hua, MD, MPH**; Weig

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

Clinical Trials: Targeted Therapy

Clinical  
Cancer  
Research

## First-in-Human Phase I Study of the Selective MET Inhibitor, Savolitinib, in Patients with Advanced Solid Tumors: Safety, Pharmacokinetics, and Antitumor Activity

Hui K. Gan<sup>1,2,3</sup>, Michael Millward<sup>4</sup>, **Ye Hua**<sup>5</sup>, Chuan Qi<sup>5</sup>, Yang Sai<sup>5</sup>, Weiguo Su<sup>5</sup>, Jian Wang<sup>5</sup>, Lilin Zhang<sup>5</sup>, Melanie M. Frigault<sup>6</sup>, Shethah Morgan<sup>7</sup>, Liu Yang<sup>8</sup>, and Jason D. Lickliter<sup>9,10</sup>



JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized, Double-Blind, Placebo-Controlled, Multicenter Phase II Study of Fruquintinib After Two Prior Chemotherapy Regimens in Chinese Patients With Advanced Nonsquamous Non–Small-Cell Lung Cancer

Shun Lu, Jianhua Chang, Xiaoqing Liu, Jianhua Shi, You Lu, Wei Li, Jin-ji Yang, Jianying Zhou, Jie Wang, Tongtong An, Lei Yang, Zhe Liu, Xiangdong Zhou, Mo Chen, **Ye Hua**, and Weiguo Su

## 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,<sup>1</sup> Arthur F. Kavanaugh,<sup>2</sup> John T. Sharp,<sup>3</sup> Hyman Tannenbaum,<sup>4</sup> **Ye Hua**,<sup>5</sup> Leah S. Teoh,<sup>5</sup> Steven A. Fischkoff,<sup>5</sup> and Elliot K. Chartash<sup>5</sup>



# Triple Jump - Pipeline Build-up and Growth Strategy

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## □ **“Jump start” with licensing in clinical or IND-ready assets**

- Quickly build-up pipeline with near-term clinical catalysts
- Focus on China right in areas that present with huge unmet medical needs but less “crowded”
- Innovative development and regulatory pathways that add value to partners

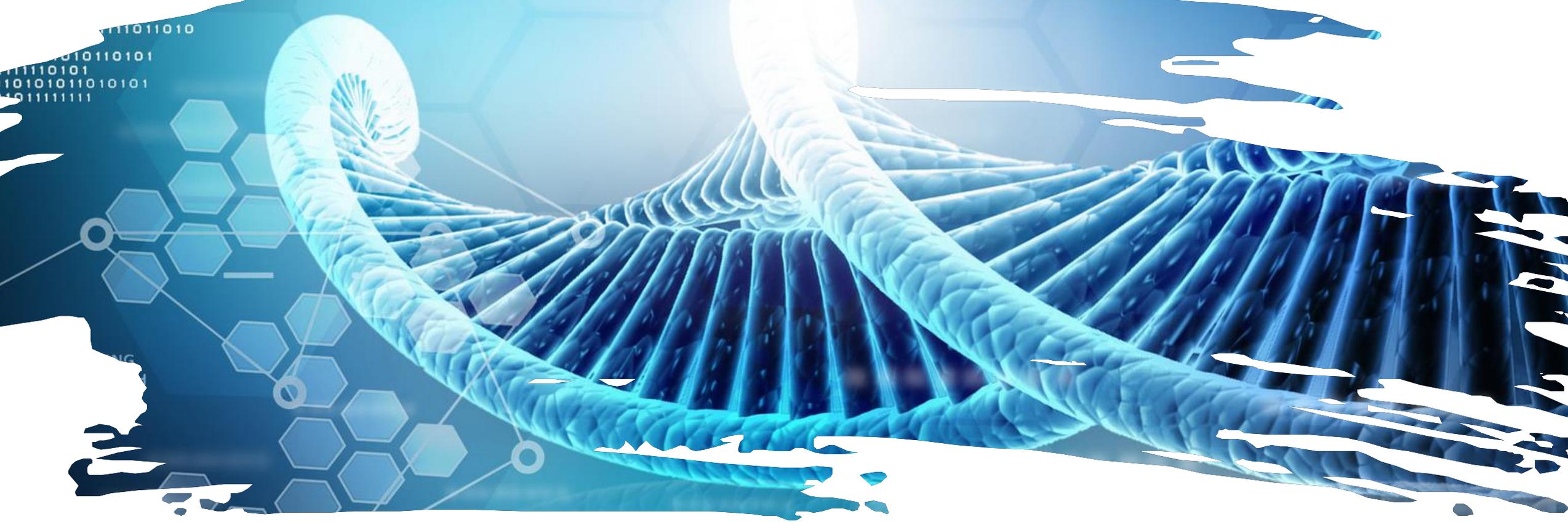
## □ **“Walking with 2 legs” by selective discovery for novel targets**

- Carefully chosen targets with proven biology and fast to market potential
- Speedy discovery by capable partners with track record and capabilities
  - 1 year to PCC
  - 1.5 to 2 years to IND
- Limited investment with fully owned IP and substantial upside

## □ **Biotech with global presence**

- US IND for “home grown” novel target agents for global simultaneous development
- Out-licensing opportunities for ex-China development and commercialization



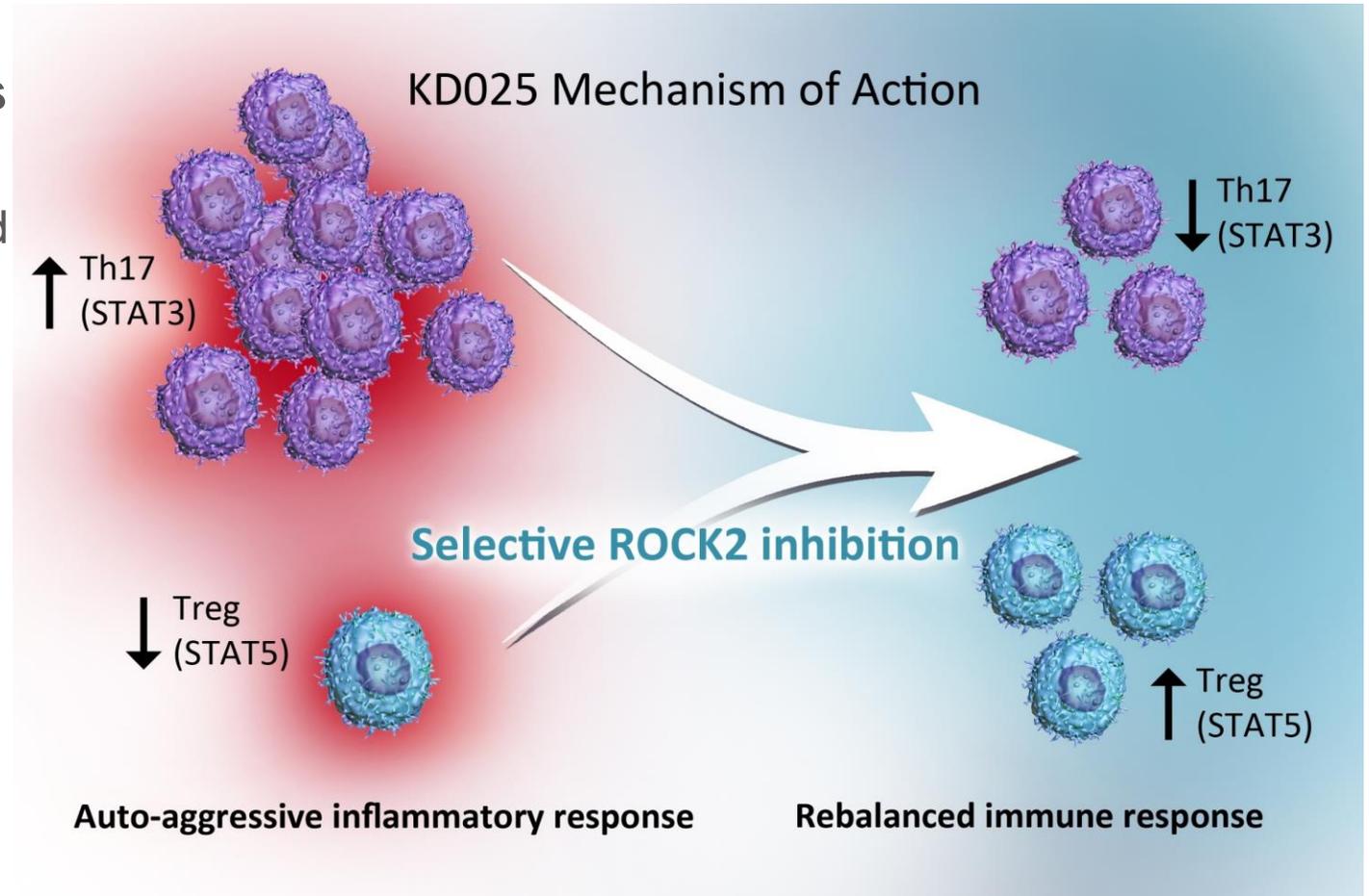


**BN101**

FDA and NMPA Breakthrough Therapy Designation for cGVHD

# BN101 / KD025 – A selective ROCK2 Inhibitor

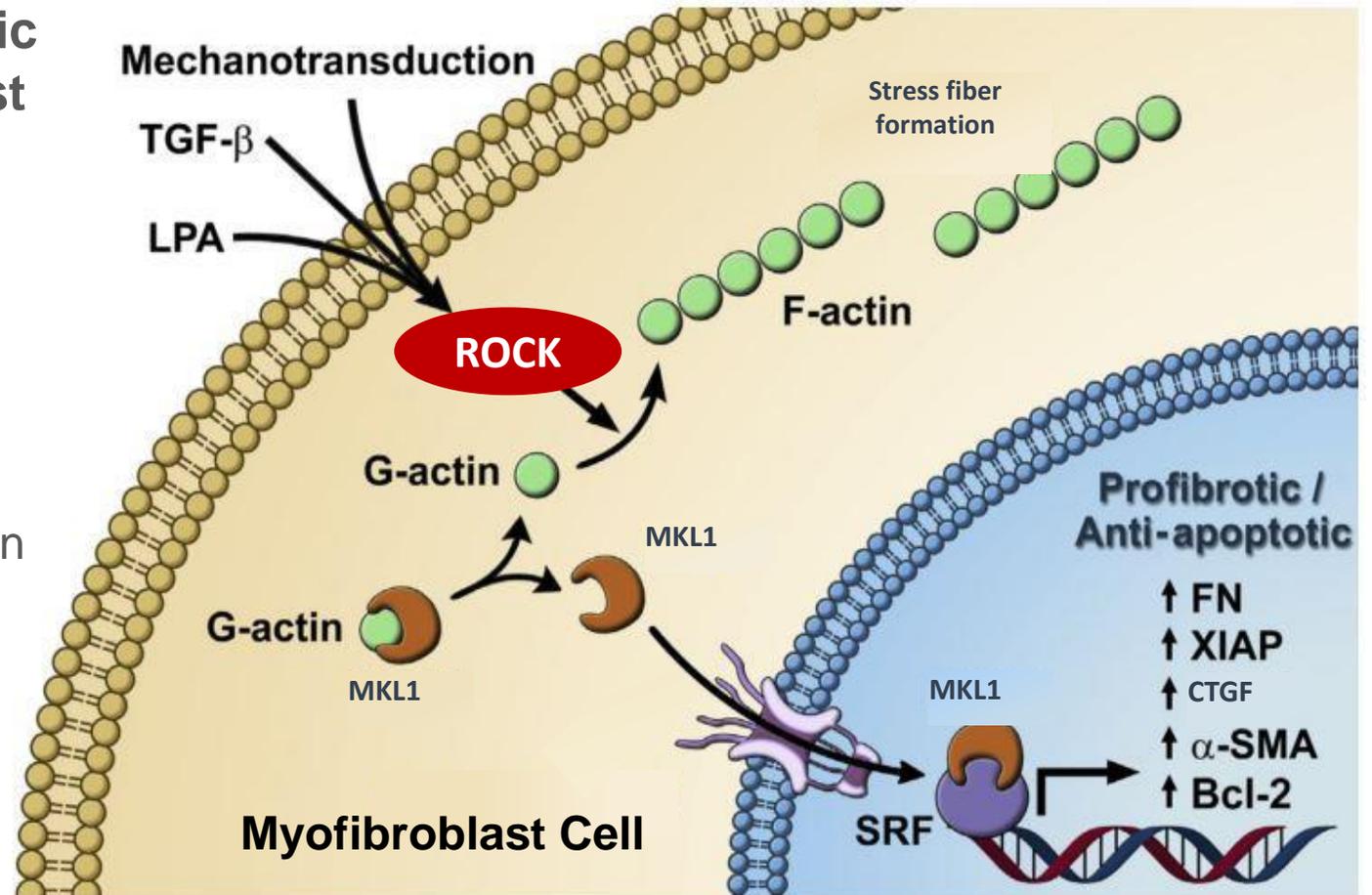
- ROCK2 inhibition downregulates pro-inflammatory Th17 responses and increases Treg function
  - Reduces STAT3 phosphorylation and increases STAT5 phosphorylation
- ROCK2 inhibition re-establishes immune homeostasis



# 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



# BN101/KD025 Clinical Development Summary

CT Code	Phase	Objective	Status
SLx-2119-09-01	Phase 1	Dose-Escalating, Safety, Tolerability, and PK Study in Healthy Male Subjects	Completed
KD025-101	Phase 1	Dose-Escalating Study to Examine the Safety and Tolerability of KD025 in Healthy Male Subjects	Completed
KD025-102	Phase 1	Dose-Escalating Study to Examine the Safety and Tolerability of KD025 in Healthy Male and Post-Menopausal Female Subjects	Completed
KD025-103	Phase 1	Study to Examine the Safety, Tolerability, and Pharmacokinetics of 500 mg KD025 Administered Twice Daily in Healthy Male and Post-Menopausal Female Subjects	Completed
KD025-105	Phase 1	Study to Examine the Safety, Pharmacokinetics, and Food Effect of 500 mg KD025 Administered Orally in Fed and Fasted States to Healthy Male Subjects	Completed
KD025-106	Phase 1	Study to Compare the Bioavailability of KD025 Tablet and Capsule in Healthy Male Subjects	Completed
KD025-107	Phase 1	Study to Evaluate the Effect of Itraconazole, Rifampicin, Rabeprazole and Omeprazole on the Pharmacokinetics of KD025	Completed
KD025-108	Phase 1	Study to assess the absolute bioavailability of KD025 and to determine the mass balance recovery, metabolite profile and identification of metabolite structures for [14C]-KD025 in healthy male subjects	Completed
KD025-109	Phase 1	Hepatic Impairment Study in Subjects With Normal Hepatic Function and Subjects With Varying Degrees of Hepatic Impairment	Ongoing
KD025-208	Phase 2	Study to Evaluate the Safety, Tolerability, and Activity of KD025 in Subjects With Chronic Graft Versus Host Disease	Completed
KD025-213	Phase 2	Study to Evaluate the Efficacy and Safety of KD025 in Subjects With cGVHD After At Least 2 Prior Lines of Systemic Therapy	Ongoing
KD025-110	Phase 1	Randomized, double-blind, placebo-control complete QT study in healthy volunteers	Ongoing
BN101-101	Phase 1	Randomized, double-blind, placebo-control single ascending dose study in healthy volunteers	Completed



# GVHD: A Debilitating Disease with High Unmet Need

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- Despite recent progress in the treatment of hematologic malignancies, bone marrow transplant remains the mainstay curative treatment
- With the emergence of highly effective CAR-T cell therapy, the number of patients eligible for allogeneic stem cell transplant will grow significantly
- Graft versus Host Disease (GVHD) is a major complication post transplant. It is a serious, life threatening complications which often lead to multiple organ injuries and even to patient death.
- Acute GVHD (aGVHD) usually occurs within weeks or up to 100 days post transplant. Chronic GVHD (cGVHD) usually develops 3-6 months post transplant with or without prior aGVHD and can persist for years
- Approximately 30%-70% of stem cell transplant patients will develop a chronic form of GVHD with or without preexisting aGVHD
- Current standard care remains empirical with corticosteroid being the first line therapy albeit serious side effects. More recently, targeted therapies such BTK inhibitor and JAK inhibitor have shown promising results in clinical trials, and ibrutinib has been approved in the US for relapsed/refractory cGVHD



# Spectrum of Manifestations in Chronic GVHD

Ocular sicca

Oral ulcers

Nail dystrophy

Skin sclerosis

Deep sclerosis

Bronchiolitis obliterans

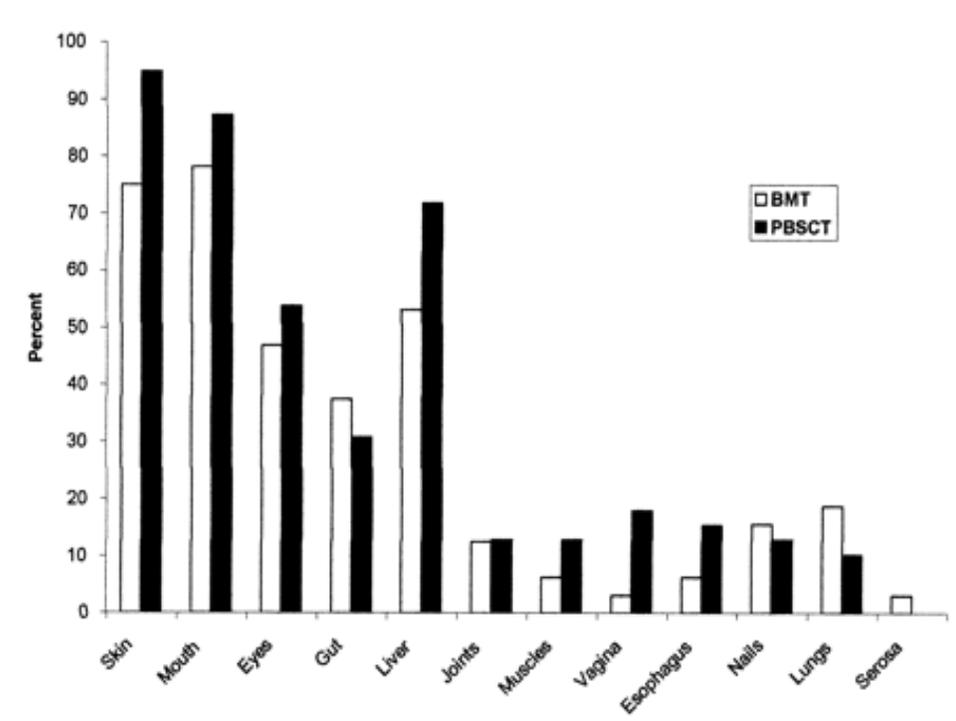
Loss of bile ducts

Fasciitis

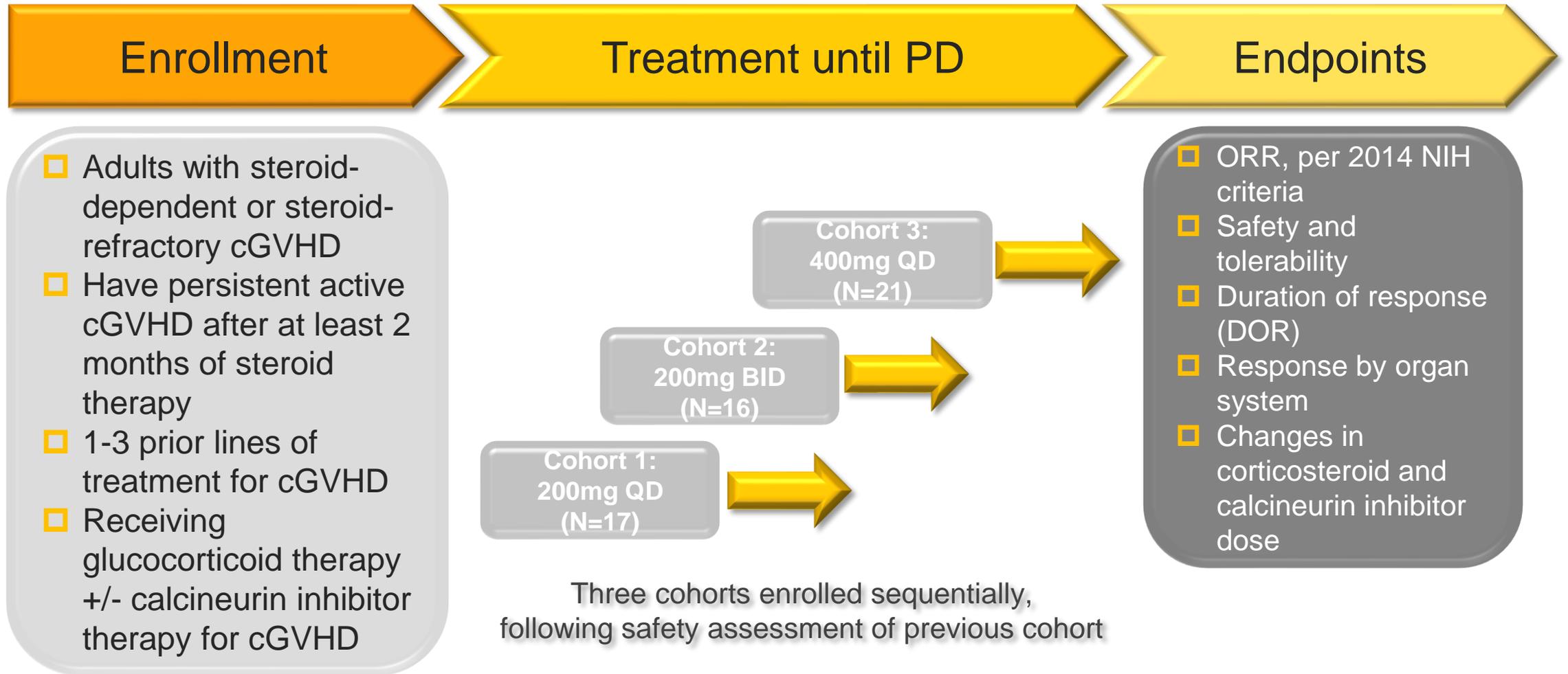
Skin ulcers

Infections  
Disability  
Quality of life  
Endocrine  
Metabolism  
Nutrition  
Pain

cGVHD involves multiple organs



# KD025-208: PoC Trial in cGVHD



# KD025-208: Demographics and Baseline Characteristics

Demographics and Baseline Characteristics	Cohort 1 200 mg QD (N=17)	Cohort 2 200 mg BID (N=16)	Cohort 3 400 mg QD (N=21)
Median age [years (range)]	50 (20-63)	55 (30-75)	46 (25-75)
Male (%)	76	56	57
Median time cGVHD diagnosis to study (months)	26	18	16
Organ involvement, n (%)			
≥4 organs involved	8 (47)	10 (63)	9 (43)
Eyes	14 (82)	11 (69)	17 (81)
Skin	13 (76)	12 (75)	15 (71)
Mouth	13 (76)	11 (69)	11 (52)
Joints and fascia	11 (65)	11 (69)	12 (57)
Lungs	4 (24)	3 (19)	10 (48)
Upper GI	2 (12)	4 (25)	2 (10)
Esophagus	2 (12)	0 (0)	4 (19)
Lower GI	1 (6)	2 (13)	1 (5)
Liver	0 (0)	2 (13)	0 (0)

50% of all patients had ≥4 organs affected - included both inflammatory and fibrotic manifestations



# KD025-208: Baseline Severity and Prior Therapies

Demographics and Baseline Characteristics	Cohort 1 200 mg QD (N=17)	Cohort 2 200 mg BID (N=16)	Cohort 3 400 mg QD (N=21)
Severe cGVHD <sup>1</sup> , n (%)	12 (71)	14 (88)	16 (76)
Median prednisone dose at BL (mg/kg/day)	0.22	0.19	0.15
Prior lines of therapy <sup>2</sup>			
Median	3	2	2
≥2 prior lines of therapy, n (%)	15 (88)	8 (50)	12 (57)
Refractory to prior line of therapy <sup>3</sup> , n (%)	11/15 (73)	9/13 (69)	15/20 (75)

<sup>1</sup>Defined as at least 1 organ with NIH Activity Assessment score of 3, or lung score ≥2 at baseline

<sup>2</sup>ECP was not counted as a prior systemic therapy

<sup>3</sup>Status unknown for 6 subjects

- 65% of all patients had received ≥2 prior lines of cGVHD therapy
- 73% refractory to prior line of therapy<sup>3</sup>

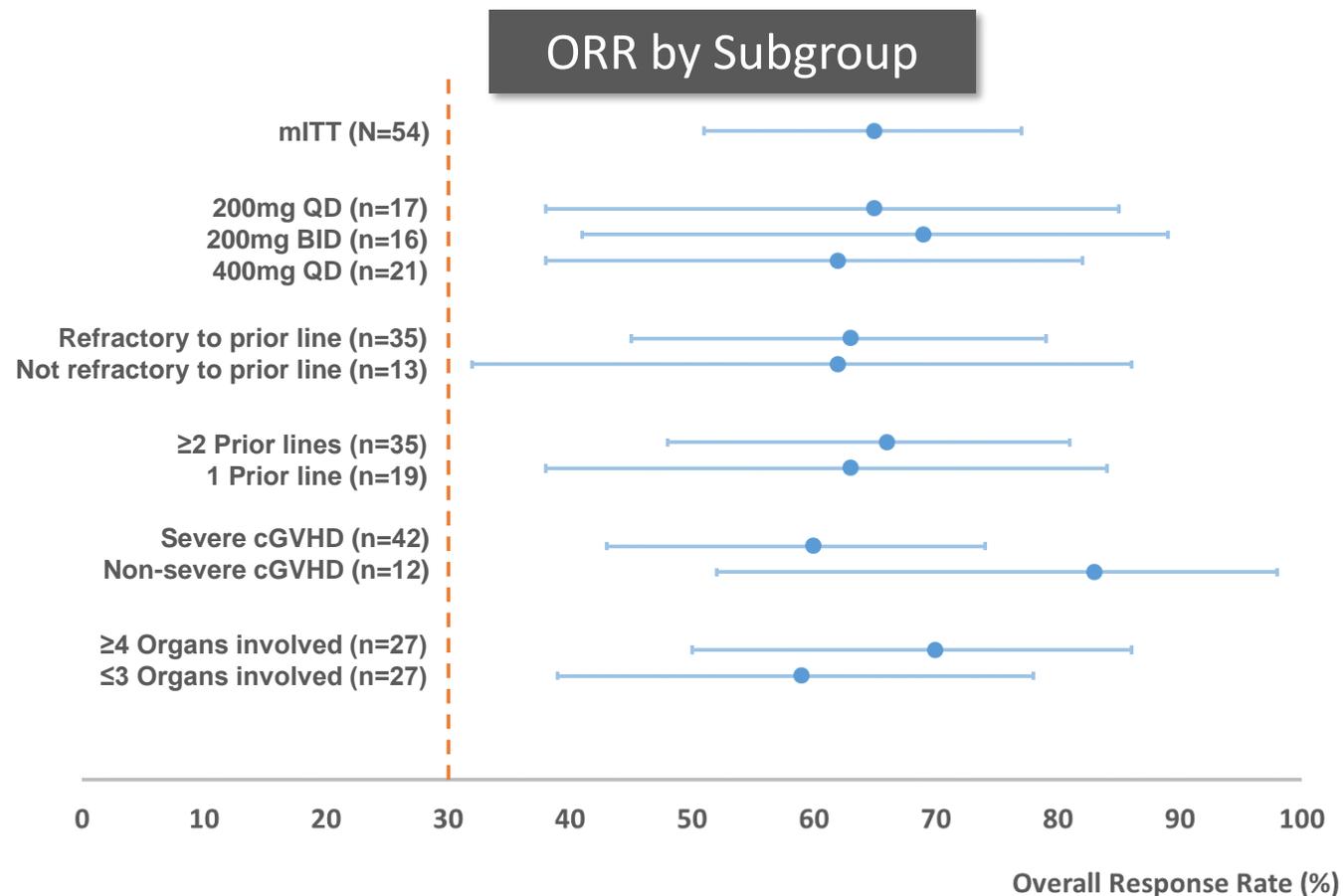


# KD025-208: Overall Response Rate (ORR)

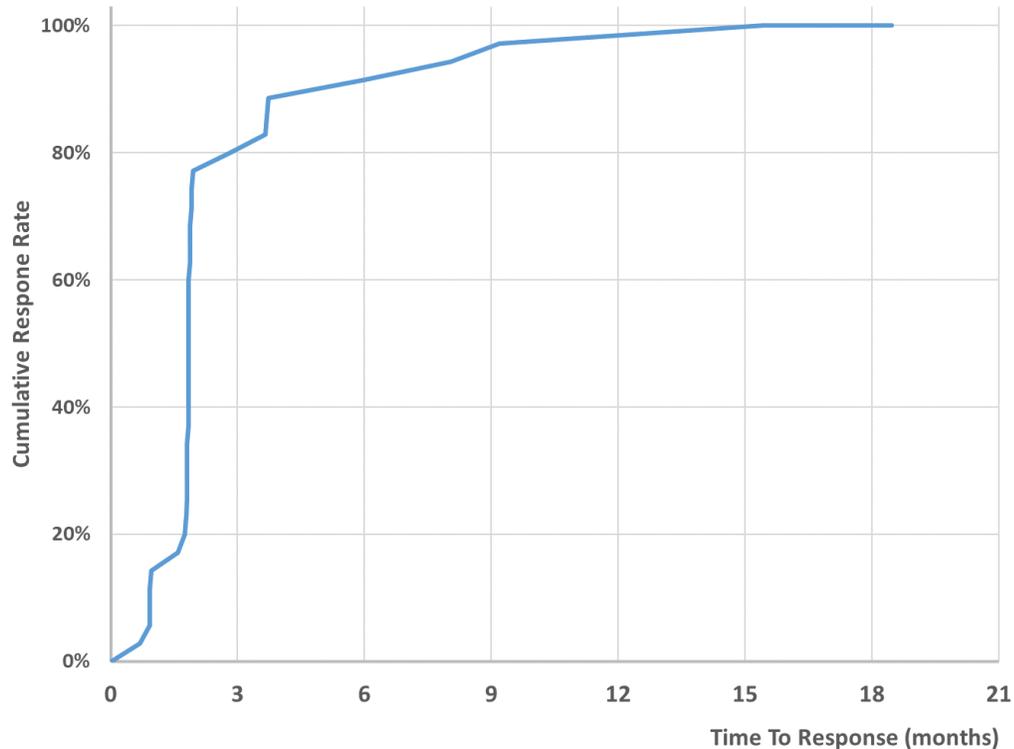
Cohort	N	ORR	95% CI
mITT	54	65%	(51, 77)
200 mg QD	17	65%	(38, 86)
200 mg BID	16	69%	(41, 89)
400 mg QD	21	62%	(38, 82)

## Responses observed across key subgroups

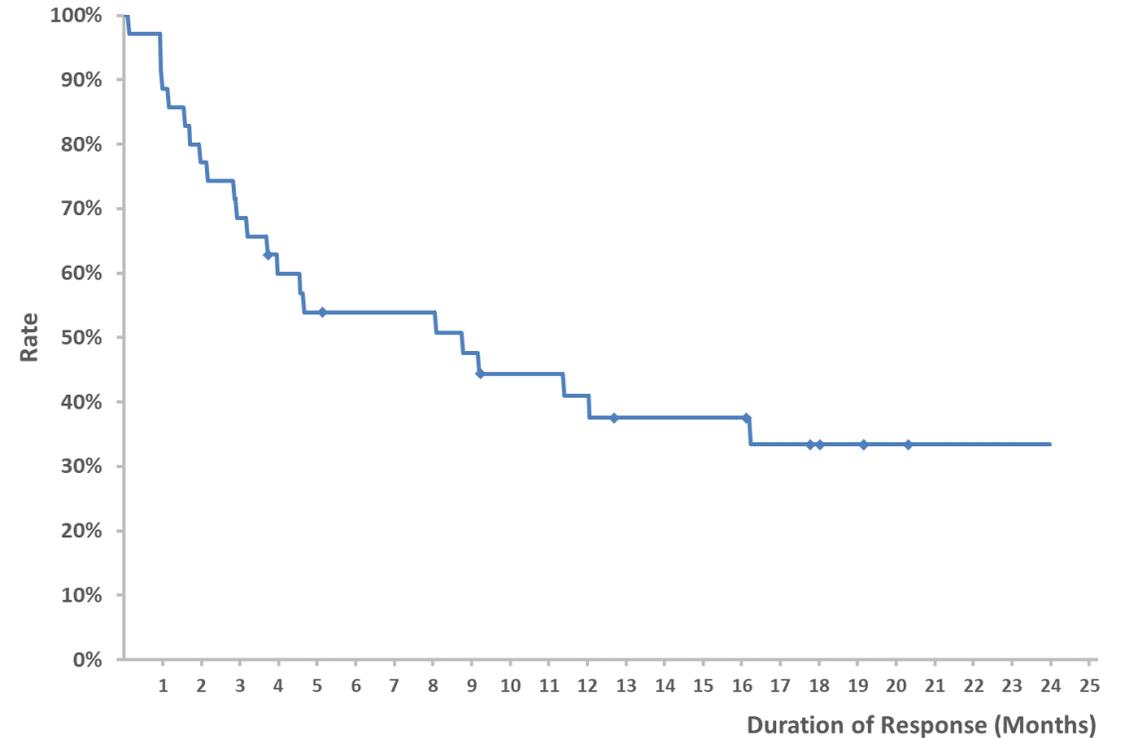
- ☐ Refractory to prior line: 63%
- ☐ ≥2 Prior lines of therapy: 66%
- ☐ Severe cGVHD: 60%
- ☐ ≥4 Organs involved: 70%



# KD025-208: Timely and Durable Response



Amongst responders, 75% of responses occurred by week 8 assessment



Median DoR of 35 weeks (8 months) in mITT responders with 51% maintained for  $\geq 20$  weeks



# KD025-208: Corticosteroid Dose Reduction during Therapy

Cohort	Cohort 1 (N=17) n (%)	Cohort 2 (N=16) n (%)	Cohort 3 (N=21) n (%)
Patients with corticosteroid dose reduction	13 (76)	9 (56)	13 (62)
Responders, % (n)	75 (n=11)	55 (n=11)	65 (n=13)
Non-Responders, % (n)	21 (n=6)	33 (n=5)	0 (n=8)

- ❑ 19% of patients have completely discontinued corticosteroids
- ❑ 65% achieved corticosteroid dose reductions
- ❑ Median corticosteroid dose reduction: 50%
- ❑ Corticosteroid dose reductions observed in responders and non-responders



# KD025-208: Safety and Tolerability

Safety Overview	Cohort 1 (N=17) n (%)	Cohort 2 (N=16) n (%)	Cohort 3 (N=21) n (%)	ITT (n=54) n (%)
Median weeks of treatment	37	33	39	36
Any Adverse Event (AE)	17 (100)	16 (100)	20 (95)	53 (98)
Grade 3/4 AE	9 (53)	11 (69)	10 (48)	30 (56)
SAE	5 (29)	6 (38)	12 (57)	23 (43)
Drug related AE				
Any related AE	7 (41)	9 (56)	14 (67)	30 (56)
Related AE leading to discontinuation <sup>1</sup>	2 (12)	0	1 (5)	3 (6)
Related Grade ≥3 event	1 (6)	4 (25)	2 (10)	7 (13)

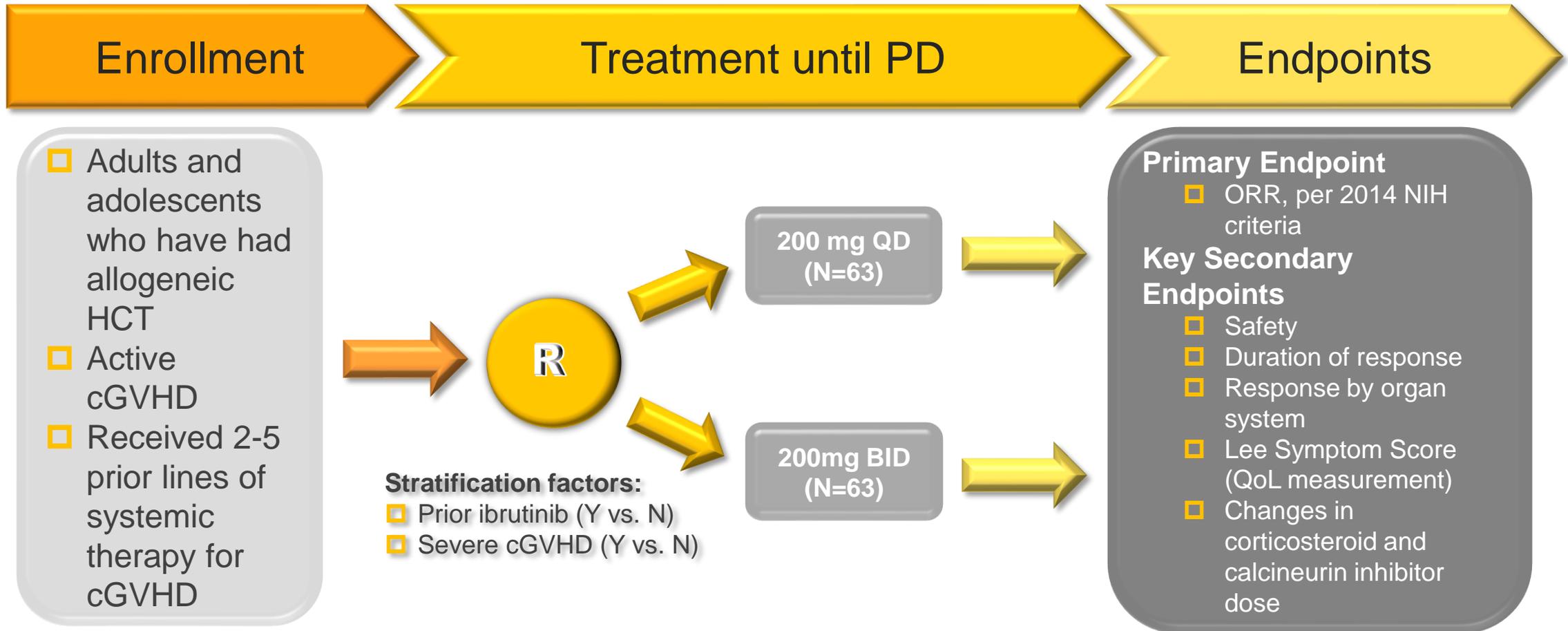
<sup>1</sup> Cohort 1: Headache; Diarrhea. Cohort 3: Fatigue

- AEs were overall consistent with those expected in cGVHD patients receiving corticosteroids
- No apparent increased risk of infection
  - No CMV infection reported
  - No significant drug-related cytopenias

Commonly reported AE n (%)	Cohort 1 (N=17) n (%)	Cohort 2 (N=16) n (%)	Cohort 3 (N=21) n (%)	ITT (n=54) n (%)
All Grade AE (≥20%)				
Upper respiratory tract infection	9 (53)	9 (56)	7 (33)	25 (46)
Diarrhea	6 (35)	5 (31)	7 (33)	18 (33)
Nausea	6 (35)	4 (25)	8 (38)	18 (33)
ALT/AST increased (SMQ Broad)	8 (47)	7 (44)	3 (14)	18 (33)
Fatigue	5 (29)	3 (19)	9 (43)	17 (32)
Dyspnea	3 (18)	6 (38)	7 (33)	16 (30)
Headache	4 (24)	3 (19)	6 (29)	13 (24)
Edema	3 (17)	4 (25)	6 (29)	13 (24)
Cough	1 (6)	4 (25)	7 (33)	12 (22)
Hypertension	5 (29)	2 (13)	4 (19)	11 (20)
Grade ≥3 AE (≥5%)				
Dyspnea	1 (6)	2 (13)	5 (24)	8 (15)
Lung Infection / Pneumonia	1 (6)	2 (11)	5 (24)	8 (15)
ALT/AST increased (SMQ Broad)	2 (12)	3 (19)	0	5 (9)
Hypoxia	1 (6)	1 (6)	3 (14)	5 (9)
Hyperglycemia	2 (12)	0	2 (10)	4 (7)
Anemia	2 (12)	1 (6)	0	3 (6)

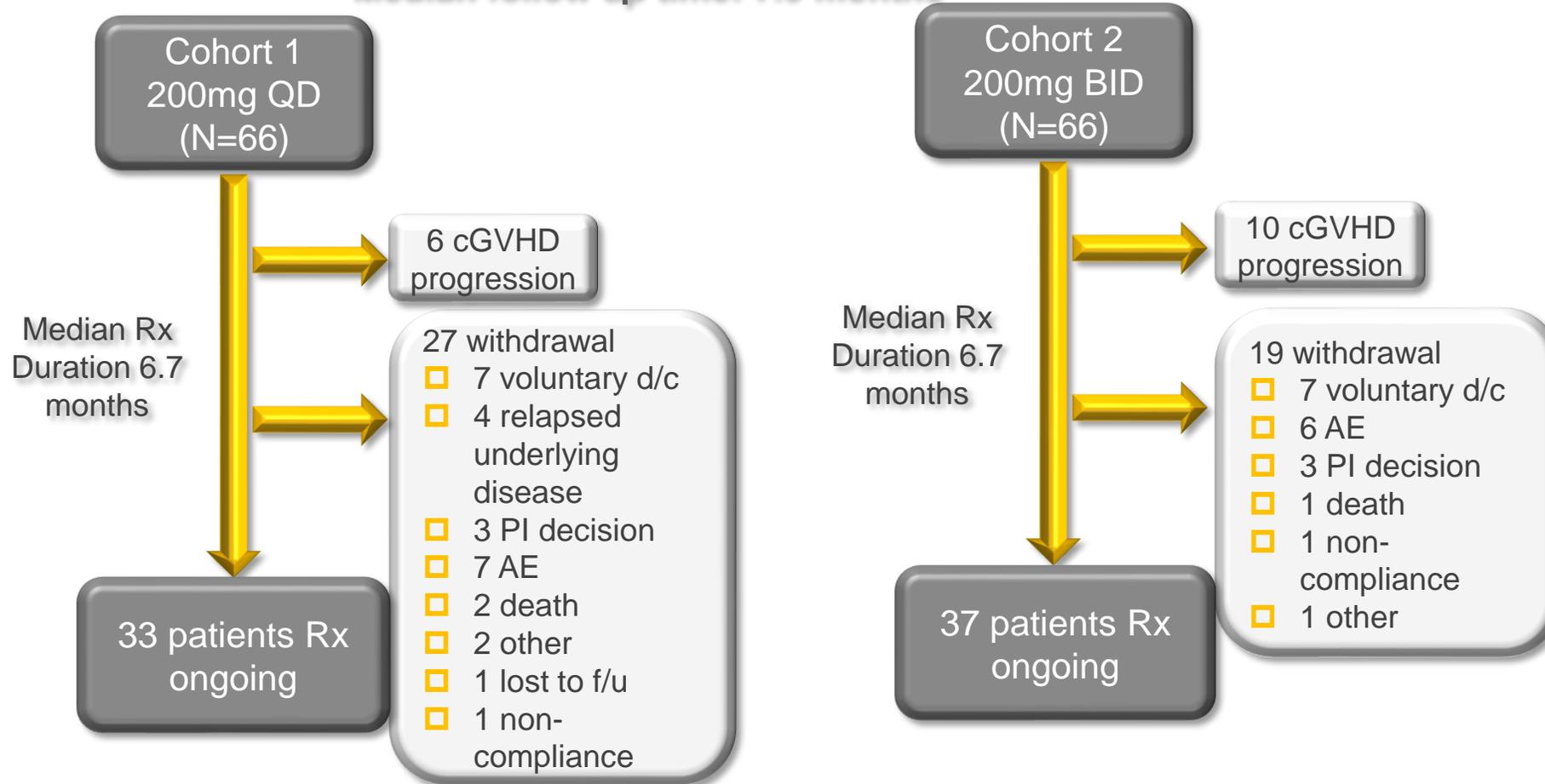


# ROCKstar (KD025-213) Registration Trial for cGVHD



# ROCKstar (KD025-213) Patient Disposition

Data as of Feb 2020  
Median follow up time: 7.9 months



# ROCKstar (KD025-213) Baseline Severity and Prior Therapies (Data as of August 2020, ASH Data)

Demographics	Belumosudil 200 mg QD (n=66)	Belumosudil 200 mg BID (n=66)
Median age, y (range)	53 (21-77)	57 (21-77)
Male, %	64	50
Median prior lines of therapy, n	3	4
Median time from cGVHD diagnosis to enrollment, mo	25	30
NIH moderate cGVHD, n (%)	18 (27)	23 (35)
NIH severe cGVHD, <sup>a</sup> n (%)	46 (70)	43 (65)
Median prednisone dose, mg/kg/d	0.19	0.20
≥4 organs involved, n (%)	33 (50)	35 (53)
Prior ibrutinib treatment, <sup>a</sup> n (%)	22 (33)	23 (35)
Prior ruxolitinib treatment, n (%)	20 (30)	18 (27)
Refractory to last prior line of systemic therapy, n (%)	44 (79)	35 (65)

<sup>a</sup>Defined as at least 1 organ with NIH Activity Assessment score of 3, or lung score ≥2 at baseline; stratification factor

- ❑ Majority of patients had received ≥2 prior lines of cGVHD therapy
- ❑ Majority of patients had ≥2 organ involved
- ❑ Majority of patients refractory to prior line of therapy

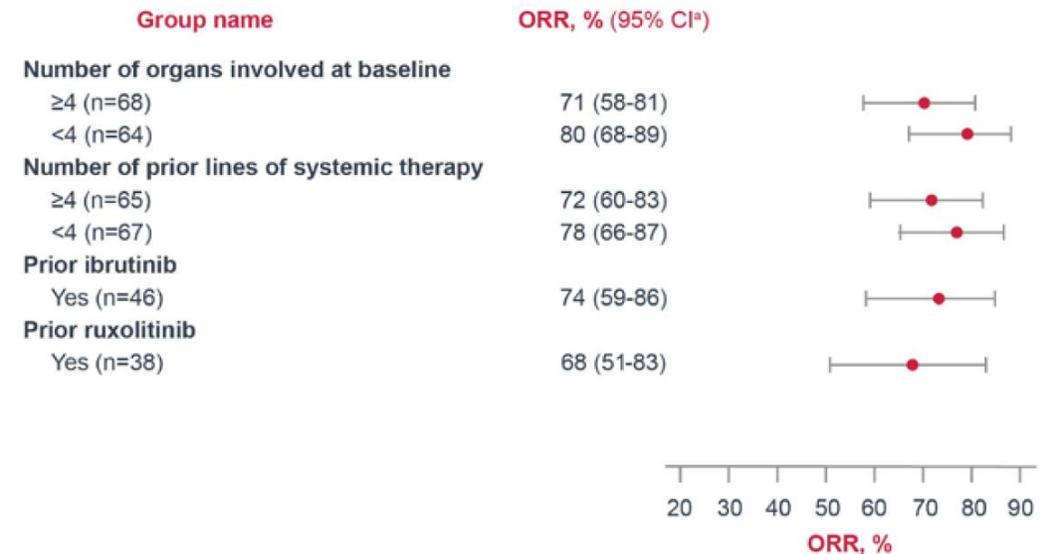
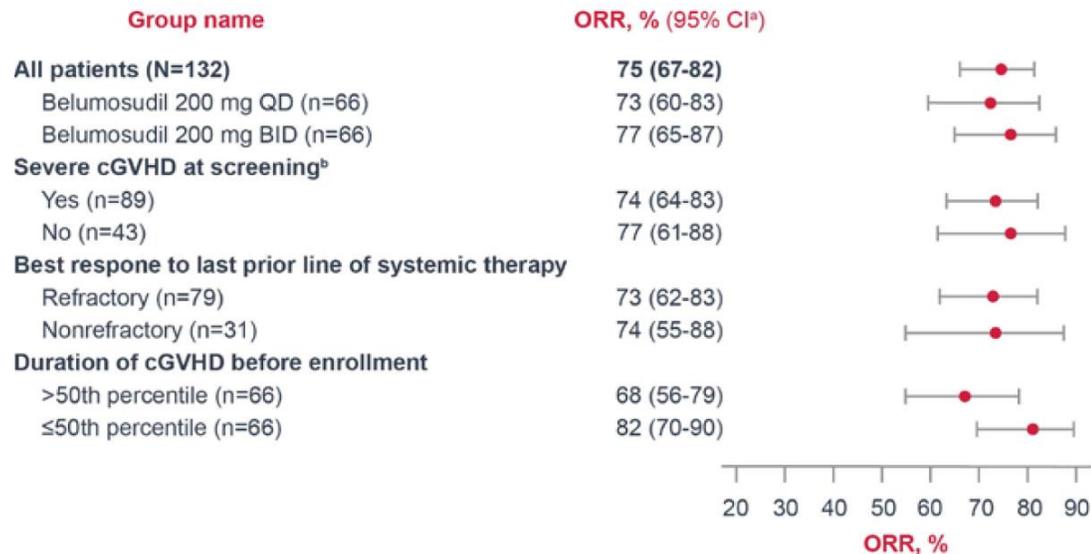


# ROCKstar (KD025-213) Results of Primary Analyses

(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 systems
- Seven patients achieved overall CR
- Consistent ORRs across all key subgroups
- Durable responses at 6 months data cut-off (median follow-up=34 weeks)
  - The median DOR was 50 weeks, and 60% of responders maintained response status for ≥20 weeks.



# ROCKstar (KD025-213) Safety and Tolerability

(Data as of August 2020, ASH Data)

Safety Overview n (%)	Cohort 1 200 mg QD (N=66)	Cohort 2 200 mg BID (N=66)	Overall (N=132)
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 <sup>1</sup>	4 (6)	4 (6)	8 (6)

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

Commonly reported AE n (%)	Cohort 1 200 mg QD (N=66)	Cohort 2 200 mg BID (N=66)	Overall (N=132)
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 (23)
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)



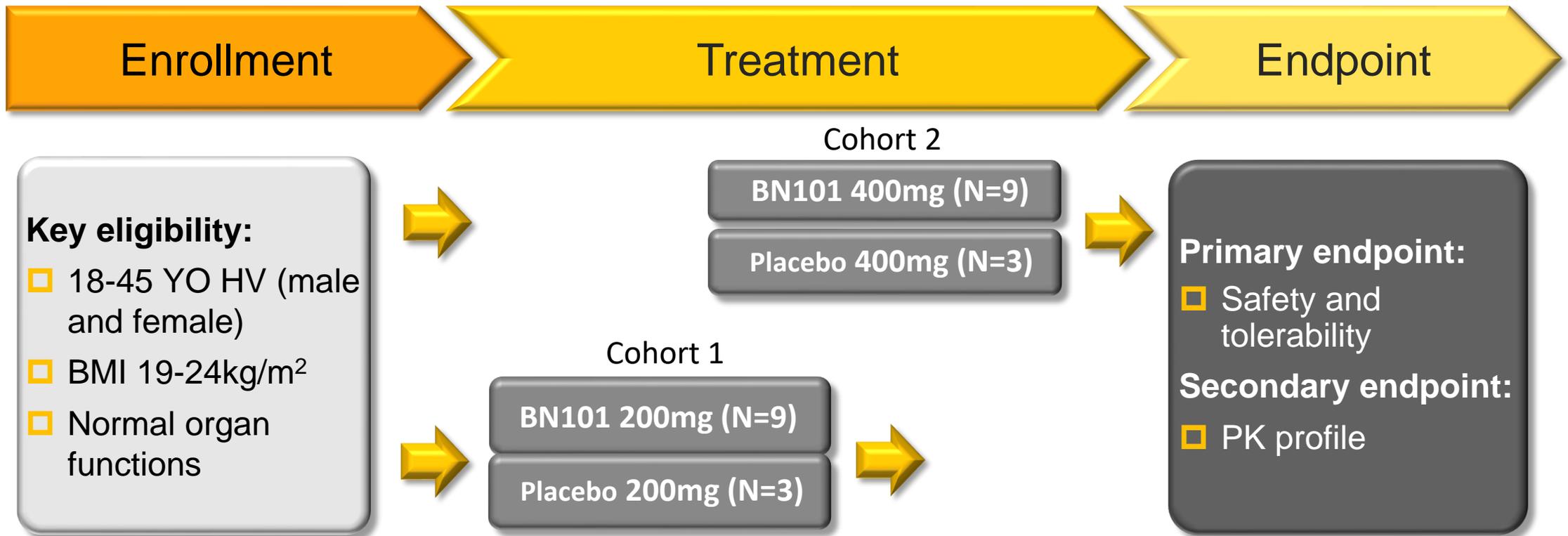
# BN101/KD025 in cGVHD: US Regulatory Pathway

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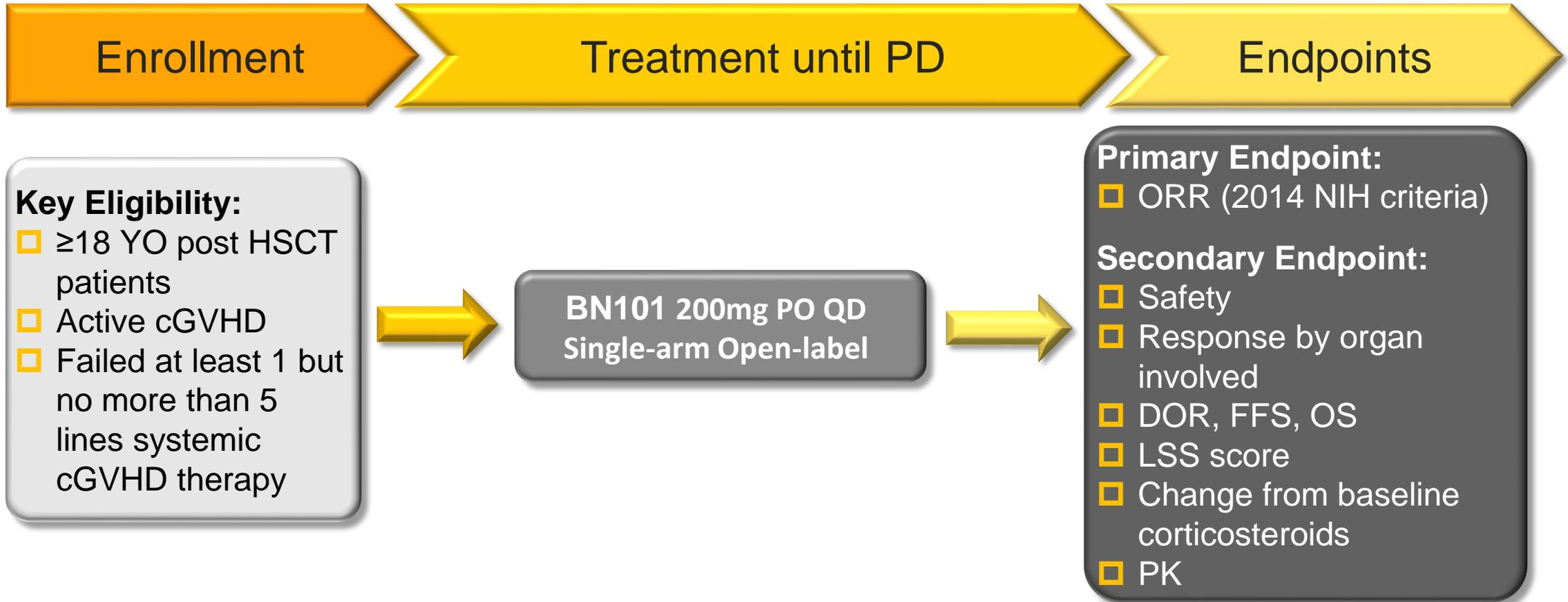
- ❑ FDA granted Breakthrough Therapy Designation in cGVHD after at least 2 prior lines of systemic therapy (Oct 2018)
- ❑ Positive pre-NDA meeting with FDA for BN101/KD025 in cGVHD 12Mar2020
- ❑ Belumosudil met the primary endpoint at the pivotal trial (KD025-213) in cGVHD with superb topline results released on 21May2020 and complete data presented at 2020 ASH annual meeting
- ❑ Kadmon completed belumosudil NDA rolling submission on 30Nov2020 under the Real-Time Oncology Review (RTOR)
- ❑ PDUFA date 30Aug2021



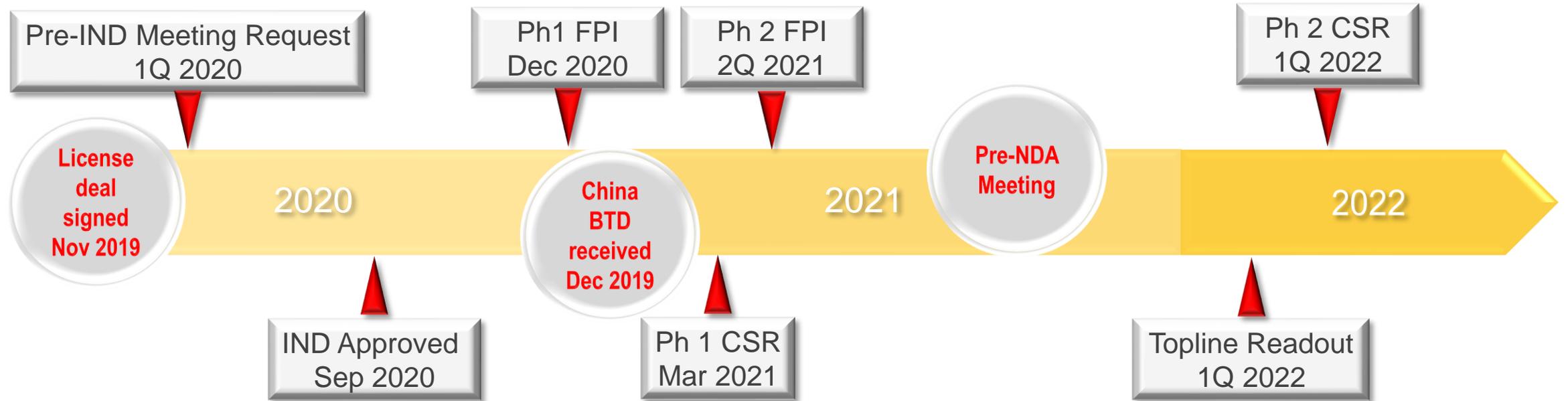
# Belumosudil China Phase 1 Healthy Volunteers' Trial (Completed)

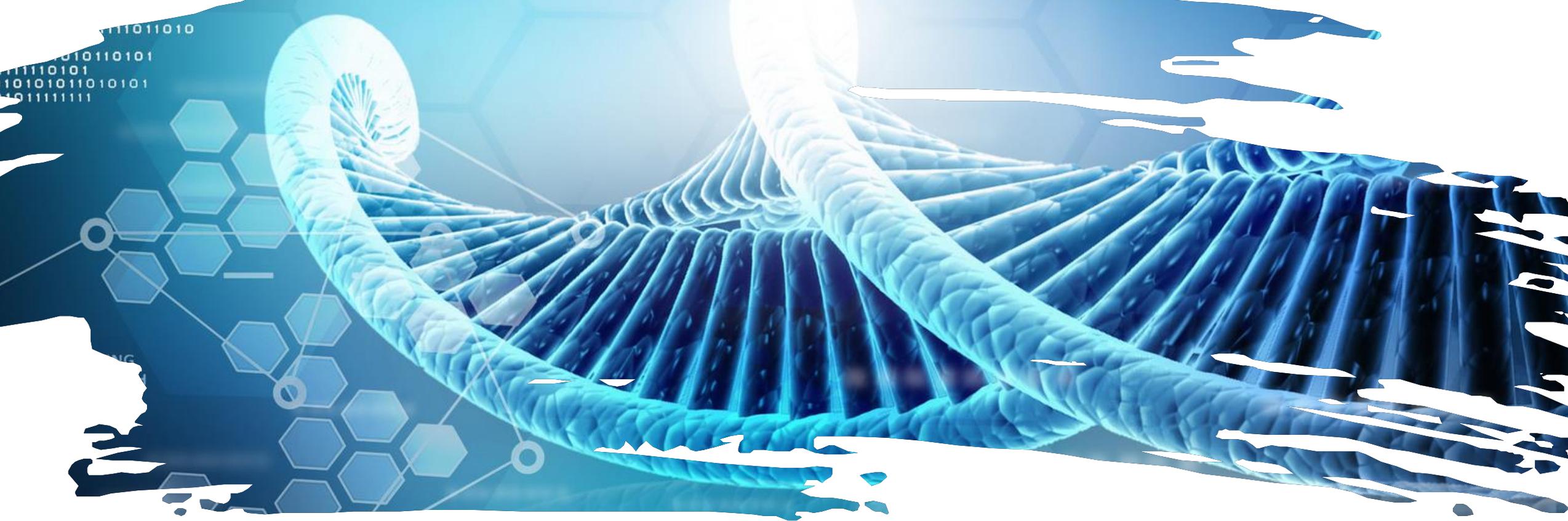


# Belumosudil China Phase 2 cGVHD Trial (Ongoing)



# Belumosudil Development Timeline in China





# BN102

A highly selective, potent reversible BTK inhibitor

# BTK - The Validated Target in B-cell Signaling Pathway

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## □ First generation covalent bound BTK inhibitors have achieved great success

- First generation BTK inhibitors are covalent bound and irreversible
- 2019 global sales were >8B USD; peak sales is expected to be >9B USD in 2024
- Irreversible BTK inhibitors are expected to become a mainstay therapy for B-cell malignancies such as CLL/SLL, MCL, MZL and WM

## □ However, acquired resistance to first generation BTK inhibitors are emerging

- C481S mutation, the most common type of treatment resistance occurs in >50% CLL patients treated with irreversible BTK inhibitors
- No effective therapy to date for patients developed C481S mutation which presents a high unmet medical need and large commercial opportunity

## □ Next generation reversible BTK inhibitors are effective against BTK WT & MT

- Currently 2 reversible BTK inhibitors are in Phase 1/2 clinical stage in the US, but none in China
- While 3 reversible BTK inhibitors are approved in China and more drugs in development stage, next generation reversible BTK inhibitor is yet to advance to clinical stage in China



# Reversible BTK Inhibitors in Development

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## □ Most advanced reversible BTKi ARQ531 (Merck/ArQule)

- Completed Phase 1 dose escalation, entering Phase 2 dose expansion
- Good response rate in relapsed/refractory CLL patients with C481S

## □ SNS-062 (Sunesis)

- Phase 1 dose escalation completed
- No responses observed; project terminated in 2020

## □ LOXO-305 (now Lilly)

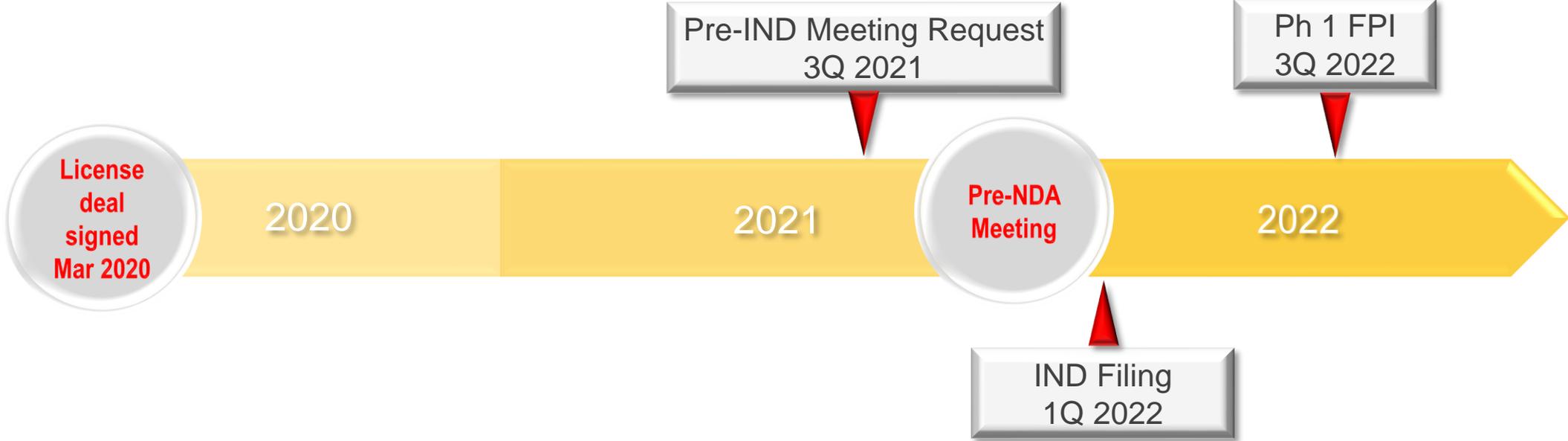
- Promising initial efficacy data presented at ASH 2020
- Safety profile appears favorable

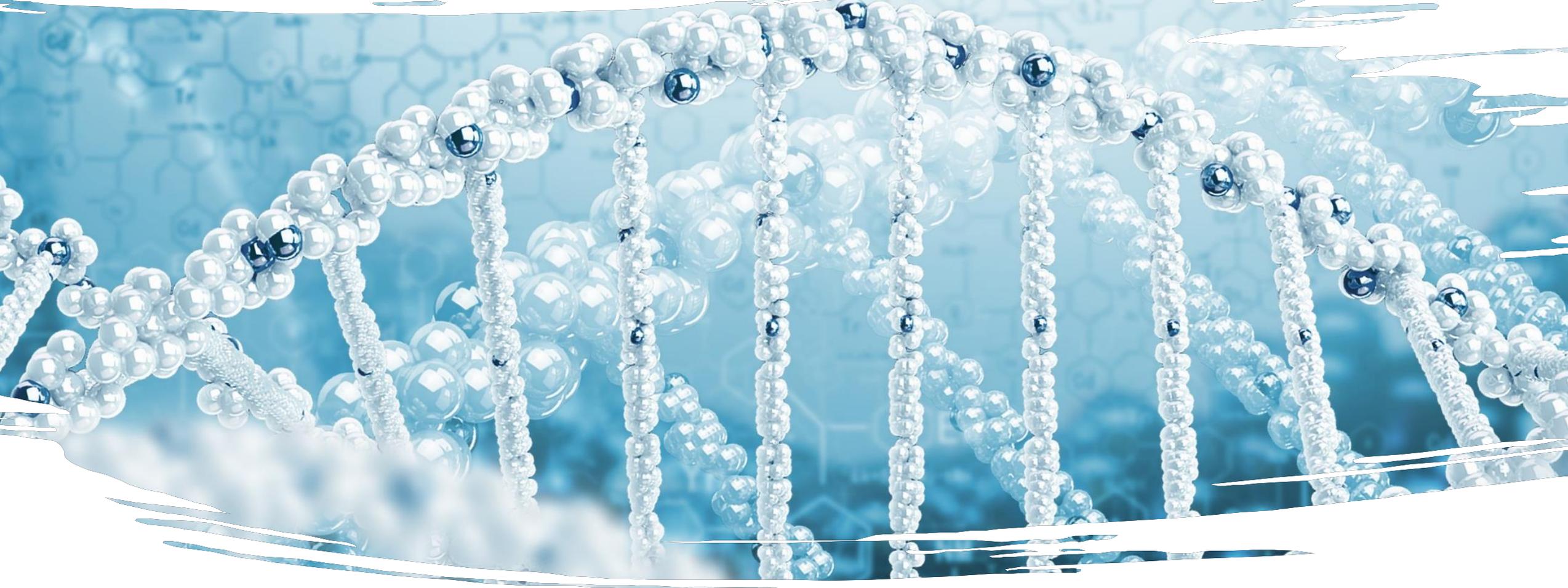
## □ **BN102** is a highly selective and potent reversible BTK inhibitor

- IND enabling stage
- EU CTA approved and Phase 1 SAD trial is to be initiated in 2Q2021 by Carina Biosciences
- China IND preparation on track in 1Q2022



# BN102 Development Timeline in China





**Thank You**