2022 WuXi AppTec Investor Day

WuXi DDSU: Enabling Innovation for Chinese Customers 2.0

Shuhui Chen, Ph.D.

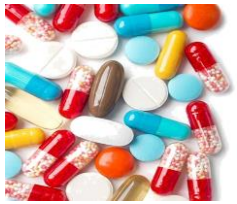
Executive Vice President, Chief Scientific Officer, Head of DDSU

Business Model of DDSU 1.0

Supporting Chinese customers with a novel integrated R&D service model centered on IP creation :

Customer needs → Target selection → **IP creation** → PCC selection → Preclinical development → **IND filing CTA**

Through IP generation and success sharing to conduct new drug R&D in exchange for future royalties, we share risk and reward with partners.



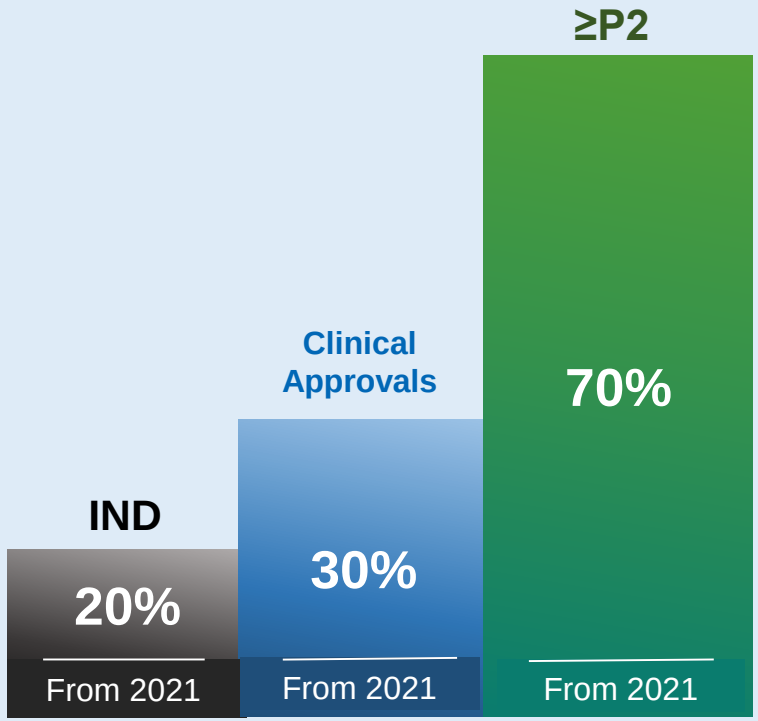
30 (IND applications) x 1/3 (success rate) x ~5% (royalty share) = **0.5** new drug

June 30, 2021 Pipeline Status

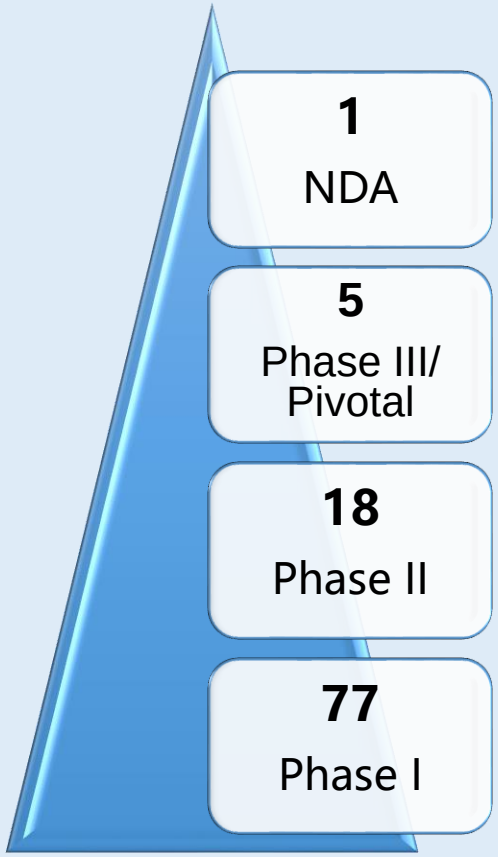
IND: **127** Clinical Approvals: **99** Phase II+: **2+12**

Pipeline Progress Greatly through June 30, 2022

153 INDs, **129** Clinical Trial Approvals, **24** projects at Phase II trials and beyond



2022.6	**153**	**129**	**24**
2021.6	127	99	14



Qilu's Iruplinalkib

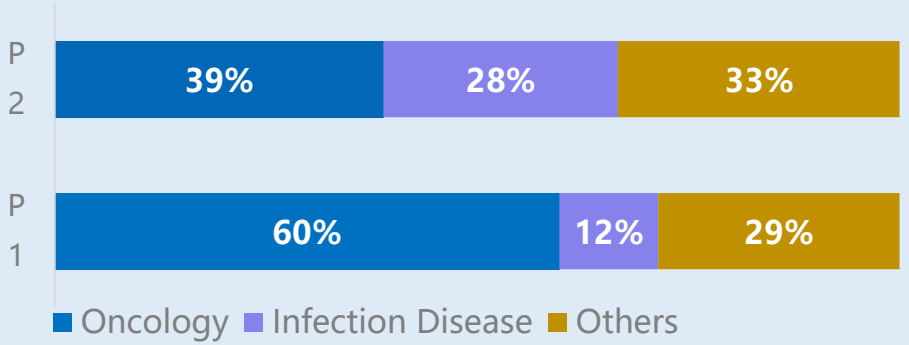
Chiatai Tianqing TQB3616

Joyo Sudapyridine

Yangtze River YZJ-1139

Chiatai Tianqing TQB3525

Zhongsheng ZSP1273



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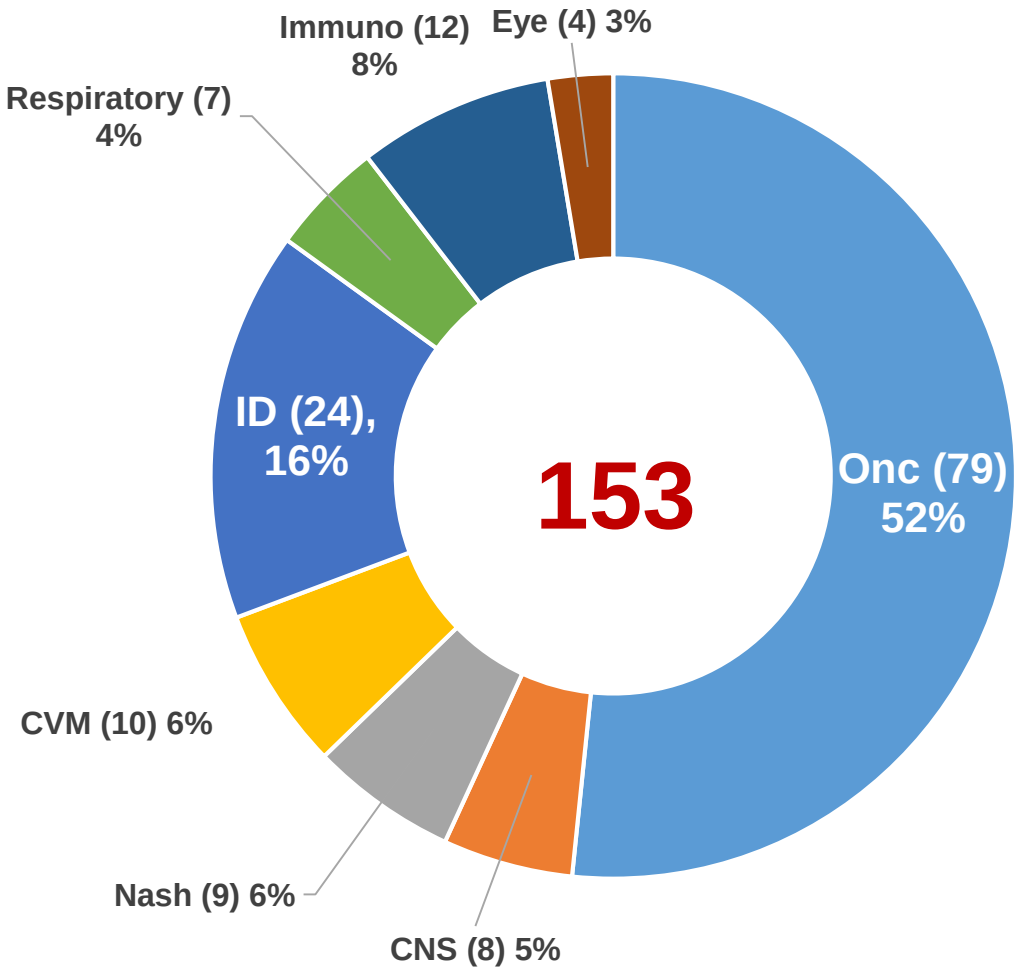
DDSU 1.0 Pipeline Breakdown

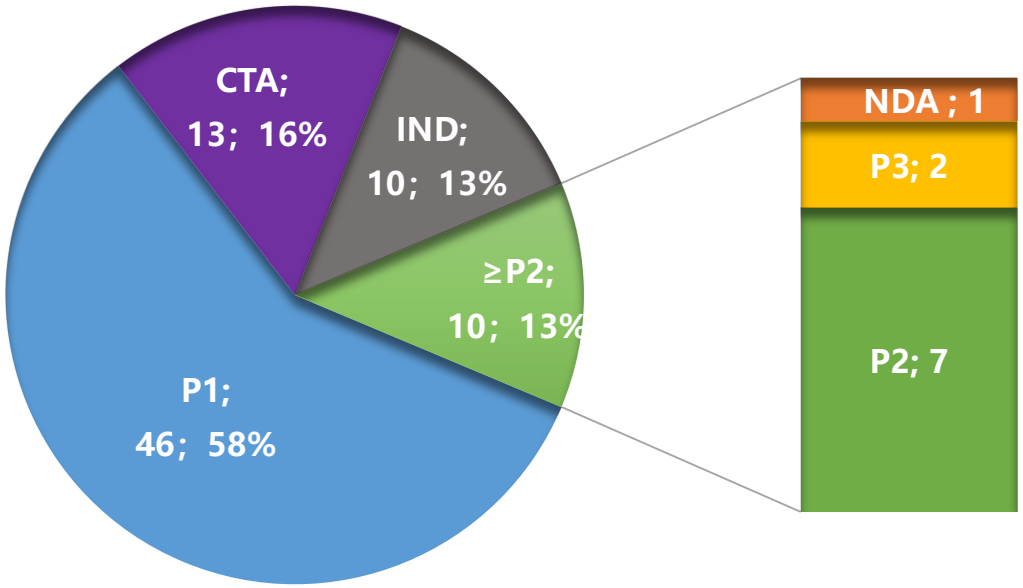


- Comprehensive tumor targets coverage
- Strengthening targets coverage in infectious diseases, metabolic and immune disorders
- Gradually expanding into CNS
- Focus on specialty diseases (respiratory, ophthalmic)

Oncology Drugs: Comprehensive Coverage

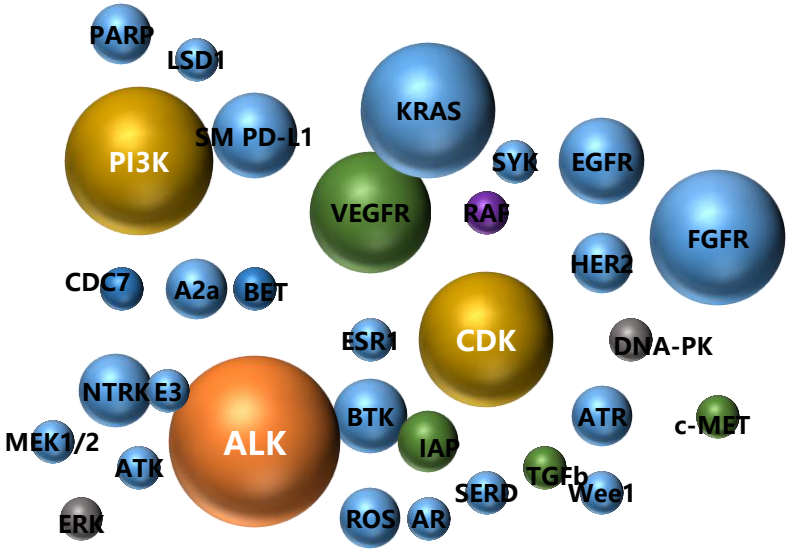
Aggregate **79** INDs, accounting for **52%** of pipeline

1 NDA, **2** ongoing pivotal clinical trials



Cover **95%** of clinically validated targets

Signaling | DNA repair | I-O | Epigenetic | Cell cycle



Continually deploying new targets

PolQ | HPK1 | PKYMT1 | USP1 | SETD2

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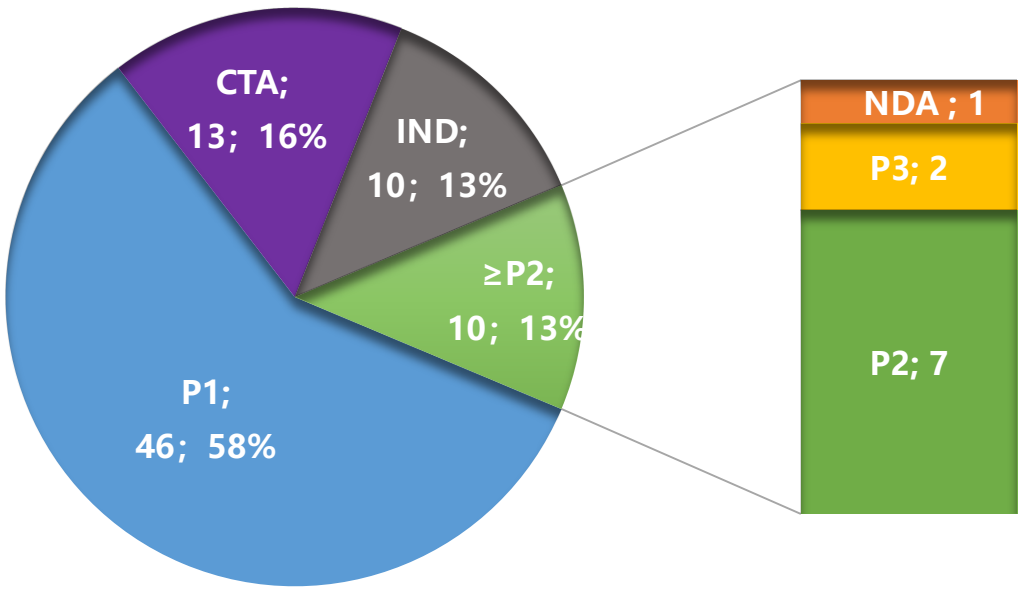
Oncology Drug Candidate Pipeline: Comprehensive Coverage

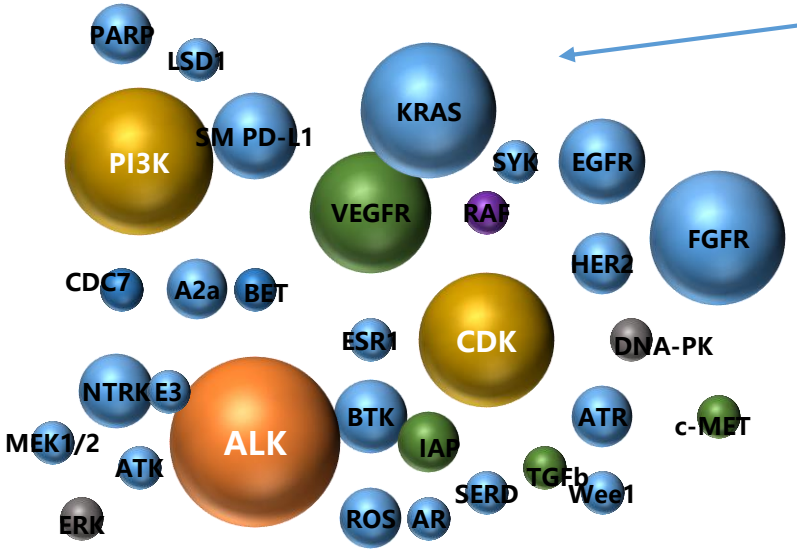
Aggregate **79** INDs, accounting for **52%** of DDSU's pipeline

1 NDA, **2** ongoing pivotal clinical trials



Cover **95%** of clinically validated targets

Signaling | DNA repair | Immuno-oncology | Epigenetic | Cell cycle



Continually deploying new targets

PolQ | HPK1 | PKYMT1 | USP1 | SETD2

RAS Pathway Targets Full Coverage

Phase II: 2
- PI3K
- mTOR

Phase I: 4
- RAF
- MEK
- AKT
- KRAS G12C

IND: 2
- ERK
- SHP2

PCC & LO: 3
- pan-KRAS
- SOS
- KRAS G12D

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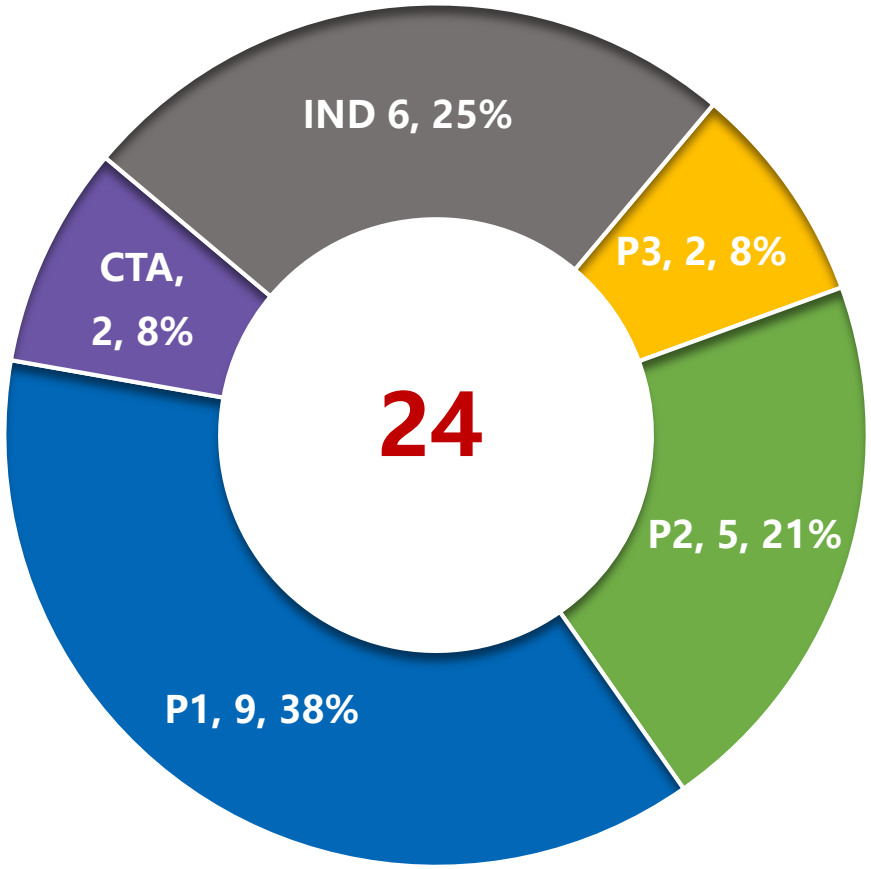
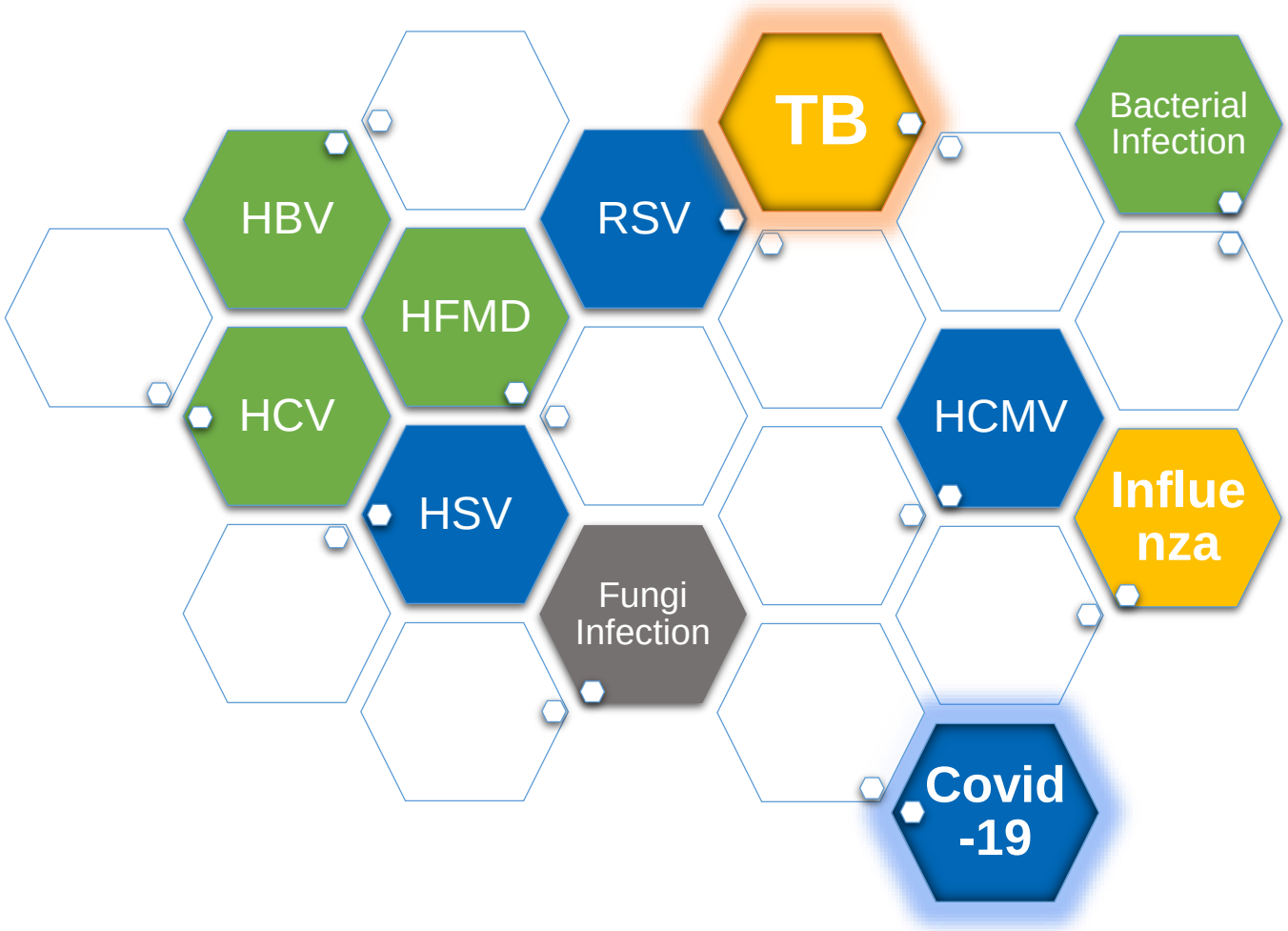
Infectious Disease Drug Candidate Pipeline

- ✓ Full coverage: **antiviral**, **antibiotic**, **antifungal**
- ✓ Aggregate **24** INDs, accounting for **16%** of the pipeline





Enabling Customers to Build Diversified Pipeline

Partnering with Chinese pharmaceutical companies:

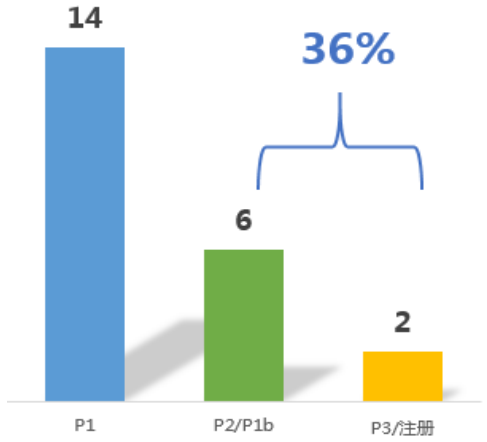
20 provinces & cities

70+ companies

250+ new drug projects

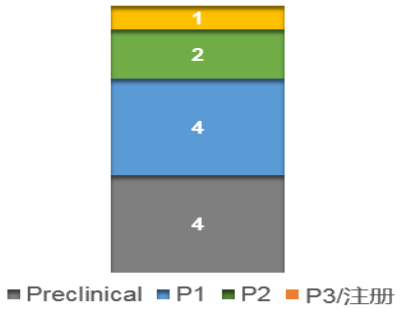
Enabling Company A to Build R&D Pipeline

- ✓ Cover **tumors, liver disease, respiratory system**, and other therapeutic areas
- ✓ 10 years' collaboration, with total of **30+** projects, **22** in clinical development, **2** at P3/pivotal clinical trial stage
- ✓ Accounting for **45%** of its pipeline of small molecule new drugs in clinical stage



Enabling Company B to Establish its Pipeline

- ✓ Established pipelines for **infectious disease**, **metabolic disorders**, **tumors**
- ✓ 10 years' collaboration, with total of **10+** projects, **7** in clinical development, **1** at P3/pivotal clinical trial stage



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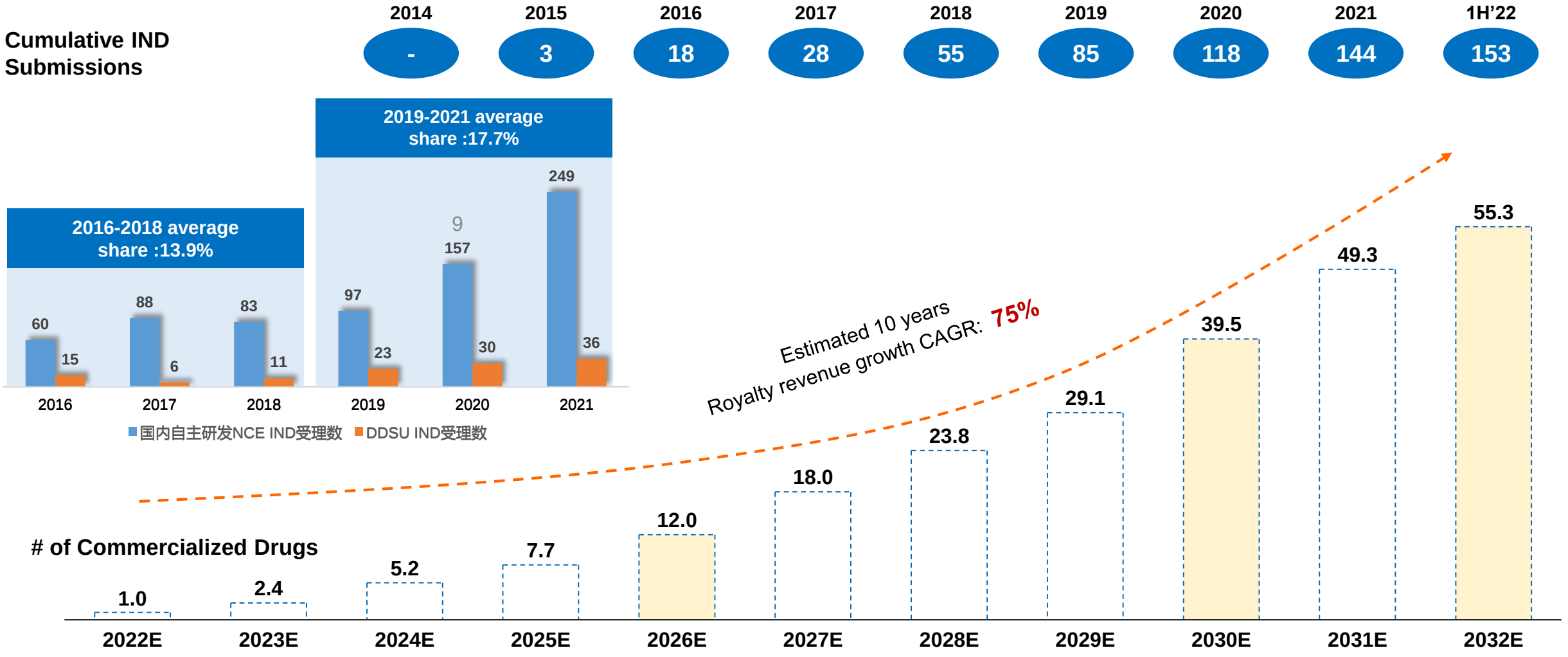
Long-term Sustainable Royalty Stream from DDSU 1.0 to Come



Key Changes of New Drug R&D Landscape in China

The Impact of Centralized Procurement Policy and Capital Market on Innovative Drug R&D

Traditional pharmaceuticals：Margins are shrinking

Biotech: Cold winter in capital market and financing difficulties

Serious Homogenization of New Drug R&D

Intense competition for popular targets, involution of R&D

Diversification of New Modalities

New modalities such as ADC, PROTAC®, RNA and Cell & gene therapies

***Note**: PROTAC® is a registered trademark of Arvinas Operations, Inc., and is used under license.*

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一切过往 皆为序章

-- 莎士比亚《暴风雨》

What's past is prologue

-- Shakespeare "Tempest"

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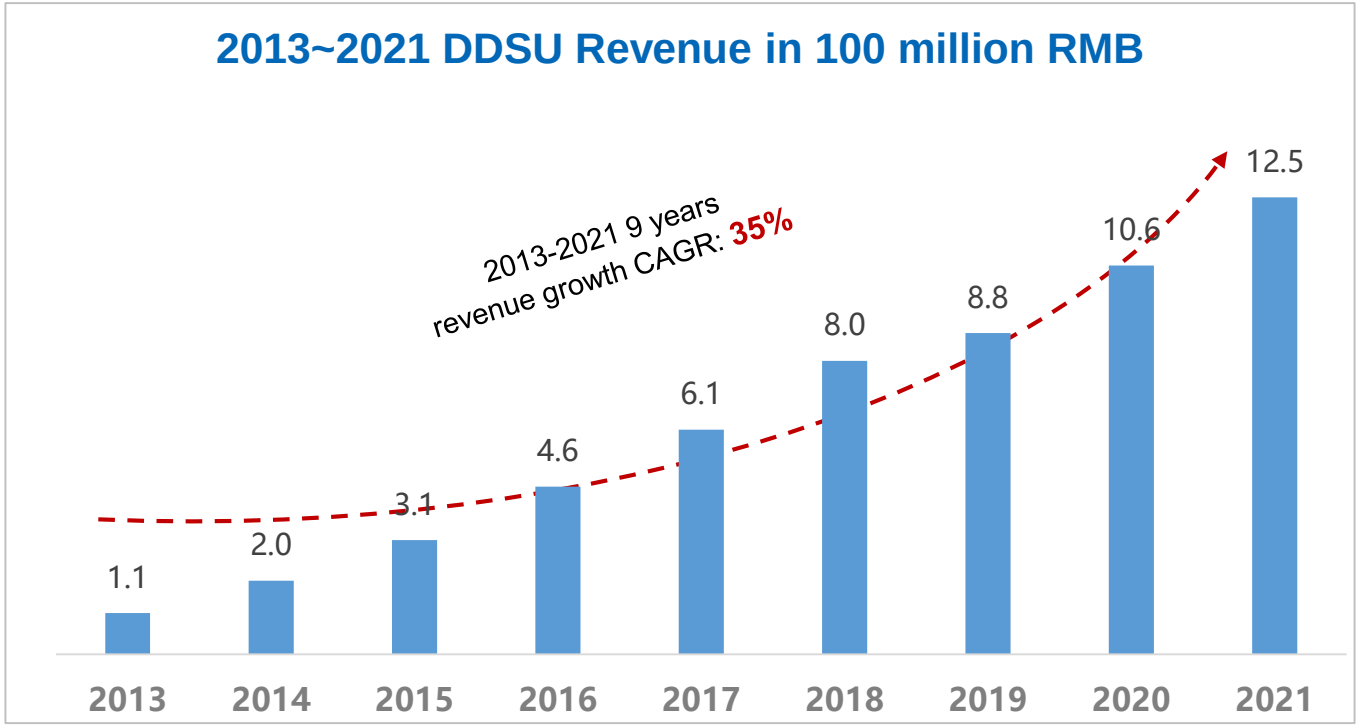
DDSU Business Evolution to Meet Customers' Needs

DDSU 1.0

- Fast-follow
- Me-too and Me-better
- Traditional small-molecule drugs

DDSU Business Evolution to Meet Customers' Needs



DDSU 1.0

- Fast-follow
- Me-too and Me-better
- Traditional small-molecule drugs

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DDSU Business Evolution to Meet Customers' Needs

DDSU 2.0

- Best-in-class
- New modality
- Top three INDs in China
- Integrated clinical R&D services

DDSU 1.0

- Fast-follow
- Me-too and Me-better
- Traditional small-molecule drugs

Sudapyridine (WX-081): A Better Therapy for Drug-Resistant Tuberculosis

Pulmonary tuberculosis

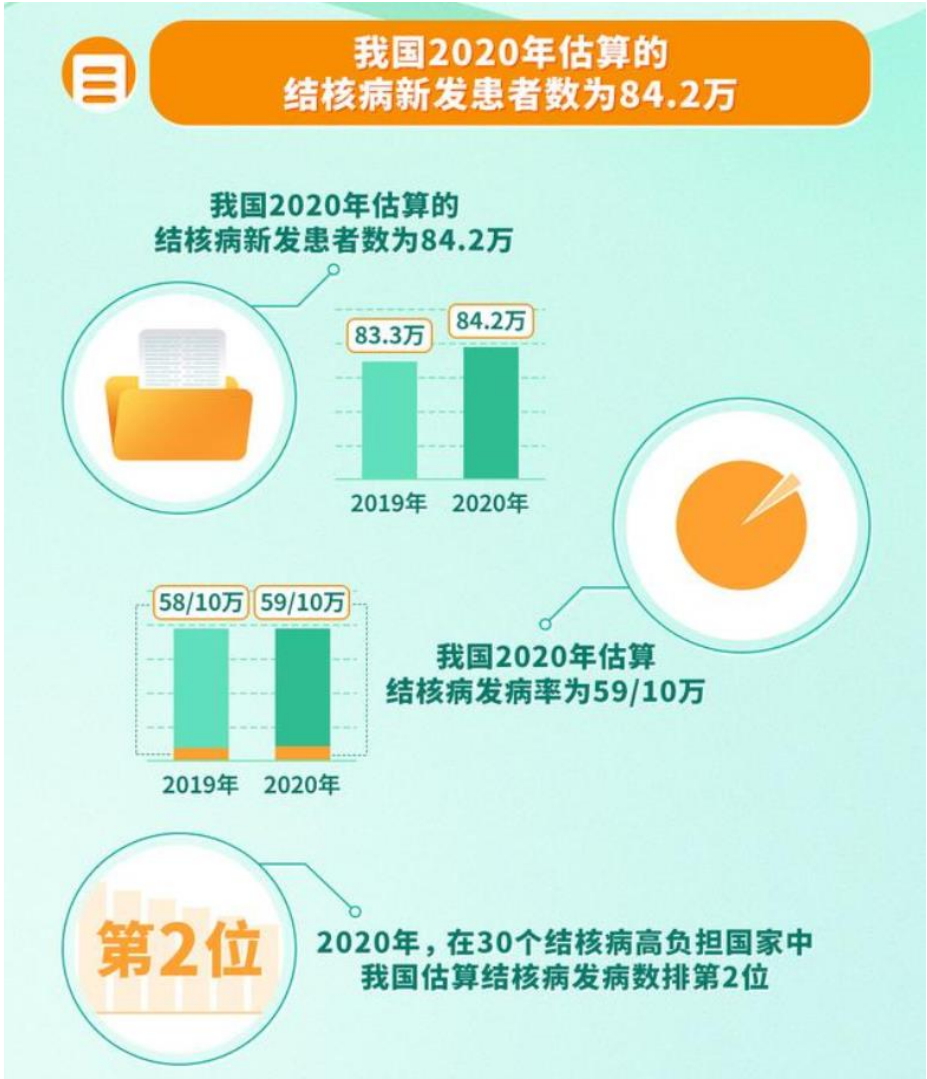
- Global TB patients are wide spread
- High proportion of them is MDR-TB
- Effective therapy is not available

Bedaquiline

- First FDA-approved tuberculosis drug with new MoA in 40 years
- Side effects limit its wide use
- Expensive

Sedapyridine (WX-081)

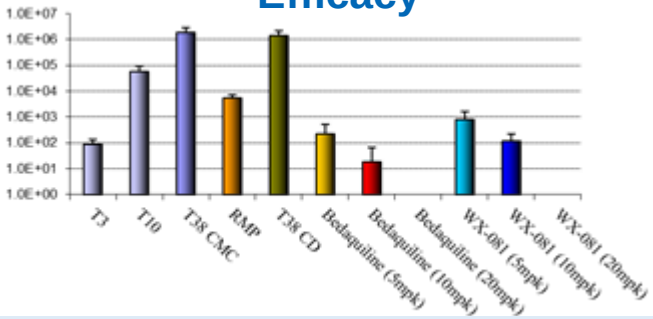
- The same MOA as Bedaquiline
- Comparable or better clinic al efficacy than bedaquiline
- No cardiotoxicity



Superior Preclinical Data of Sudapyridine (WX-081) Translated into its Clinical Advantage

Preclinical profile

Efficacy



Sudapyridine (WX-081) is as effective as bedaquiline in mouse TB infection model, and can achieve TB bacteria clearance at high dose (20 mpk).

Pharmacokinetic Studies

Parameter	Bedaquiline	WX-081
Dose (*iv*/*po*) (mg/kg)	1/6.25	1/6.25
Cl (*iv*) (mL/min/kg)	7.76	3.59
Vd (*iv*) (L/kg)	6.21	10.4
$T_{1/2}$ (*iv*) (h)	21.3	46.3
C_{max} (*po*) (ng/mL)	608	503
$AUC_{0\text{-}last}$(*po*) (ng.h/mL)	6038	10155
F%	47.1	40.7

Animal PK and lung concentration of Sudapyridine (WX-081) are superior to bedaquiline.

Cardiac Safety Study

Parameters	WX-081-M3	BDQ-M2
hERG IC_{50} (μM)	1.89	1.73
hCav1.2 IC_{50} (μM)	> 3	0.75
Nav1.5 IC_{50} (μM)	> 10	> 10
Rabbit Purkinje fiber assay AP conc. (μM)	≥ 10	0.3

New Zealand white rabbits Purkinje fibers study proves lower cardiac toxicity risk of Sudapyridine (WX-081) than Bedaquiline.

Clinical observations

Clinical efficacy of Sudapyridine √

Sudapyridine vs. bedaquiline
No significant difference in sputum negative conversion rate (%)
WX-081 group：69.2%
Bedaquiine group：66.7%

Clinical Pharmacokinetics√√

- Better than bedaquiline
- Supports QD dose
- No significant difference between pulmonary tuberculosis patients and healthy volunteer

No clinical cardiac side effects√√

- Phase I: No Q-T interval prolongation was found, no adverse reactions of grade 3 and above
- phase II: no drug-related adverse reactions of grade 3 and above

❑ China's first innovative anti-drug-resistant tuberculosis drug entered clinical phase III development, meeting the original goal of "**Best-in-Class**" profile.

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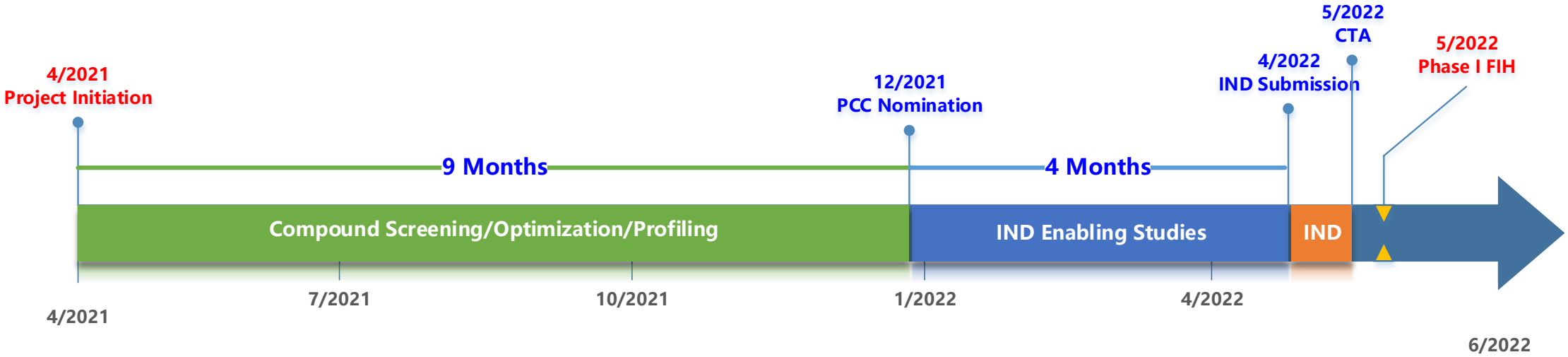
Faster: 14 Months From Project Initiation to Phase I FIH

COVID-19 pandemic poses a great threat to global health and economy

- Prevention: Although vaccines are being widely administered virus mutation and immune escape lead to low protection rate.
- Treatment: 3CL inhibitors are more efficacious, safer and more accessible than neutralizing antibodies and RdRp inhibitors.
- Project Objective: Develop a novel 3CL inhibitor drug with independent IP, great efficacy and high accessibility.



Good preclinical efficacy: High potency against different variants. Improved survival rate and reduced lung virus titer significantly in animal models.

Excellent PK properties: Higher drug exposure in mono-drug administration than the approved 3CL drug.

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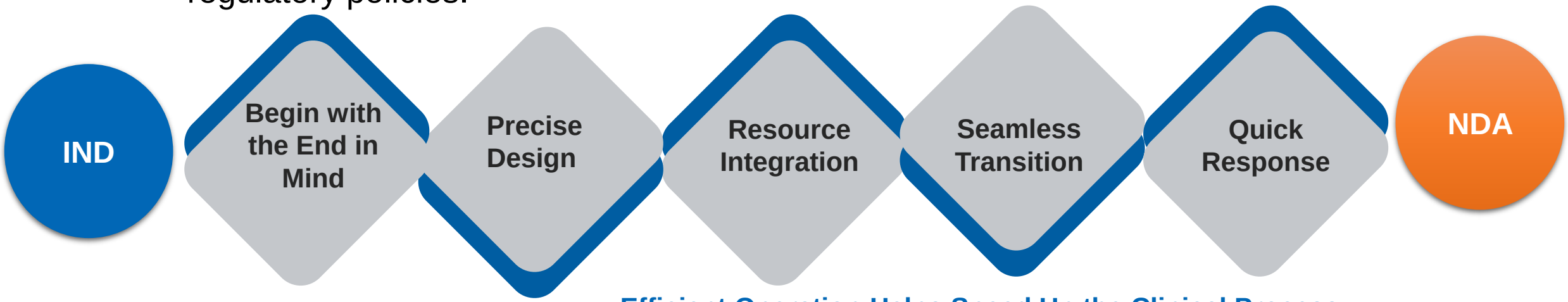
Faster： Integrated Services to Accelerate Clinical Development

Speed by Design： Save~ 2~3 years

Precise clinical and registration design through in-depth interpretation of non-clinical profiles, clinical needs and regulatory policies.

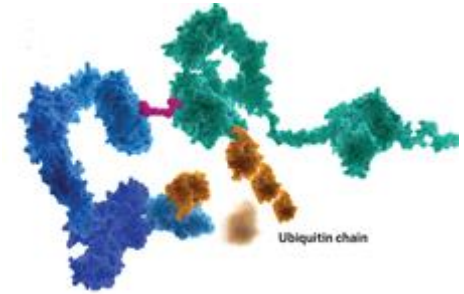


Efficient Operation Helps Speed Up the Clinical Process: Save ~1 year

Eliminate gaps between different modules through DDSU project management

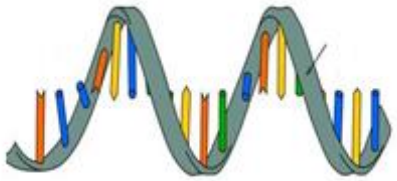
3 Clients ● **4 Clinical Integrated Service Projects** ● **1 in Phase II** ● **3 in Phase I**

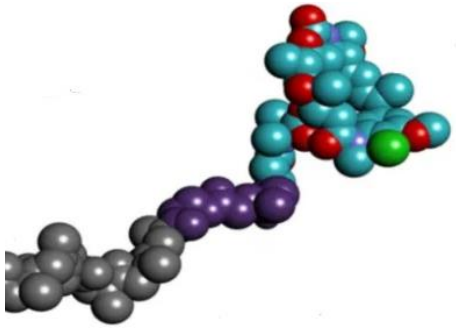
Newer： New Modalities



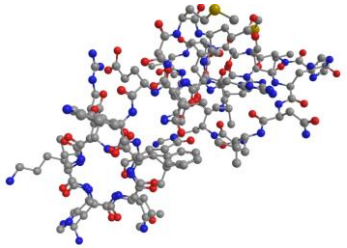
Molecular Glue PROTAC®*

RNA





Peptide PDC



- PROTAC® refers to Proteolysis Targeting Chimeras

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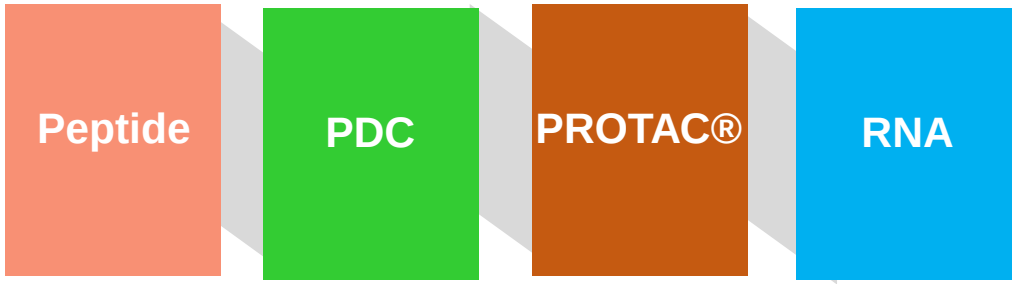
New Modality Pipeline

Cover Multiple New Modality Pipelines



Therapeutic Areas Mainly in Oncology and Metabolism

Prostate cancer	HBV	Hypertension	Obesity
T2D	NSCLC	Breast cancer	Solid tumor
DLBCL	NASH	RA	DME

Multiple Pipelines into preclinical development, will submit IND in 6-12 months

Projects	2022Q2	2022Q4	2023H1	2023H2	2024H1	2024H2
Peptide		IND				
		IND				
				IND		
					IND	
PDC		IND				
				IND		
PROTAC®		IND				
			IND			
			IND			
			IND			
RNA		IND				
					IND	
						IND

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DDSU1.0 → DDSU2.0: Leap from Quantity to Quality

Better: Best-in-class

Newer: New modality

Faster: First Tier IND-in-China