

Innovative chemistry for a better future

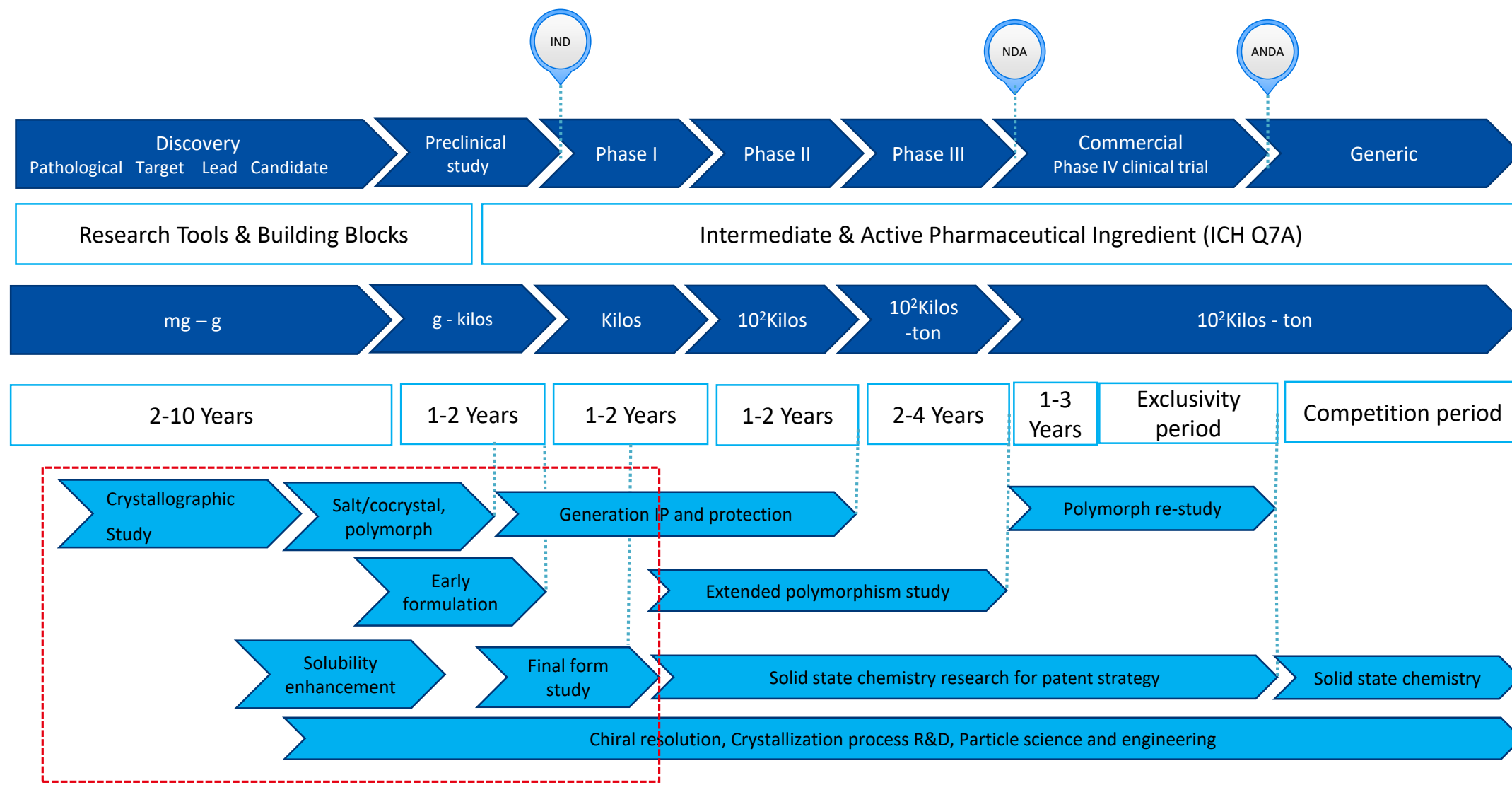
PharmaBlock

Solid State & Crystal Engineering Capabilities

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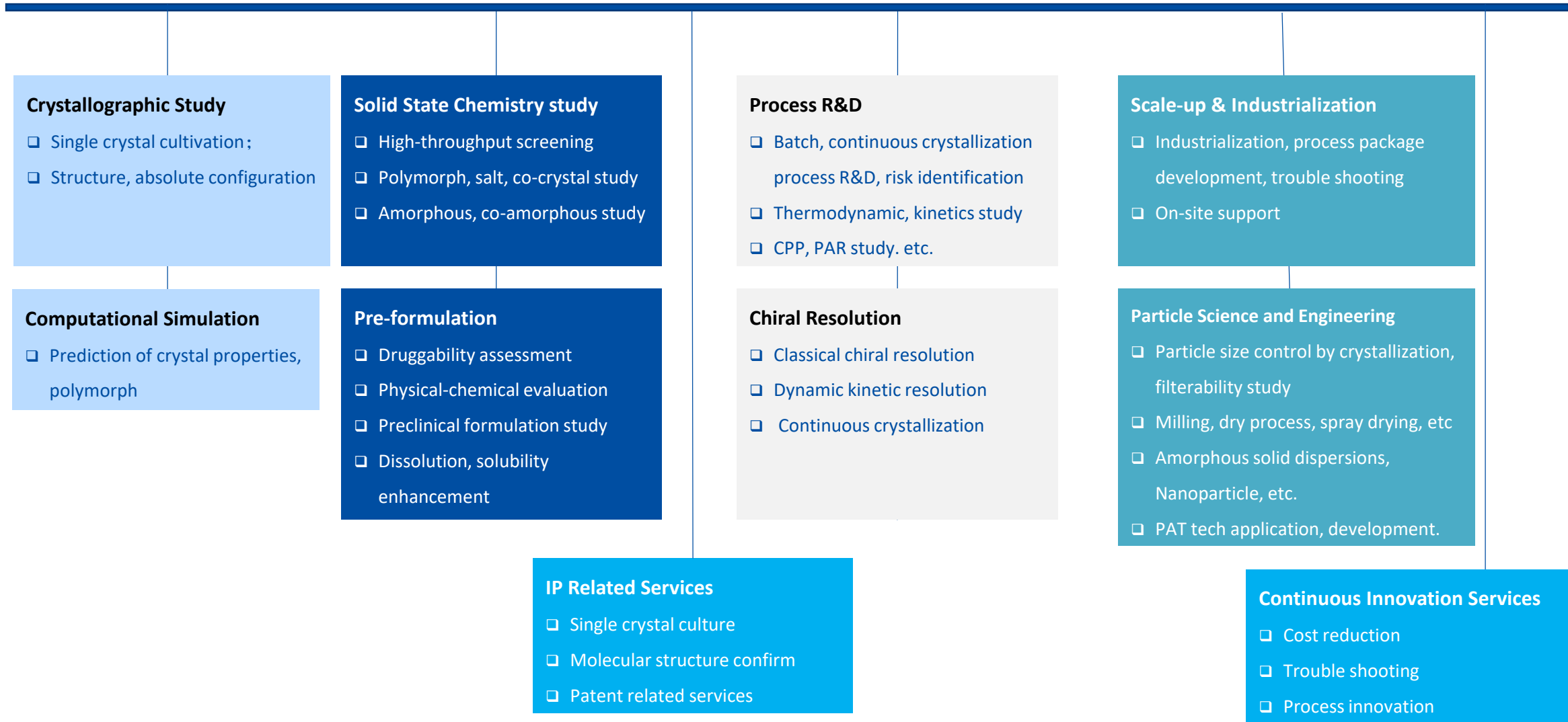
PharmaBlock

How We Support the Entire Pharmaceutical Life-cycle

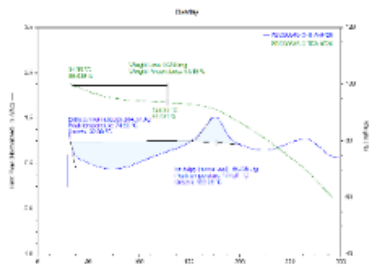


 : Need to be completed before IND

Our Comprehensive Capabilities



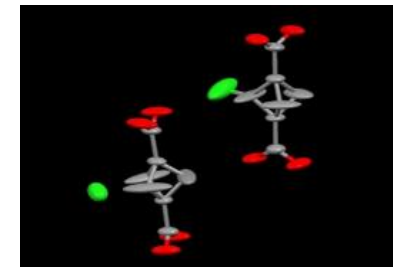
Pharmaceutical Crystallographic Study



Stability, solubility, melting point, etc. Solid state chemistry properties test



Single crystal cultivation. Normal methods: 1. Cool; 2. Evaporation; 3. Solvent; 4. Thermal treatment; 5. Crystallization from the melt; 6. Thermal de-solvation; 7. liquid-liquid.



chemical structure confirmed

Pharmaceutical Sciences (Nanjing), Inc. PharmaBlock

Single Crystal Cultivation and Analysis Project Report

Project Summary			
Project	Drug name	Name	Date
Client	Pharmaceutical Company	Department	00/00/00
Author	Pharmaceutical Company	Project No.	00-000000

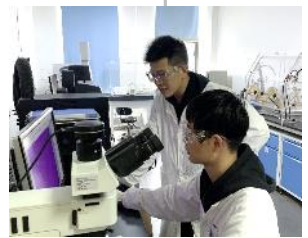
Final report



Start material



Choose suitable ligands from ligand library



Selection of high quality crystals



Data collection, structure solution refinement the chemical structure confirmed by x-ray analysis

Freeform assessment (1 week)

- BCS classification assessment;
- Stability, solubility, hygroscopicity assessment to determine the solid state chemistry research strategy
- (the solvent, counter-ion, co-former, methods)

Salt screening (6-8 weeks)

- Temperature controlled shaker with 48, 96 wells plate
- Tailor temperature controlled HTS platform (<1ml vial, Magnetic stirring)
- High throughput screening to 100+ experiments
- XRPD, DSC/TGA , stability, solubility, etc., study to evaluate and select solid candidate

Salt screening (6-8 week)

- 10+ routine polymorph study method including cooling, evaporation, anti-solvent, thermal treatment, etc.
- Tailor HTS screening to 100+ experiments
- XRPD, DSC/TGA, stability, solubility, etc., study to evaluate and select solid candidate

Pre-formulation(1-2 weeks)

- Scale-up to 3-5g for properties study
- Particle science study
- Tox formulation screening for PK/PD
- Solubility and solubility enhancement
- Process study (amorphous solid dispersion and nanoparticle)

Compound evaluation



Salt or co-crystal HT screening, evaluation and selection



Polymorph HT Screening, evaluation and selection

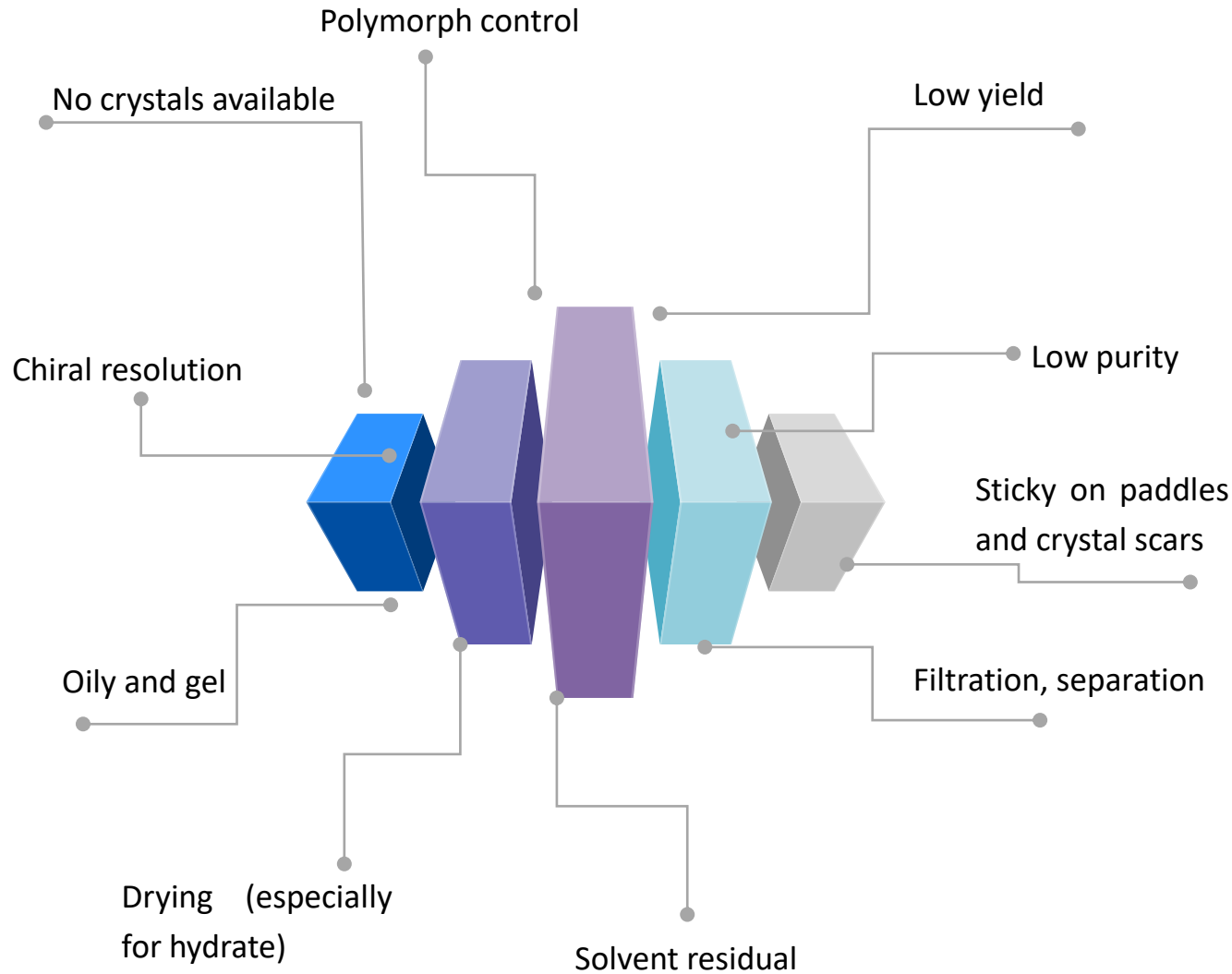


Scale-up to gram, pre-formulation study



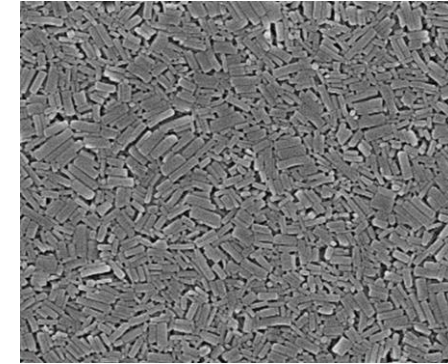
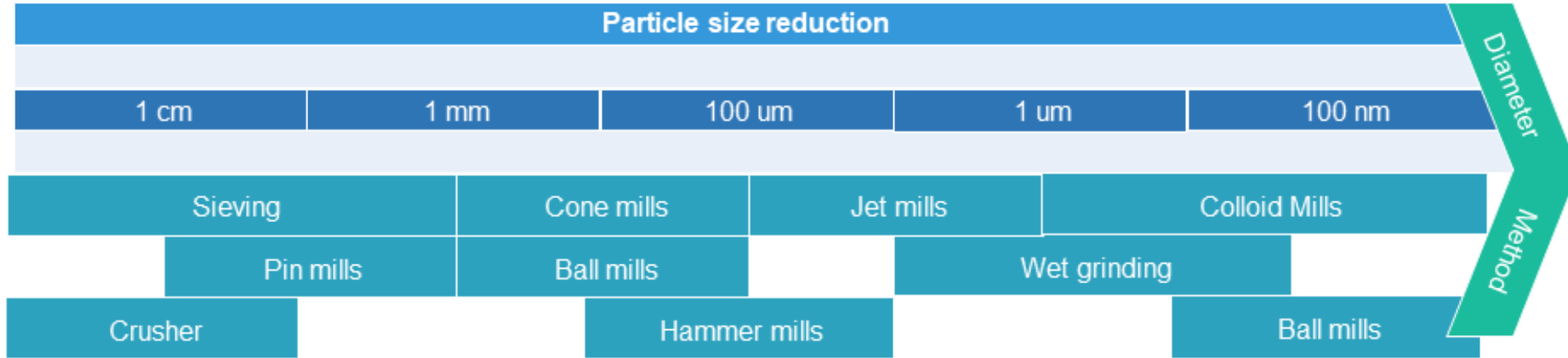
Crystallization Process Development

Statistics of 700+ delivered crystallization process R&D projects



	Tech focus	Ratio (%)	Remark
1	Polymorph Control	67	
2	PSD Control	33	
3	Robustness in Scale up	42	
4	Oil out, Crystal Scar	57	
5	Impurity	62	
6	Particle Engineering	18	
7	Color of Product	33	
8	Chiral Resolution	33	
9	Residual Solvent	42	
10	Hydrate Control	36	Increasing
11	API Stability Challenge	37	
12	Filtration Challenge	17	
13	Morphology Challenge	23	
14	Drying Process	22	

Particle Science and Engineering

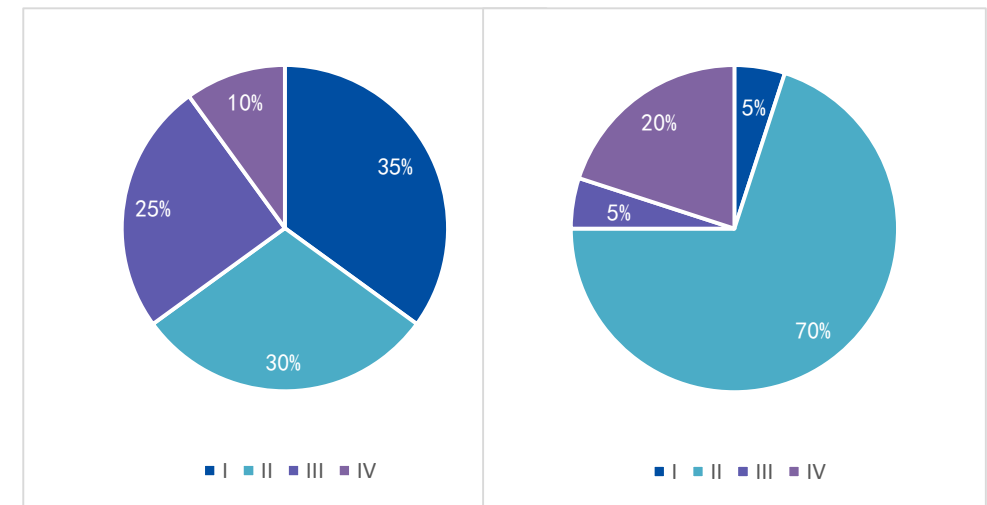
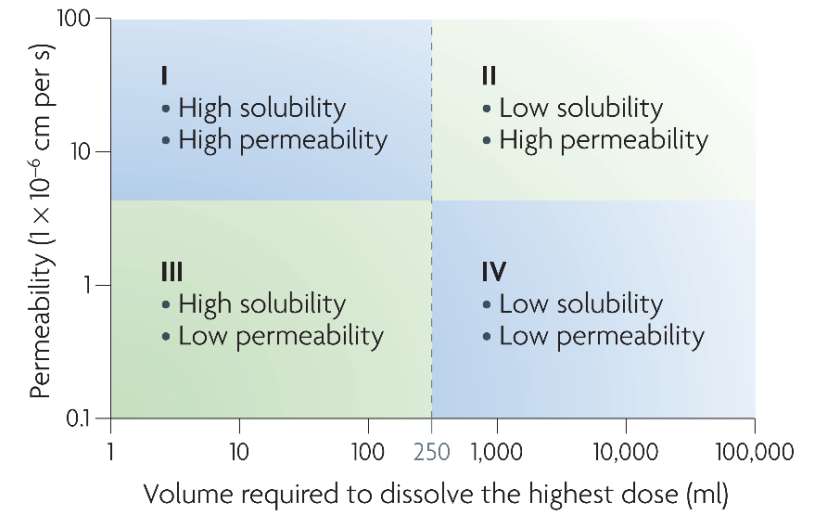
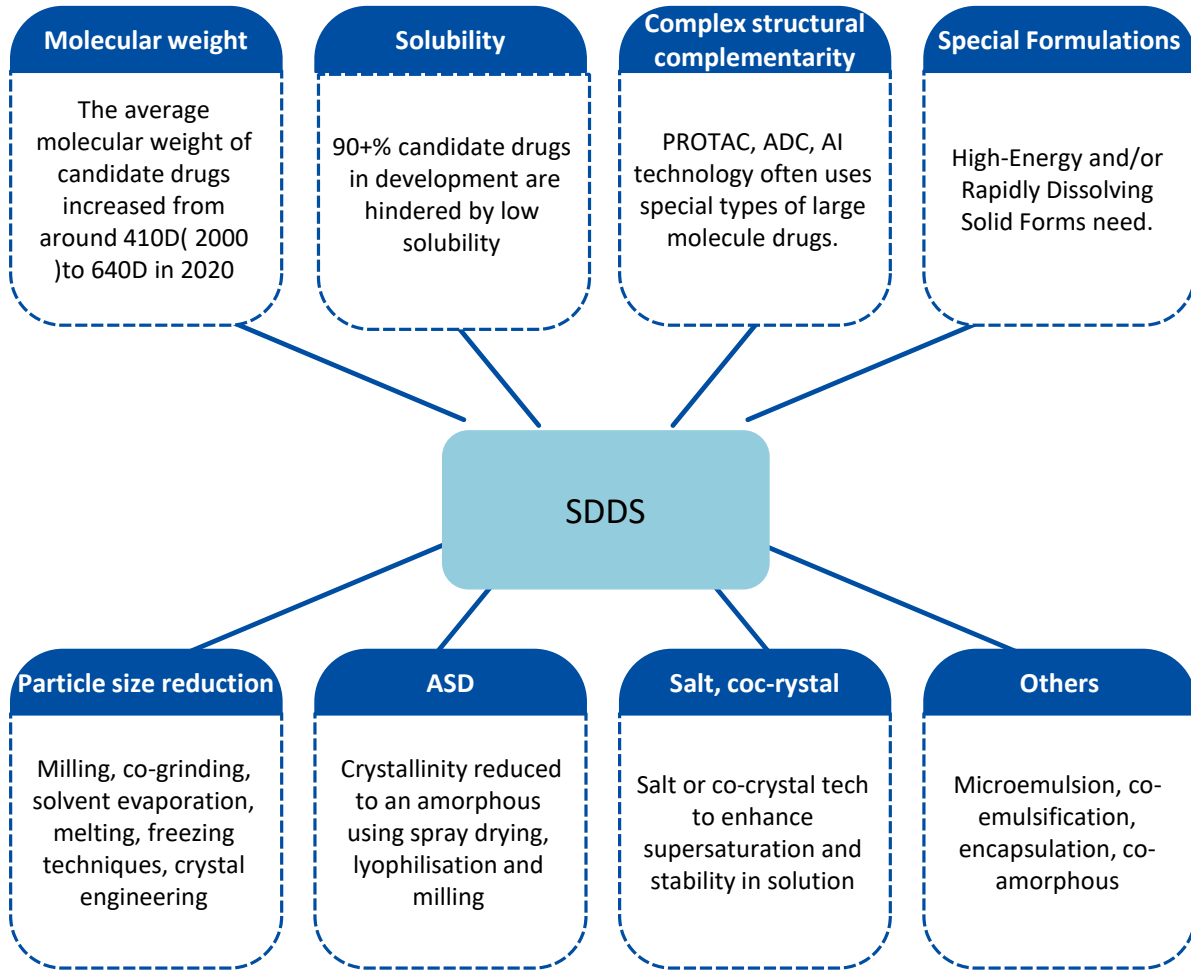


Customized PSD



Supersaturating Drug Delivery Systems

Supersaturating drug delivery systems (SDDS) takes advantage of supersaturated state to simultaneously increase the apparent solubility and permeability of insoluble drugs.



Statistics on the BCS classification of marketed and candidate drugs

Methods for obtaining chiral compounds

- ❑ Asymmetric catalysis
 - ❑ Biocatalysis
 - ❑ SFC
 - ❑ **Chiral resolution**
- Challenges →
- Difficult to synthesize
 - Limited biocatalysts
 - Difficult to industrialize
 - High cost

Advantages of chiral resolution

- ❑ Economical
- ❑ Straightforward isolation
- ❑ Speed on scale
- ❑ Industrialize

Typical Screen (12 chiral reagents x 6 solvents)

Chiral resolution reagents screening

- ❑ 12+ resolution reagents
- ❑ 6+ solvents
- ❑ >80 initial crystallization experiments
- ❑ Solids analyzed by HPLC/XRPD

Resolution & Crystallization Process Development

Conditions optimization

- ❑ Equivalents of chiral reagents
- ❑ Temperature
- ❑ Solvents

Scale-up of Dominant Chiral Reagents

- ❑ HPLC
- ❑ Yield

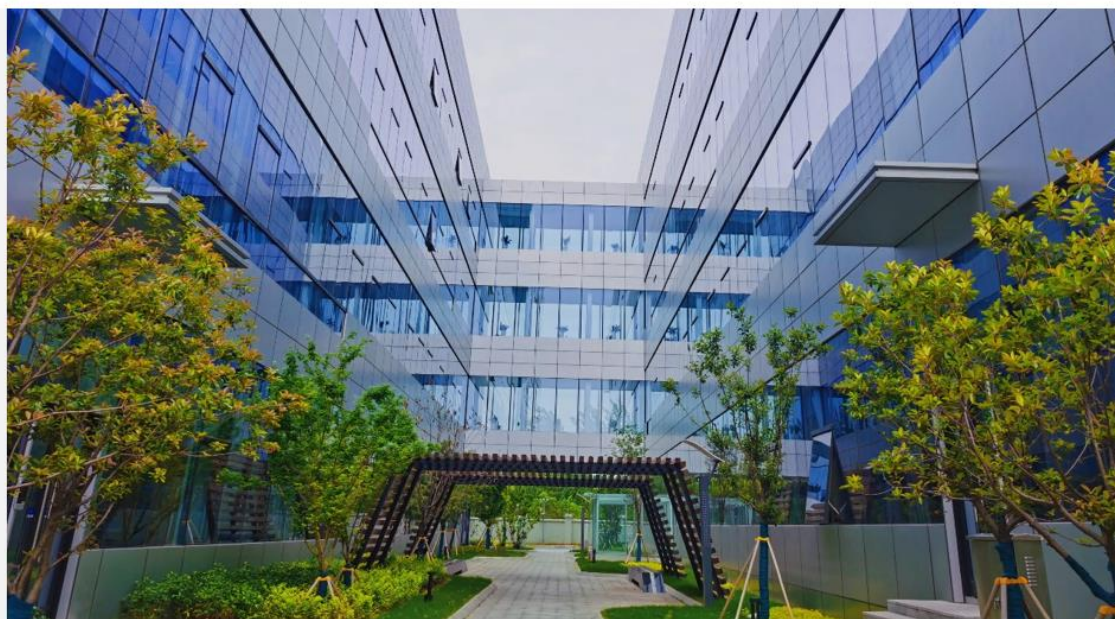
Dynamic Kinetic Resolution

- ❑ DKR conditions
- ❑ Continuous crystallization

THANK YOU

OUR VISION

To provide better products and services through innovation of chemistry and low carbon technologies in R&D and manufacturing.



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