INNOCARE
诺诚健华

InnoCare Pharma (9969.HK, 688428.SH)
2023Q3 Results NDR

November 2023

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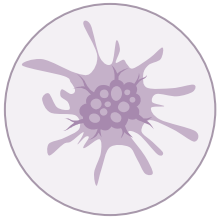
Our Vision

To Become
a **Global Biopharmaceutical Leader**
that Develops and Delivers
Innovative Therapies for Patients **Worldwide**

Oncology



Autoimmune

Our Therapeutic Focus

Strategy Execution Delivered Strong Growth & Development in 2023Q3

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Commercialization

- Total revenue reached **RMB 537mn, +21.7% yoy growth**
- Orelabrutinib rapid market penetration and hospital coverage after NRDL inclusion
- Highly experienced commercial team in hematology
- **Tafasitamab**
  - Approved for Urgent Clinical Use in the Hainan Province
  - Approved in Hong Kong
  - Access for Urgent Clinical Use in Big Bay Area

Progress of Internal R&D Pipeline

- **Orelabrutinib**
  - **r/r MZL NDA approved, first and only BTKi approved in China; r/r MCL approved in SG**
  - **r/r MCL US registrational trial finished patients enrollment, NDA submission in mid-2024**
  - **1L CLL/SLL registrational Phase III finished patients enrollment, NDA submission 2Q2024**
  - **1L DLBCL-MCD registrational Phase III** ongoing
  - **ITP PIII registrational trial initiated, FPI**
  - **SLE PIIa positive, PIIb enrollment ongoing, interim results expected by end of 2024**
  - **MS PII: 24-week results: 92.3%** relative new Gd+T1 lesion reduction at 80mg QD compared to placebo arm
- **ICP-248 PI ongoing with excellent efficacy**
- **ICP-332 PII for AD patients enrollment completed in Sept., result readout by end of 2023**
- **ICP-488** PI in healthy finished; early PoC in psoriasis cohorts started, PII initiated
- **ICP-723 registrational trial ongoing,** IND approved for pediatric arm
- **ICP-192 registration trial for cholangiocarcinoma**

License-in/Collaboration

- **ICP-B04, Tafasitamab+LEN**
  Finished enrollment in registrational trial, NDA submission 2Q2024
- **ICP-B02 (CD3*CD20)**
  Good efficacy observed in IV and SC cohorts
- **ICP-B05 (CCR8)**
  PI dose escalation ongoing

Platform

- Guangzhou manufacture facility is producing majority of commercial Orelabrutinib & all other clinical drug products
- Beijing biologics CMC facility started to operation
- Removed “B” in HKEx

Focus concerted efforts towards Company’s 2.0 objectives
Continue corporate culture of cost sensitive, strong execution & innovation

[1] ***PoC**: Proof of concept*

1 Major Program Update

Orelabrutinib (ICP-022): Phase III Registrational Trial for ITP Initiated

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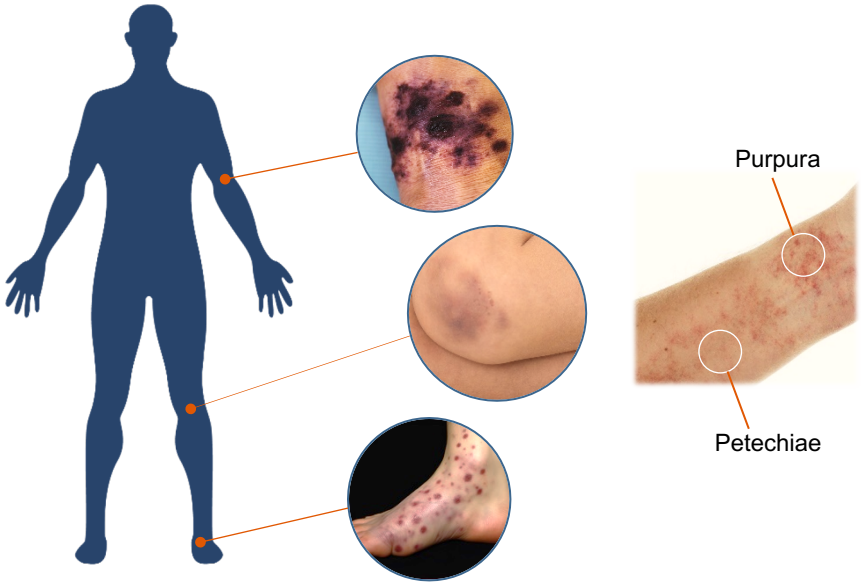
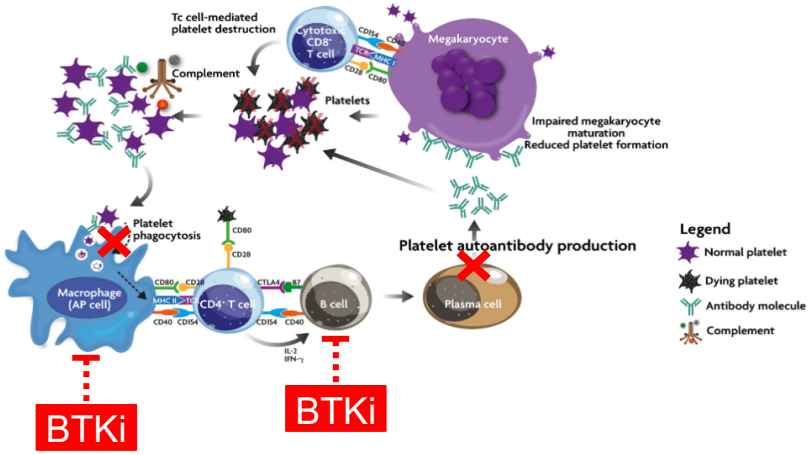
Immune Thrombocytopenia



BTKi's advantage in ITP

- Decreased macrophage (Fcγ receptor)–mediated platelet destruction
- Reduced production of pathogenic autoantibodies



- Phase II: **40% patients met the primary endpoint at 50mg QD**
- Phase III: registrational trial being initiated in China, **FPI achieved**
- Frontline BTK inhibitor gets approved for AID
- Considering global markets

Source: Drew Provan, John W. Semple, DOI:https://doi.org/10.1016/j.ebiom.2022.103820

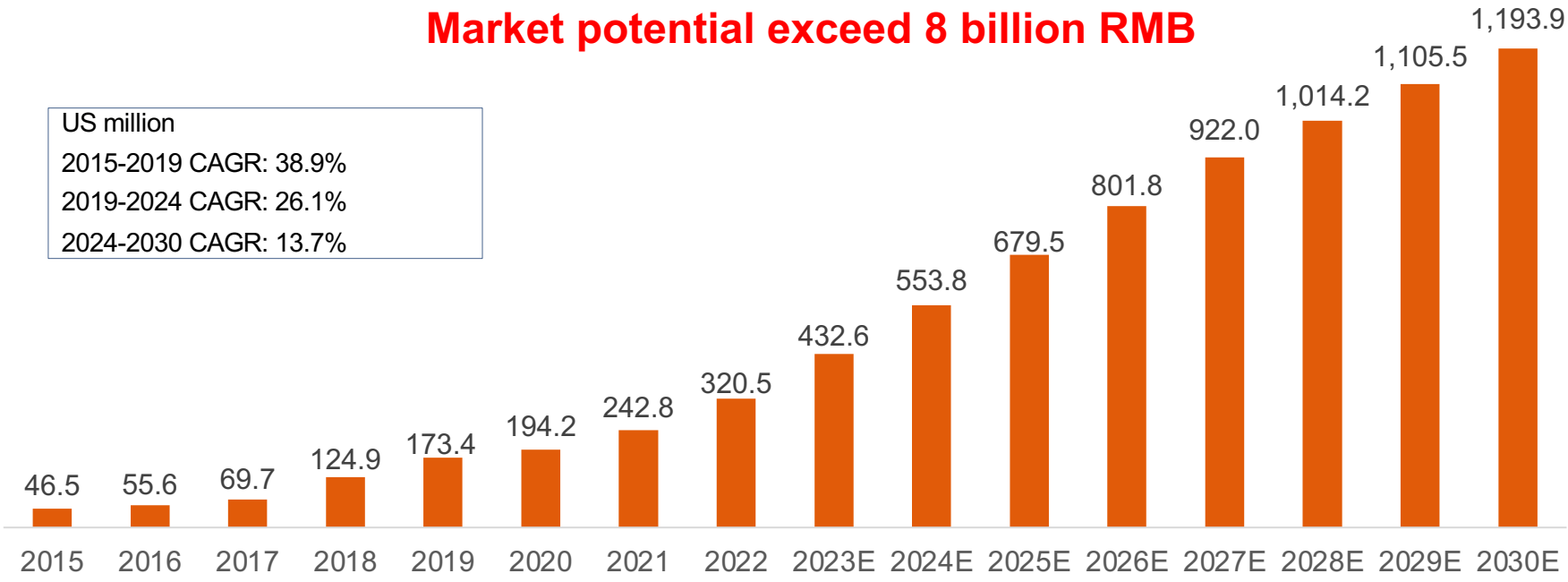
1 ITP Market Potential in China

ITP market growing rapidly, existing therapies include: :

- Hormones (glucocorticoids, dexamethasone, etc.), recurrence in 70%-80% of patients, accompanied by serious adverse events, including infection, peptic ulcer, bleeding, etc.
- TPOs(romiplostim, eltrombopag, avatrombopag, hetrombopag) can solve the "urgent need", but the duration is not satisfactory.

Huge unmet medical use for new mechanistic therapies!

Market potential exceed 8 billion RMB



Note: 血小板减少症药物的历史市场规模主要根据TPO及TPO-R激动剂的销售计算，市场预测假设自2019年起至2023年期间将随着更多创新疗法进入市场而出现加速增长

Source: Frost &Sullivan

2 Major Program Update

Tafasitamab: Potential Best Therapy for r/r DLBCL

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Current Status and Further Development

- **Registrational trial for r/rDLBCL finished enrollment in mainland China, NDA submission 2Q2024, NDA approval in 1-2Q2025**
- **Approved for Urgent Clinical Use in the Hainan Province**
- **BLA was approved in Hong Kong and approved for pilot use in GBA**

Competitive Landscape: Selected Novel Therapy in r/r DLBCL

Company	Target	Therapy	Phase	ORR (%)	CR (%)	mDOR (m)	mPFS (m)	mOS (m)
Incyte/InnoCare	**CD19**	**Tafasitamab + Lenalidomide**	**Approved ex-China**	**57.5**	**40**	**43.9**	**11.6**	**33.5**
ADC Therapeutics	CD19 ADC	Loncastuximab tesirine	**Approved ex-China**	48.3	24.1	10.25	4.93	9.92
Roche	CD79b ADC	Polatuzumab vedotin + BR vs BR	**Approved**	42 vs 18	23 vs 3	12.6 vs 7.7	9.5 vs 3.7	12.4 vs 4.7
Roche	CD20/CD3	Glofitamab	BLA	52	39	10.4	3.8	11.5
Amgen/ Beigene	CD19/CD3	Blinatumomab	II	43	19	11.6	3.7	5.0
Regeneron/ Zai Lab	CD20/CD3	Mosunetuzumab	II	33	21	N/A	N/A	N/A
AbbVie	BCL2	Venetoclax+R+Pola	II	65	31	5.8	4.4	11

Source: Frost & Sullivan Analysis as of the end of 2022; Insight; Pharma Intelligence

3 Major Program Update

ICP-248 (BCL2 Inhibitor): Best Combination Partner for Orelabrutinib

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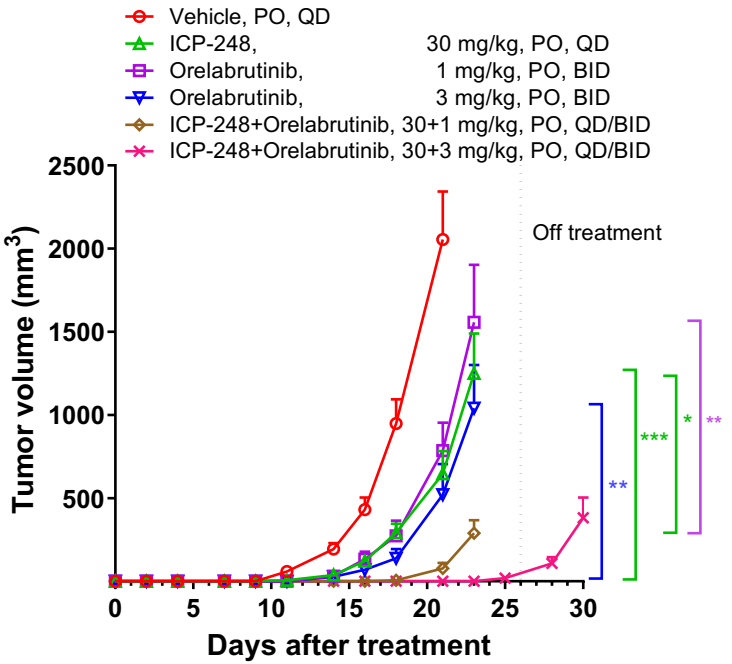
Phase I dose escalation in NHL

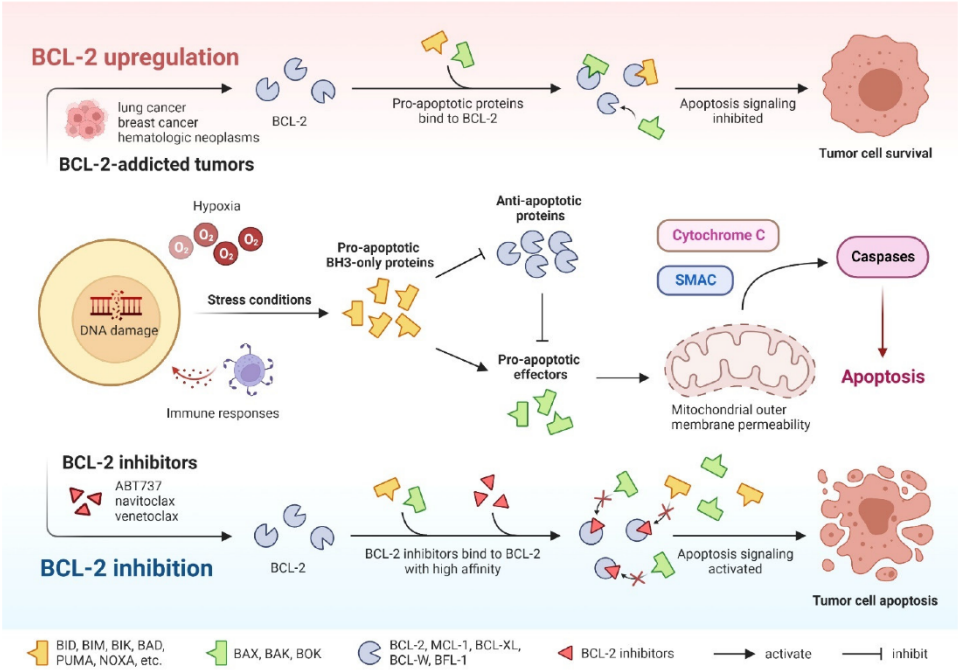
- Phase 1 dose escalation in patients with r/rCLL/SLL, r/rMCL and other NHL underway; Excellent PK profile
- Six patients dosed that show outstanding efficacy (**2 CR with uMRD, 2 SD out of 4 evaluated**)
- Great **combo potential with Orelabrutinib** for global markets

Dose level	Subject #	Lines of prior Tx	Diagnosis	DLT	SAE	Overall Assessment	MRD
100mg	1	4 (BTKi failure)	r/r MCL	No	No	**CR**	**PB uMRD**
100mg	2	3 (BTKi failure)	r/r SLL	No	No	**CR**	**BM uMRD by Flow**
100mg	3	1 (FCR)	r/r CLL	No	No	SD (normal LN/ALC; normal hematology)	**4.7%**
100mg	4	1 (FCR)	r/r CLL	No	No	SD(-47%)/normal Hb	**pending**

Combination of ICP-248 and Orelabrutinib showed superior anti-tumor activity compared to monotherapy



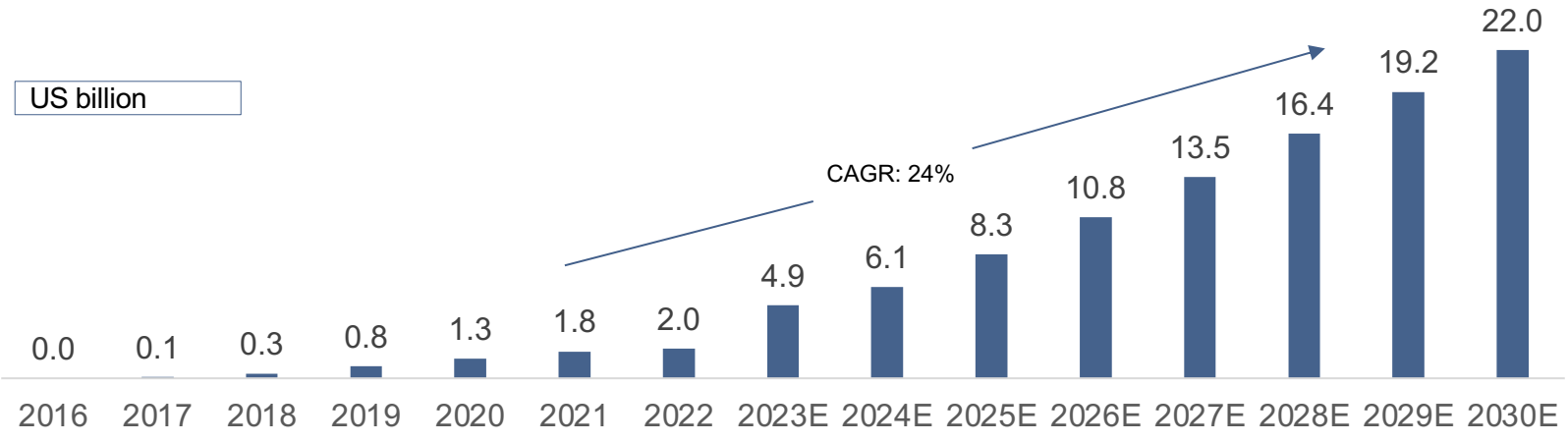
3 BCL-2 Inhibitors: An Effective Weapon Against Cancers



BCL-2 inhibitors

Monotherapy or combo with different therapeutic agents for hematologic malignancies and solid tumors

- CLL/SLL
- MCL
- AML
- MM
- FL
- DLBCL
- ALL
- LBL
- Breast Cancer
- Lung Cancer
- Pancreatic Cancer
- Hepatocellular carcinoma
- Sarcoma
- colorectal cancer



Source: Xu, J.; Dong, X.; Huang, D.C.S.; Xu, P.; Zhao, Q.; Chen, B. Current Advances and Future Strategies for BCL-2 Inhibitors: Potent Weapons against Cancers. *Cancers* **2023**, *15*, 4957. https://doi.org/10.3390/cancers15204957

Frost & Sullivan

Major Program Update

ICP-332:TYK2 JH1 Inhibitor for Oral Treatment of AD and Other Indications

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Atopic Dermatitis

ICP-332 (TYK-2, JH1)

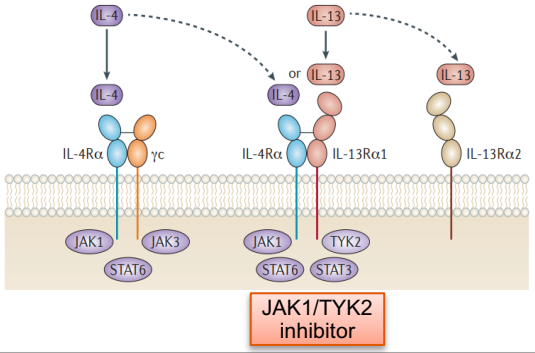
- Phase I study: SAD, MAD, food effect completed
  - Demonstrated a dose proportional and favorable PK profile, no significant food effect observed
  - Safe and well-tolerated, **no significant decrease of platelet and hemoglobin (JAK2-related AE) observed** and **no DLT observed**
- **Phase II** trial for **atopic dermatitis** (80 and 120 mg QD doses) finished patients enrollment in Sept. 2023, study readout by end of 2023

Selectivity

Drug	TYK2 vs. JAK1 (fold)	TYK2 vs. JAK2 (fold)	JAK1 vs. JAK2 (fold)
ICP-332	~40	~400	10

Evaluate JAK1/TYK2 inhibitor for AD and other indications

Strategies: Targeting Type 2 Inflammation by JAK-Inhibitor



Source: Global Burden of Disease (GBD) study 2022

4 Most Expensive Skin Disease in the World: Atopic Dermatitis

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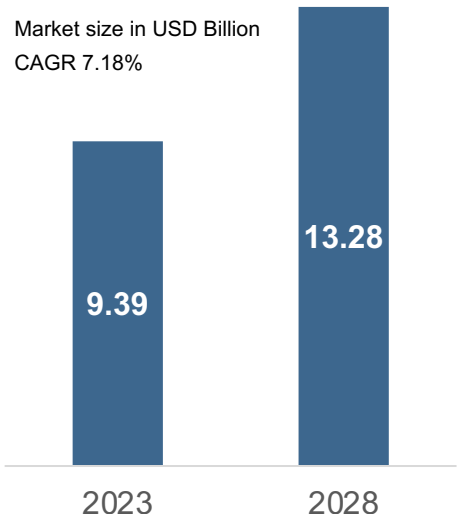
Global Atopic Dermatitis Market



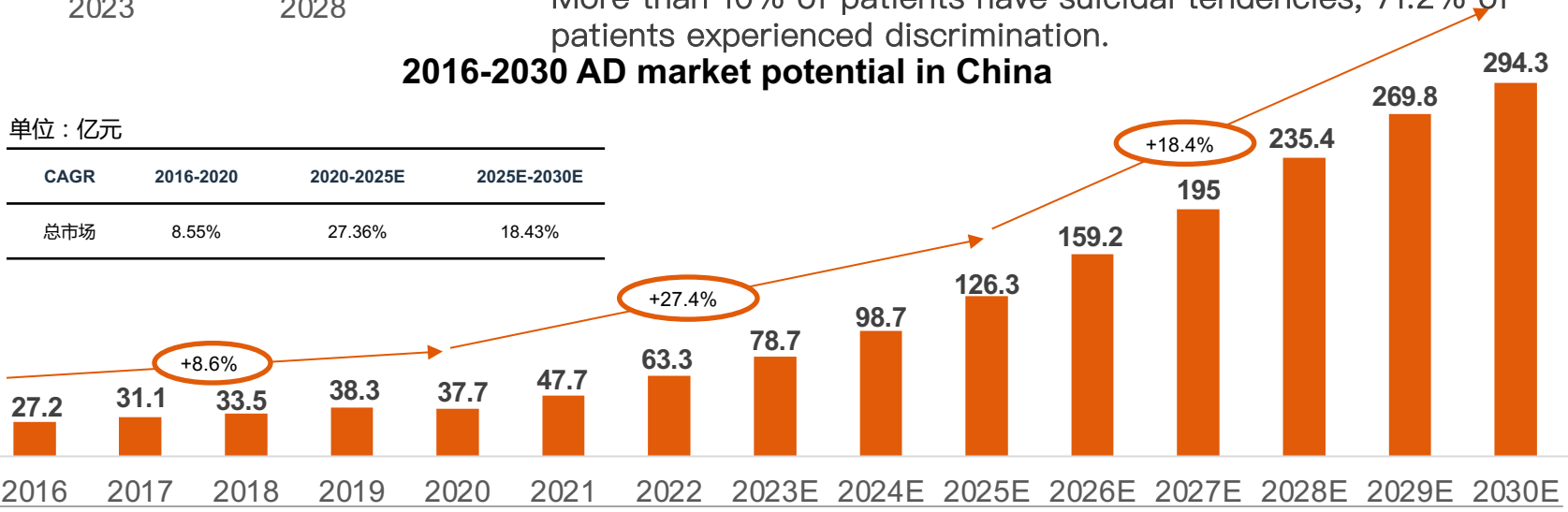
According to the "Survey Report on the Survival Status of Chinese Patients with Atopic Dermatitis":

- More than half of the patients were first diagnosed at the age of less than 20, the average duration of the disease was nearly 10 years, and most of them were complicated with other diseases
- More than 75% physicians are dissatisfied with existing treatment options
- Most patients had difficulty sleeping due to itching, reducing itching was an urgent need for 75.8% of patients with moderate to severe disease.
  More than 10% of patients have suicidal tendencies; 71.2% of patients experienced discrimination.

2016-2030 AD market potential in China

单位：亿元

CAGR	2016-2020	2020-2025E	2025E-2030E
总市场	8.55%	27.36%	18.43%



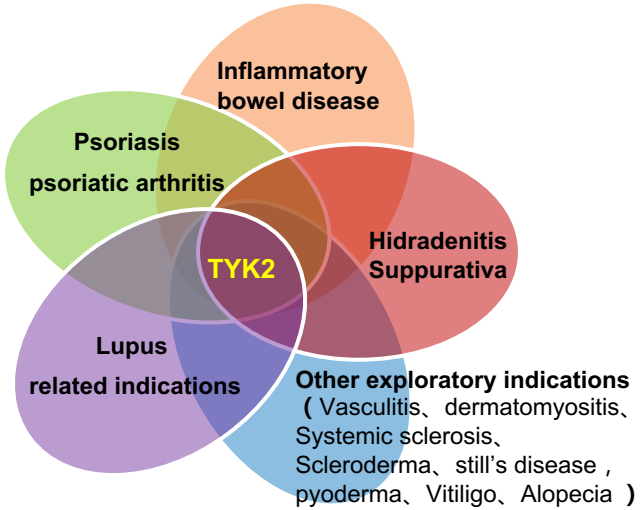
Source: Global Burden of Disease (GBD) study 2022, 健识局，Mordor Intelligence, 数据统计：中金企信国际咨询

Major Program Update

ICP-488:TYK2 JH2 Inhibitor for Oral Treatment for Psoriasis and Other Indications

Psoriasis

Indications to be developed



ICP-488 (TYK-2, JH2)

- An oral, potent and allosteric TYK2 inhibitor that selectively binds to the JH2 pseudokinase domain **with no activities on JAK1-3**
- Phase I study
  - Completed SAD (maximum dosage to 36mg), MAD and food effects arms, **no DLT observed**
  - Cohort of **psoriasis patients being evaluated for early PoC**
- Phase II being initiated
  - Potential to show significant advantages in safety profiles verse other JAK family inhibitors.

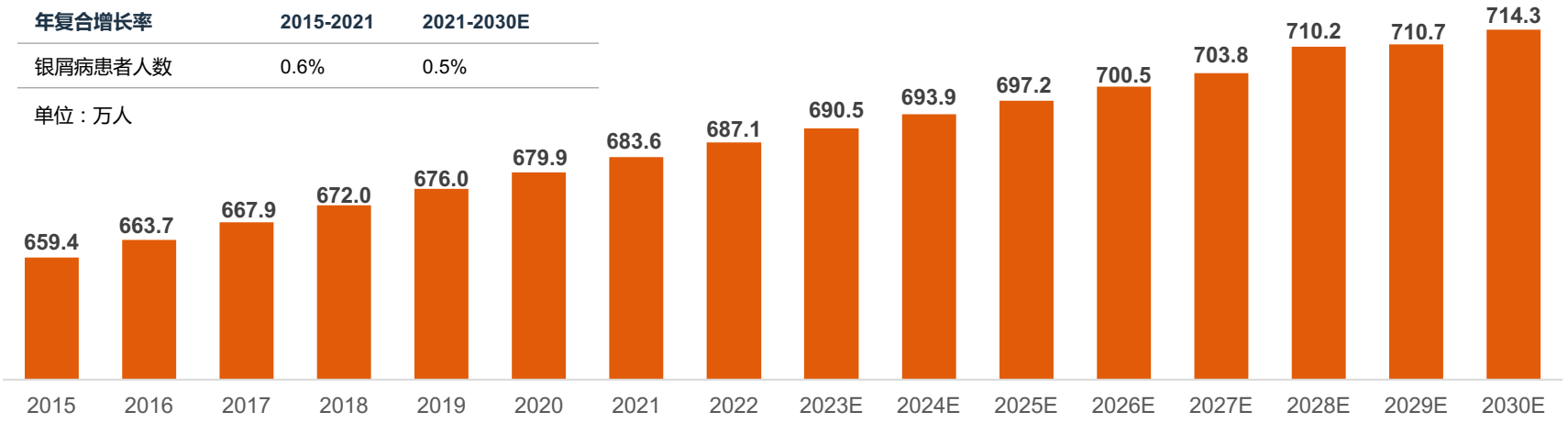
Source: Silvio Danese, MD, PhD, Laurent Peyrin-Biroulet, MD, PhD, Selective Tyrosine Kinase 2 Inhibition for Treatment of Inflammatory Bowel Disease: New Hope on the Rise, Inflammatory Bowel Diseases, Volume 27, Issue 12, December 2021, Pages 2023–2030

5 Psoriasis Market Potential in China

Psoriasis prevalence in China 2015-2030

年复合增长率	2015-2021	2021-2030E
银屑病患者人数	0.6%	0.5%

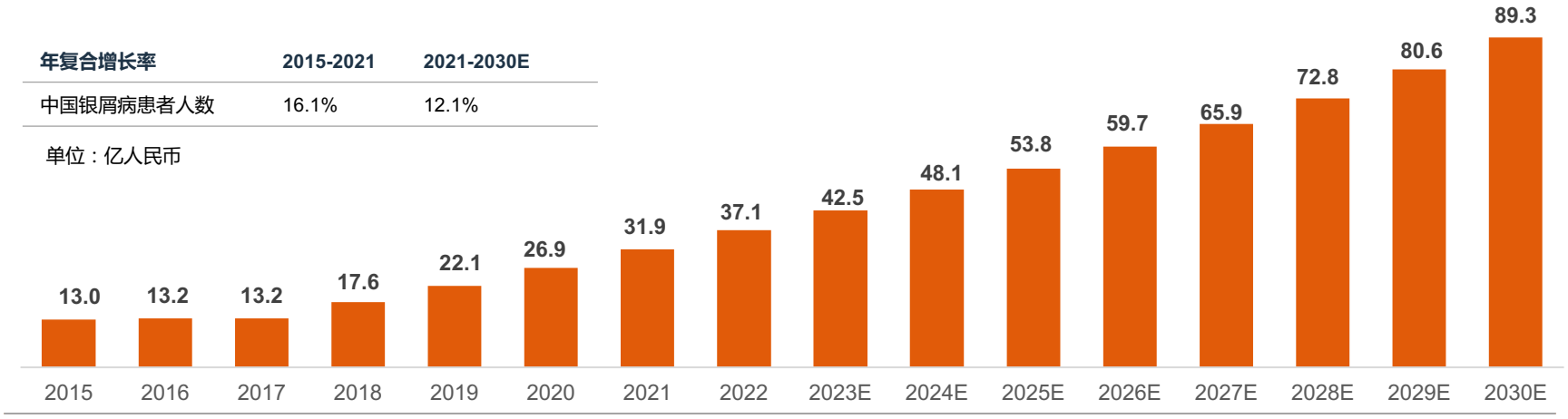
单位：万人



Psoriasis market potential in China 2015-2030

年复合增长率	2015-2021	2021-2030E
中国银屑病患者人数	16.1%	12.1%

单位：亿人民币



Anticipated Milestones & Catalysts in Next 12 Months

Liquid Cancer	■ **Orelabrutinib** ❑ NRDL-renew and indication expansion ❑ 1L CLL/SLL NDA submission ❑ r/r MCL NDA submission in the U.S.	■ **Tafasitamab** ❑ NDA submission in mainland China
	■ **ICP-248** ❑ Preliminary data readout; U.S. IND filing ❑ Combo with Orelabrutinib for CLL/SLL in the U.S. and CN ❑ Phase II pivotal study in r/r CLL/SLL	
Auto-immune Diseases	■ **Orelabrutinib** ❑ Complete SLE PIIb patient enrollment, interim readout by end of 2024 ❑ Complete ITP PIII patient enrollment ❑ MS path-forward	■ **ICP-332** ❑ Phase II AD data readout ❑ Phase III study initiation ■ **ICP-488** ❑ PoC in psoriasis; PII psoriasis initiation
Solid Tumors	■ **ICP-189** ❑ Phase I data readout ❑ Start combo study with EGFR in NSCLC	■ **ICP-723:** Complete patient enrollment of registrational trial; NDA submission ■ **ICP-192:** Strive to complete patient enrollment

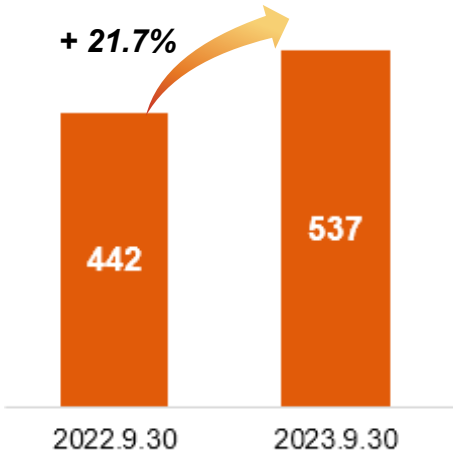
标题	报告详情
口头报告	
A Prospective Multicenter Phase II Study of Orelabrutinib-Lenalidomide-Rituximab (OLR) in Patients with Untreated Mantle Cell Lymphoma (MCL) in China (POLARIS Study): Preliminary Analysis on Efficacy, Safety, Mutation Spectrum and Impact of Mutation Profiling on Treatment Responses **一项奥布替尼-来那度胺-利妥昔单抗联合方案治疗初治MCL前瞻多中心II期研究（POLARIS研究）：疗效、安全性、突变谱和突变谱对治疗应答影响的初步分析**	摘要代码: 736 分会场：623. Mantle Cell, Follicular, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological: Poster II 美东时间：2023年12月11日（星期一）上午11:15 第一作者/通讯作者：张会来
海报展示	
Orelabrutinib monotherapy in patients with relapsed or refractory Waldenström's macroglobulinemia in a single-arm, multicenter, open-label, phase 2 study: long term follow-up results **奥布替尼单药治疗复发或难治性华氏巨球蛋白血症患者的单臂、多中心、开放标签2期研究：长期随访结果**	摘要代码：3039 分会场：623. Mantle Cell, Follicular, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological: Poster II 美东时间：2023年12月10日（星期日）晚上 6:00-8:00 第一作者：曹欣欣
在线发布	
Preliminary safety, pharmacological and efficacy data from patients with relapsed or refractory B-cell malignancies treated with the ICP-248, a next generation BCL2 inhibitor **下一代BCL2抑制剂ICP-248治疗复发或难治性B细胞恶性肿瘤患者的初步安全性、药理学和疗效数据**	摘要代码：6149 第一作者/通讯作者：易树华
Orelabrutinib plus R-CHOP regimen in treatment-naïve patients with TP53-mutated diffuse large B-cell lymphoma (DLBCL) **奥布替尼联合R-CHOP治疗伴有TP53突变的初治DLBCL临床研究**	摘要代码：6289 第一作者/通讯作者：肖毅

标题	报告详情
在线发布	
Efficacy and safety of orelabrutinib- containing TORM regime as first-line therapy in primary central nervous system lymphoma (PCNSL): a retrospective analysis **一项以奥布替尼为基础的TORM方案一线治疗原发中枢神经系统的回顾性研究**	摘要代码：6322 第一作者：吴少杰 通讯作者：李玉华
Phase 1 Trial of Orelabrutinib in Combination with Rituximab, Methotrexate, and Dexamethasone in Patients with Newly Diagnosed Primary CNS Lymphoma Implementing Bayesian Design for Dose-Seeking **奥布替尼联合利妥昔单抗、甲氨蝶呤、地塞米松（ORMD）治疗中枢神经系统淋巴瘤的基于贝叶斯设计的Ⅰ期剂量探索研究**	摘要代码：6225 第一作者：袁燕 通讯作者：陈彤
Effectiveness and Safety of Orelabrutinib in Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma: A Retrospective, Real-World Study in China **奥布替尼治疗CLL/SLL的有效性和安全性：一项回顾性真实世界研究**	摘要代码：6552 第一作者：丁凯阳 通讯作者：纪春岩
Effectiveness and Safety of Orelabrutinib Combined with Rituximab As First-Line Treatment in Marginal Zone Lymphoma **奥布替尼联合利妥昔单抗治疗一线MZL的有效性和安全性**	摘要代码：6146 第一作者：徐佳岱 通讯作者：刘澎
Pomalidomide, Rituximab, Orelabrutinib, and Minichop-like (PRO-miniCHOP) in Elderly Patients with Newly Diagnosed Diffuse Large-B Cell Lymphoma: Preliminary Results from a Phase II Study **奥布替尼、泊马度胺、利妥昔单抗联合mini-CHOP样方案治疗初治老年DLBCL患者的前瞻性探索性临床研究**	摘要代码：6238 第一作者：平娜娜 通讯作者：金正明

Financial Review
Key Financials for First Three Quarters of 2023

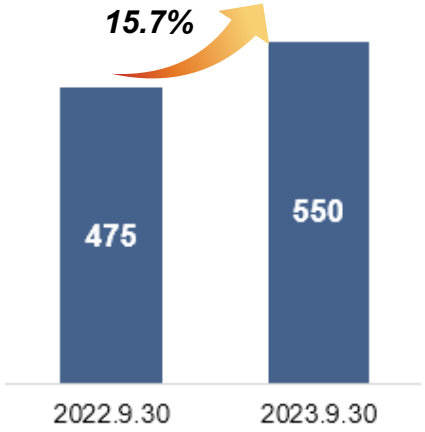
Revenue

(RMB mn)



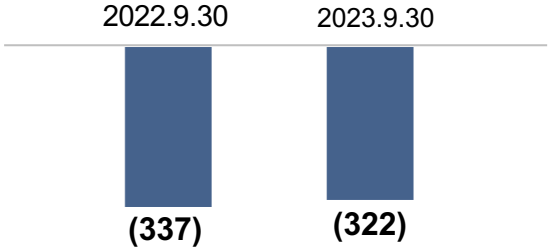
R&D Costs

(RMB mn)



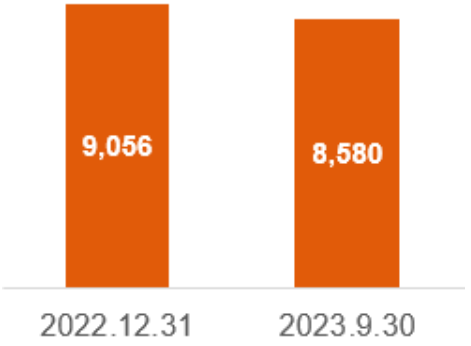
Loss for the Period (Non-HKFRS[1])

(RMB mn)



Cash and Cash Equivalents[2]

(RMB mn)



[1] *Non-HKFRS: excluding foreign exchange and share-based compensation impact*
[2] *Cash and cash equivalents = investments measured at fair value investments, cash and bank balance, interest receivable*
* *Successful STAR Board listing on Sept. 21, 2022*

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科学驱动创新 患者所需为本

Science Drives Innovation for the Benefit of Patients

Research & Development
Product Pipeline – Liquid Cancer

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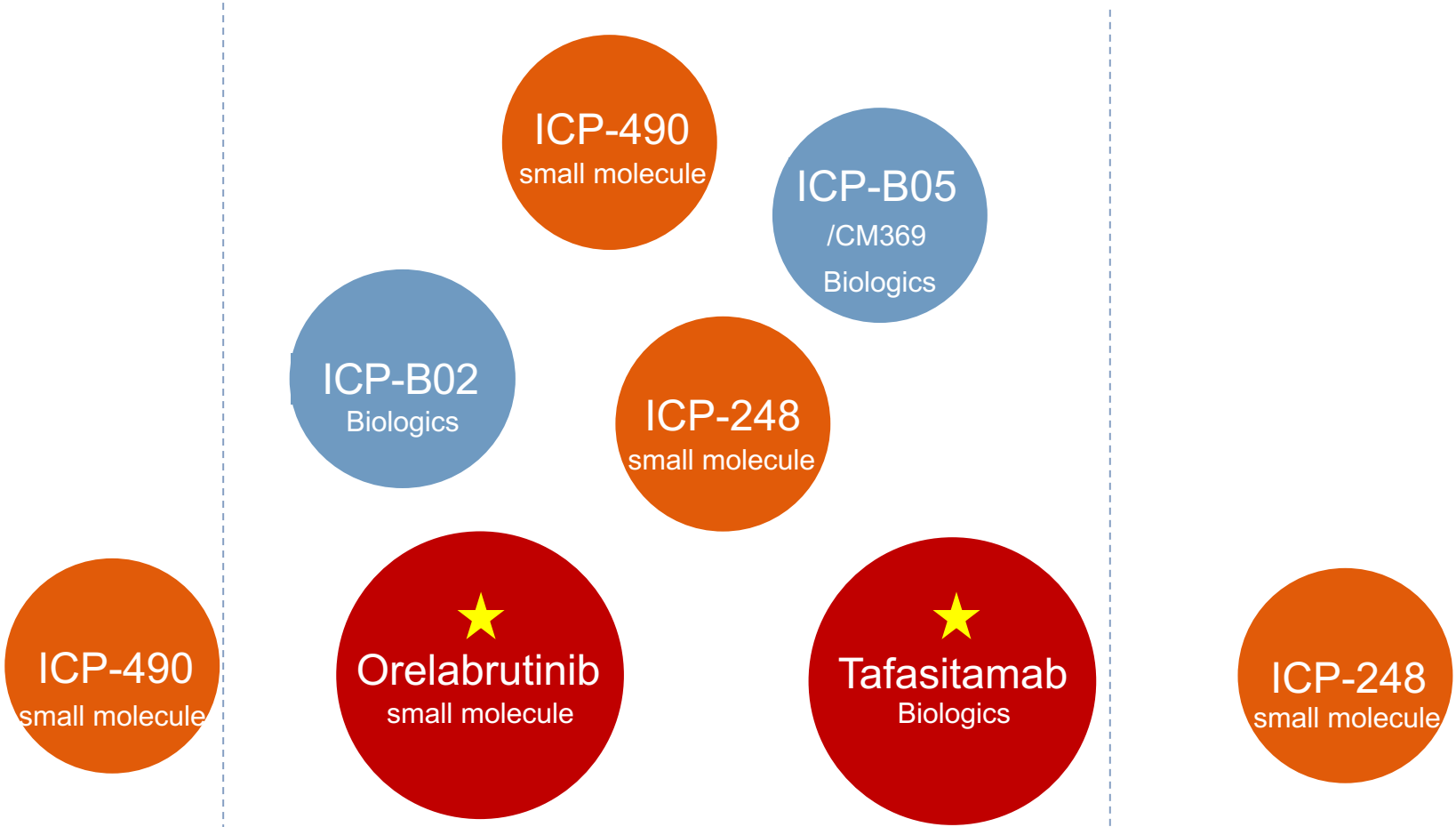
	Drug	Target	Indication(s)	Rights	IND Enabling	Dose Escalation PHIa	Dose Expansion PHIb	Dose Expansion PH2*	Pivotal Trial PH2**	Pivotal Trial PH3	Expected NDA Filing	Market
Liquid Cancer	ICP-022/ Orelabrutinib	BTK	r/r CLL/SLL		NDA approved: 25 Dec 2020							CHN
			r/r MCL		NDA approved: 25 Dec 2020							CHN,SG
			r/r MZL		NDA approved: 21 Apr 2023							CHN
			1L: CLL/SLL								2024	
			1L: MCL									
			1L: MCD DLBCL									
			r/r MCL		U.S. Development Status						2024	
	ICP-B04/ Tafasitamab	CD19	Tafa + LEN, r/r DLBCL								2024	HK
	ICP-B02	CD3 x CD20	Hemato-oncology		Dose escalating in IV&SC							
	ICP-248	BCL2	NHL/ALL/ Combo		Dose escalating							
	ICP-490	E3 Ligase	MM / DLBCL / Hemato-oncology		Dose escalating							
	ICP-B05	CCR8	Hemato-oncology		Dose escalating							

Listed drug | Registrational Trial | NDA | Commercial Product

Comprehensive Coverage for Hemato-oncology



MM	Others	CLL/SLL	MCL	MZL	WM	FL	CNSL	DLBCL	PTCL/ CTCL	AML	ALL	CML	Others
MM		NHL								Leukemia			

Strategies to Cover DLBCL

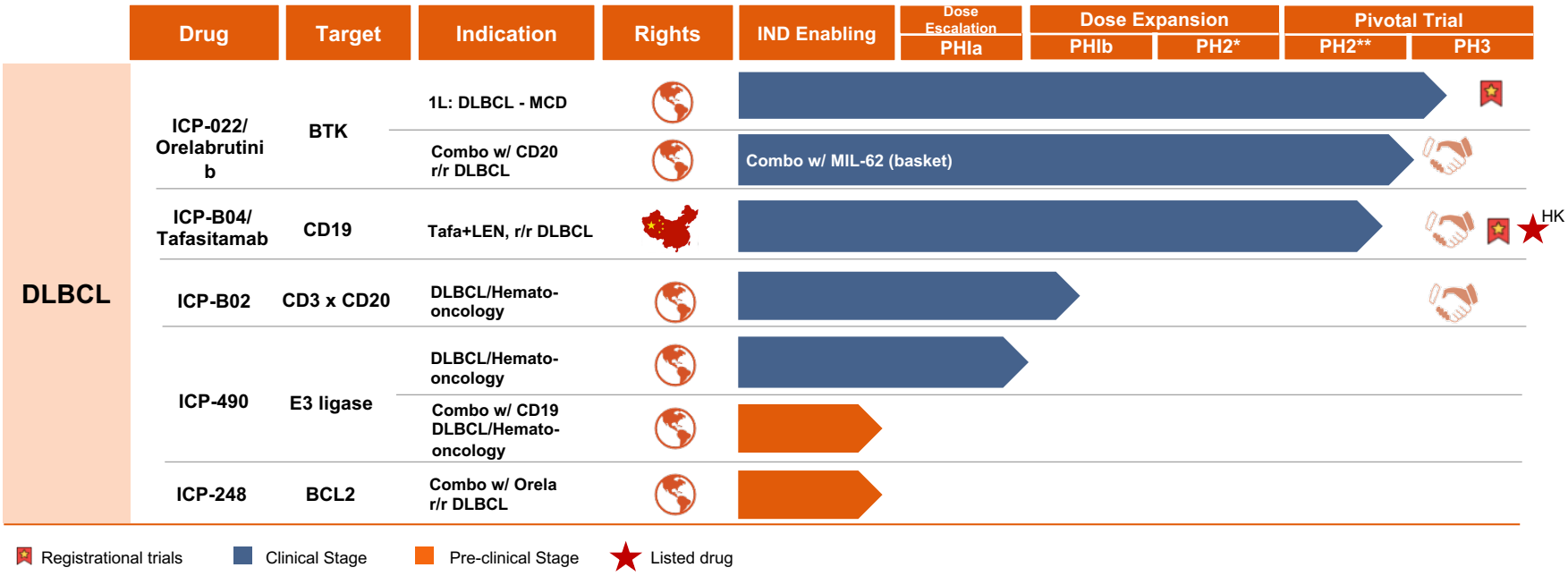
INNOCARE 诺诚健华

Orelabrutinib excellent safety profile for combo therapy

Tafasitamab CD19 Ab with improved ADCC/ADCP

ICP-490 E3 ligase modulator High selectivity/affinity Lenalidomide resistant

CD3xCD20 Highly potent, convenient w/ subQ Safety and convenient for late line patients



1 Major Program Update

Orelabrutinib: Potential Best-in-class BTKi for B-cell Malignancies

INNOCARE 诺诚健华

- **Improved Safety and Robust Efficacy Profile, No severe AF case observed after 850+ patient dosed.**

Efficacy Profile

r/r CLL/SLL

	Orelabrutinib (ICP-CL-00103, N=80)[1]	Ibrutinib Resonate (n=195) [2]	Acalabrutinib ASCEND (n=155) [3]	Zanubrutinib (BGB-3111-205, N=91) [4]
Median Follow-up Time	47 months	44 months	36 months	34 months
ORR	93.8%	91%	93%	87.9%
CR / CRi	**30%**	9%	5%	6.6 %
PR / nPR	52.5%	78%	78%	69.2%
PR-L	11.3%	4%	10%	12.1%

Safety Profile

Adverse events of special interest	Orelabrutinib N=550* (%)	Ibrutinib N= 1,476[1] (%)	Acalabrutinib N= 1,029 [2] (%)	Zanubrutinib N= 629 [3,4] (%)
Any grade diarrhea	6.0%	43.8%	31%	20%
>= Grade 3 Atrial fibrillation	**0**	4.0%	1.1%	0.6%
Second primary malignancies	0.4%	10%	12%	9%
Major hemorrhage	1.1%	4% #	2.7%	3%
≥ Grade 3 Infection	9.6%	21%	19%	23%

r/r MCL (N=106, median follow time of 39.4 months)

- 83% patients achieved ORR and 87.7% patients achieved disease control.
- CR rate, by conventional CT method, increased to 36.8% and it was expected a higher rate of in depth response may occur with prolonged treatment.
- The median PFS was 27.4 month and the median OS was not reached.

r/r MZL (N=90, median follow time of 24.3 months)

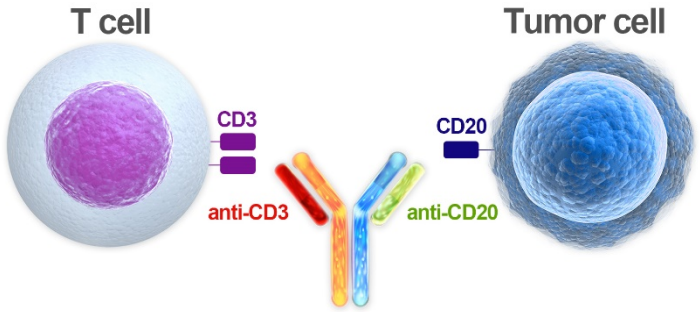
- **First BTKi for MZL in China.**
- ORR was 58.9% assessed by independent review committee (“IRC”).
- The median duration of response (“DOR”) was 34.3 months (95% CI).
- The estimated 12-month PFS and OS were 82.8% and 91%.

Sources: Imbruvica Prescribing Information, Jan 2019
Pooled Analysis of Safety Data from Clinical Trials Evaluating Acalabrutinib Monotherapy in Hematologic Malignancies, John C. Byrd, et al., Blood, 2017; 130:4326
NDA/BLA Multi-disciplinary Review and Evaluation, 210259Orig1s000, Center for Drug Evaluation and Research
Pooled Analysis of Safety Data from Monotherapy Studies of the Bruton Tyrosine Kinase (BTK) Inhibitor, Zanubrutinib (BGB-3111), in B-Cell Malignancies, S. Tam C., et al., European Hematology Association, Jun 15, 2019; 266776, PS1159 ; Xu W, et al. J Hematol Oncol . 2020 May 11;13(1):48. ; Huang X, et al. Cancer Med. 2018 Apr;7(4):1043-55. ; Byrd JC, et al. 2017 ASCO poster 272.
Ghia P, et al. J Clin Oncol . 2020 May 27:JCO1903355
“Safety Analysis of Four Randomized Controlled Studies of Ibrutinib in Patients with Chronic Lymphocytic or Mantle Cell Lymphoma” by Susan O’Brien, et al., Original Study, 2018; 18(10), 648-657. e15
Efficacy data cut off data：2022.12.30 (MCL & CLL/SLL); 2022.10.9 (WM)

- *Safety profile Note: Data cut off date 2022.12.24*
- **≥ Grade 3, serious, or any grade central nervous system bleeding events.&two cases, one with intracranial hemorrhage (65-year old patient with >10 years hypertension) and the other with vitreous hemorrhage which was assessed as unlikely related to the treatment of orelabrutinib.** Data cutoff date October 31, 2020. § one AML and one bladder cancer (based on TEAEs irrespective of causality assessment).¥ ≥ Grade 3, serious, or any grade central nervous system bleeding events. # From 2,838 pts who received ibrutinib in 27 clinical trials ## Bruising and petechiae excluded.1 Imbruvica US prescribing information2 Calquence US prescribing information3 Brukinza US prescribing information 4 Brukinza NDA Multi-Discipline Review*

Major Program Update

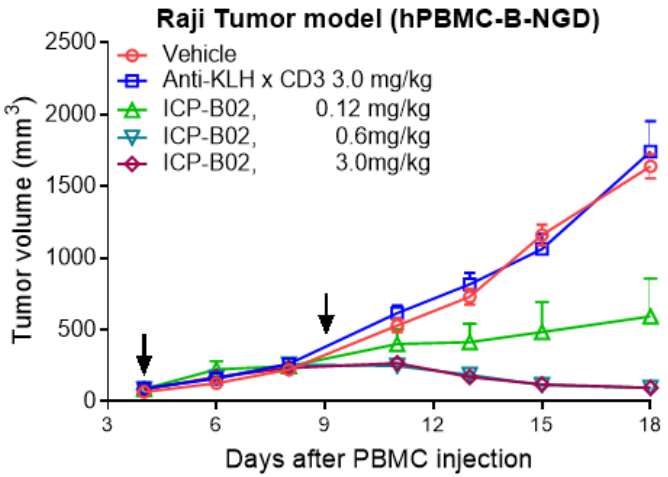
ICP-B02: Potential Best-in-class CD3 x CD20 BsAb



ICP-B02 Clinical Development Plan Targets Multi-indications and Settings

- Dose escalation of IV cohorts completed, 1st SC cohort completed
- Good efficacy observed in both IV and SC cohorts in **FL and DLBCL patients**
- **Well tolerated with no DLT observed,** low grade and manageable CRS
- SC formulation improves safety and convenience
- Significant potential across a broad range of indications in NHL as **mono or combo therapies.**

Superior anti-tumor activity



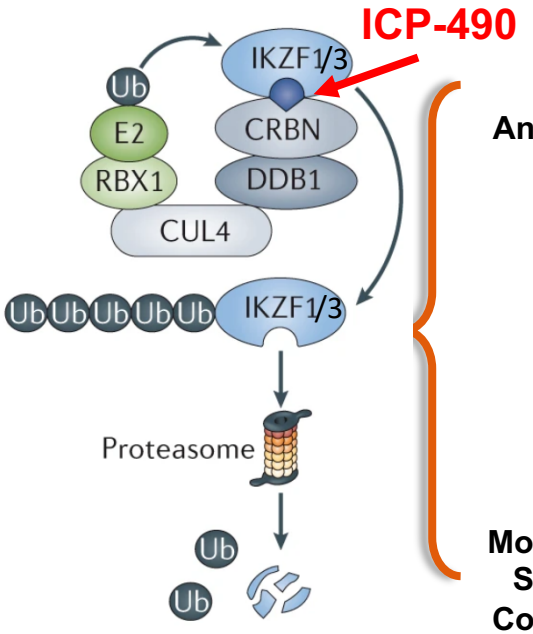
Major Program Update

ICP-490: Highly Potent Next Generation CRBN Modulator

INNOCARE 诺诚健华

Blockbuster Potential for Multi-indications

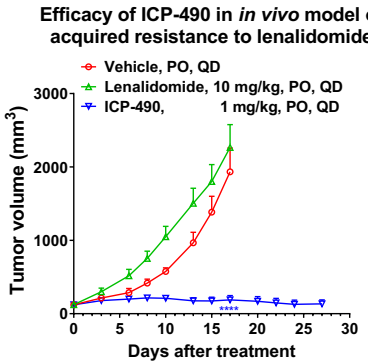
- **Superiority in potency** and overcomes acquired resistance to lenalidomide
- **Synergy with therapies** such as anti-CD38, anti-CD20, anti-CD19 mAbs etc., strong rationale for combination in the clinic
- **Revolutionary treatment of MM**
- **Immense potential in hemato-oncology, including MM, NHL as a mono therapy or in combo with others**



Direct Anti-Myeloma Effects

Immune Modulation for Synergistic Combinations

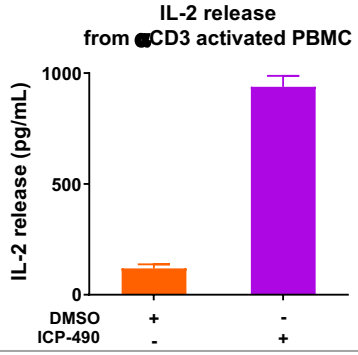
• **Overcomes acquired resistance**



MM

r/r MM
1L MM

• **Increases IL-2 modulates immune**

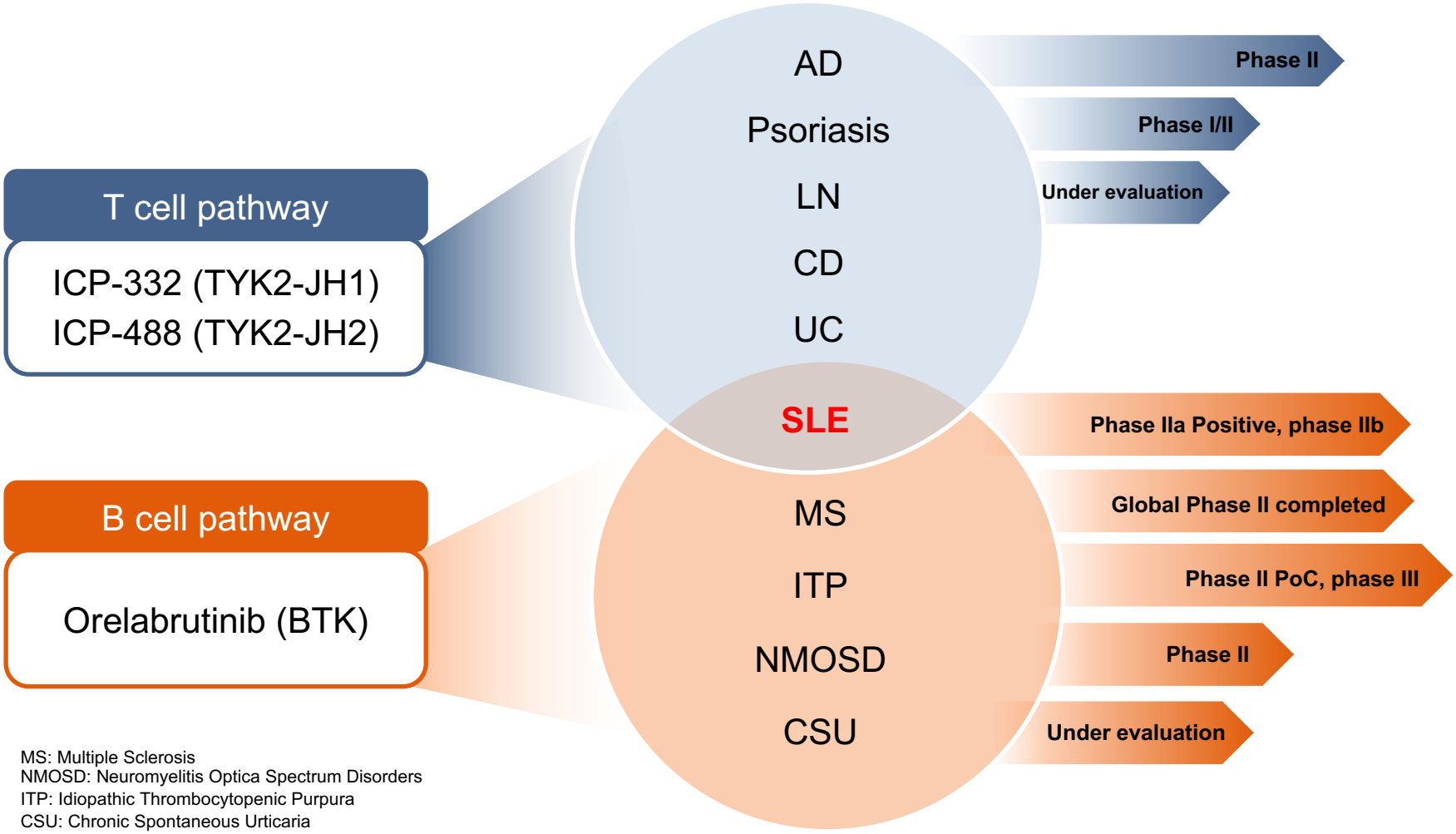


MM
NHL

MM
NHL
(CLL/SLL, MCL, MZL, WM, FL, DLBCL, etc.)

Source a: Reference: a: Jan, M., Sperling, A. S., and Ebert, B. L. (2021). Cancer therapies based on targeted protein degradation — lessons learned with lenalidomide. Nature Reviews Clinical Oncology 18, 401-417.

Autoimmune Disease Strategy



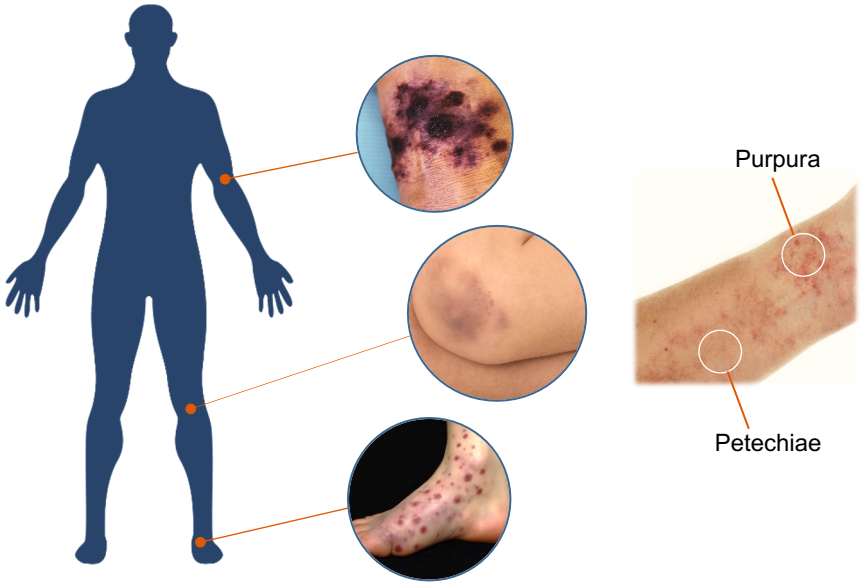
MS: Multiple Sclerosis
NMOSD: Neuromyelitis Optica Spectrum Disorders
ITP: Idiopathic Thrombocytopenic Purpura
CSU: Chronic Spontaneous Urticaria
SLE: Systemic Lupus Erythematosus
AD: Atopic Dermatitis
LN: Lupus Nephritis
CD: Crohn's disease
UC: Ulcerative Colitis

1 Major Program Update

Orelabrutinib (ICP-022): Phase III Registrational Trial for ITP Initiated

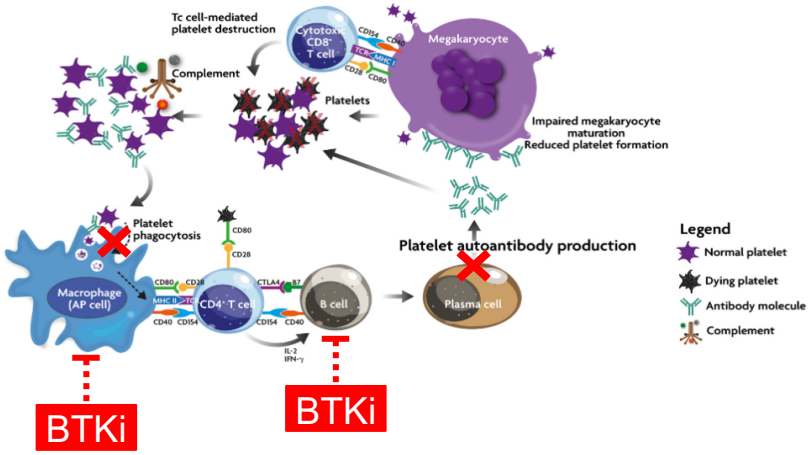
INNOCARE 诺诚健华

Immune Thrombocytopenia



BTKi's advantage in ITP

- Decreased macrophage (Fcγ receptor)–mediated platelet destruction
- Reduced production of pathogenic autoantibodies



- Phase II: **40% patients met the primary endpoint at 50mg QD**
- Phase III: registrational trial being initiated in China
- Frontline BTK inhibitor gets approved for AID
- Considering global markets

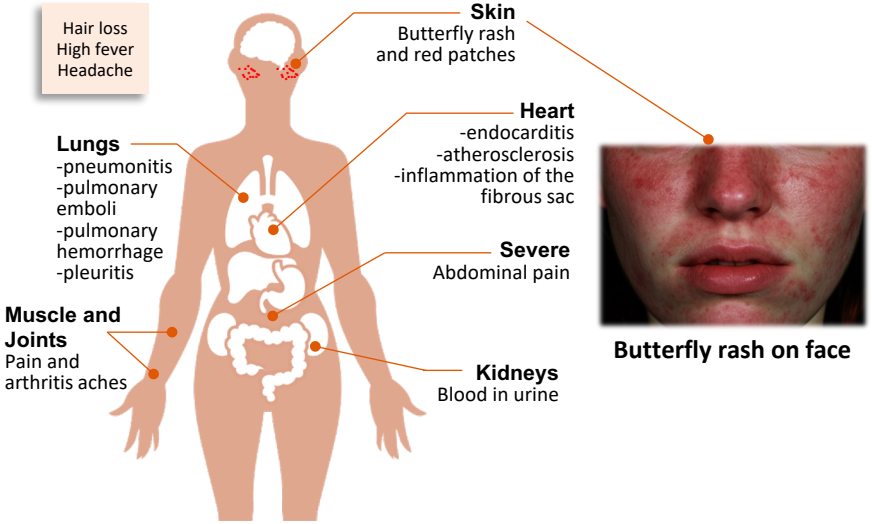
Source: Drew Provan, John W. Semple, DOI:https://doi.org/10.1016/j.ebiom.2022.103820

2 Major Program Update

Orelabrutinib (ICP-022): SLE Phase IIa Positive Results Lead to Further Development

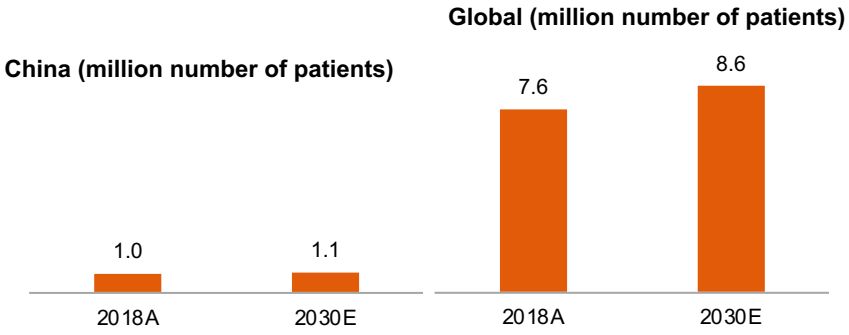
INNOCARE 诺诚健华

Systemic Lupus Erythematosus

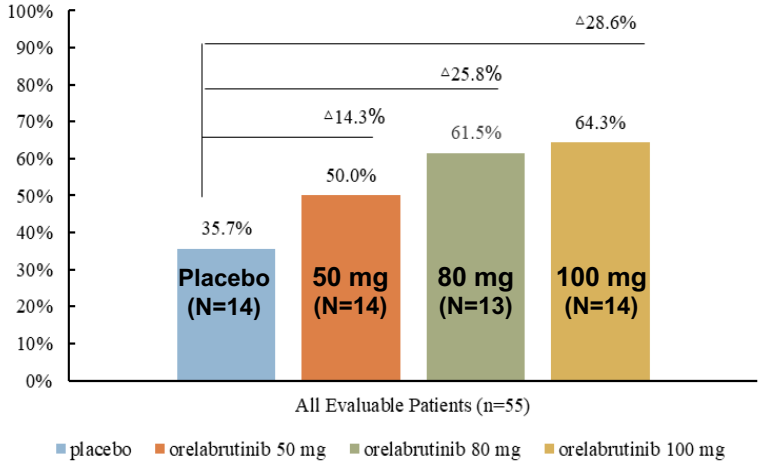


Butterfly rash on face

SLE Prevalence



SLE Phase II Study Results[1]

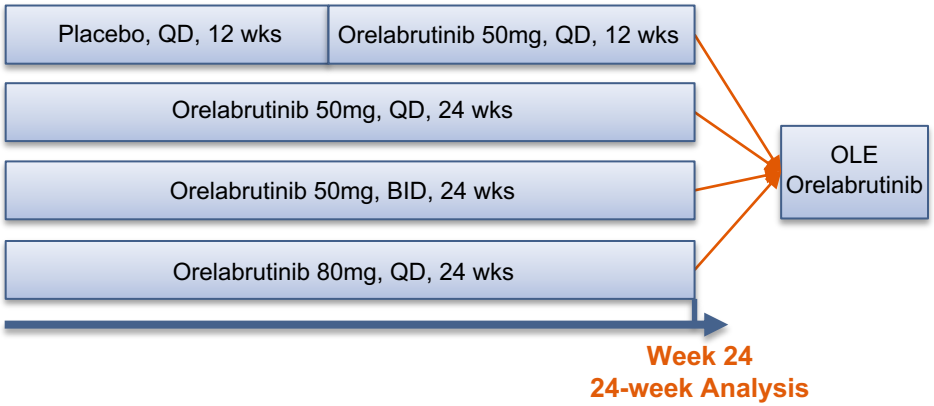


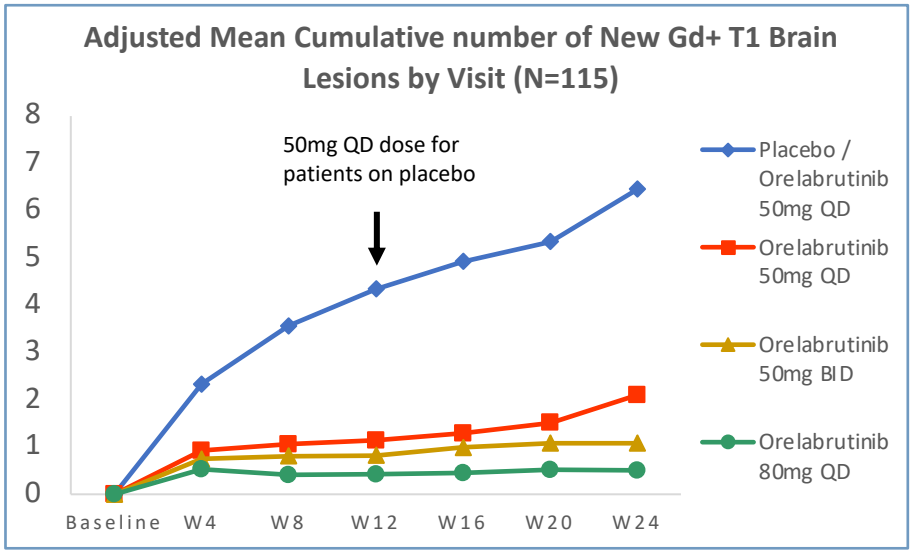
- SLE Responder Index ("SRI")-4 response rates increased in a dose dependent manner
- Trends of reduction in proteinuria level and improvement of immunologic bio-markers[2]
- The **only BTK inhibitor ever** shown efficacy in Phase II SLE trials
- **PIIb enrollment ongoing, interim results expected by end of 2024**

*[1] The Phase IIa trial evaluated the safety and efficacy of Orelabrutinib plus standard of care verse placebo plus standard of care ("**SoC**") in patients with mild to moderate SLE*
[2] Reduced immunoglobulin G and increased complements C3 and C4 were observed

3 Major Program Update: MS Phase II Results

Orelabrutinib (ICP-022): Potential Best-in-class BTKi for Multiple Sclerosis





Key Findings

- All orelabrutinib groups achieved T1 new lesion control after 4 weeks of treatment, and the effect is sustained up to 24 weeks
- **92.3%** relative reduction achieved in cumulative number of new Gd + T1 lesions 24 weeks at **80mg QD** compared to placebo arm
- **Best-in-class** profile

Cumulative number of New Gd+ T1 Lesion from Week 4 to Week 24	Placebo / Orela 50mg QD (N=27)	Orela 50mg QD (N=30)	Orela 50mg BID (N=29)	Orela 80mg QD (N=29)
Adjusted mean cumulative number (95% CI) of lesions from W4 to W24	6.45 (3.62, 11.52)	2.10 (0.62, 7.11)	1.08 (0.30, 3.81)	0.50 (0.09, 2.74)
Percent reduction		**67.4** (-22.0, 91.3)	**83.3** (33.2, 95.8)	**92.3** (56.5, 98.6)
P-value		**0.0958**	**0.0114**	**0.0037**

Notes: The adjusted mean cumulative number, percent reduction (orelabrutinib vs placebo) associated with the 95%CI and p-value are estimated from a poisson regression model with a pearson scale parameter with a log link function and offset by log number of scans as of that visit. Baseline number of Gd+ T1 brain lesions is included in the model as a continuous covariate.
The above analyses are based on PHS population that includes all randomized subjects, but excludes the subjects who missed any one of the three MRI data points within first 12 weeks due to Covid-19 or unexpected events including Ukraine war and early termination per US FDA partial clinical hold.

Major Program Update

ICP-332:TYK2 JH1 Inhibitor for Oral Treatment of AD and Other Indications

INNOCARE 诺诚健华

Atopic Dermatitis

ICP-332 (TYK-2, JH1)

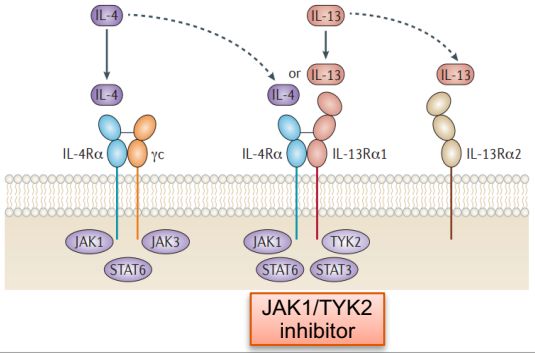
- Phase I study: SAD, MAD, food effect completed
  - Demonstrated a dose proportional and favorable PK profile, no significant food effect observed
  - Safe and well-tolerated, **no significant decrease of platelet and hemoglobin (JAK2-related AE) observed** and **no DLT observed**
- **Phase II** trial for **atopic dermatitis** (80 and 120 mg QD doses) will finish patients enrollment in Sept. 2023, study readout by end of 2023

Selectivity

Drug	TYK2 vs. JAK1 (fold)	TYK2 vs. JAK2 (fold)	JAK1 vs. JAK2 (fold)
ICP-332	~40	~400	10

Evaluate JAK1/TYK2 inhibitor for AD and other indications

Strategies: Targeting Type 2 Inflammation by JAK-Inhibitor



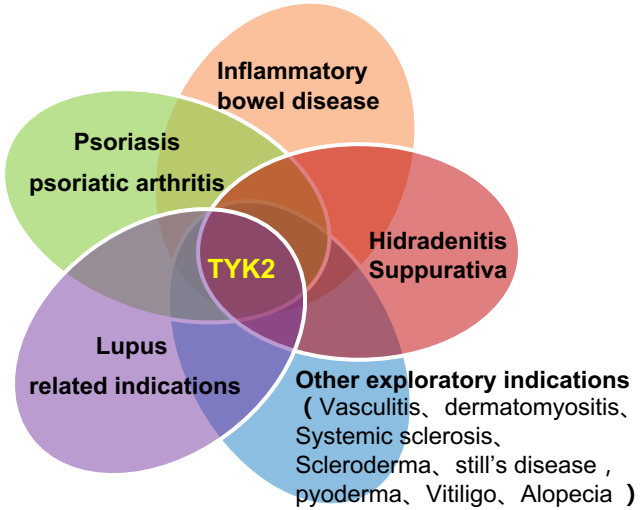
Source: Global Burden of Disease (GBD) study 2022

Major Program Update

ICP-488:TYK2 JH2 Inhibitor for Oral Treatment for Psoriasis and Other Indications

Psoriasis

Indications to be developed

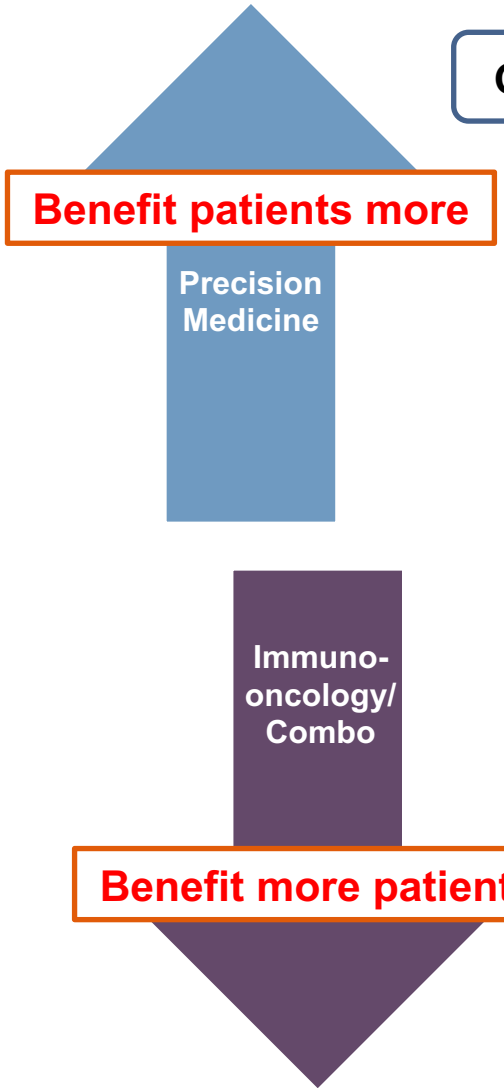


ICP-488 (TYK-2, JH2)

- An oral, potent and allosteric TYK2 inhibitor that selectively binds to the JH2 pseudokinase domain **with no activities on JAK1-3**
- Phase I study
  - Completed SAD (maximum dosage to 36mg), MAD and food effects arms, **no DLT observed**
  - 2 cohorts of **psoriasis patients for early PoC**
- Phase II being initiated
  - Potential to show significant advantages in safety profiles verse other JAK family inhibitors.

Source: Silvio Danese, MD, PhD, Laurent Peyrin-Biroulet, MD, PhD, Selective Tyrosine Kinase 2 Inhibition for Treatment of Inflammatory Bowel Disease: New Hope on the Rise, Inflammatory Bowel Diseases, Volume 27, Issue 12, December 2021, Pages 2023–2030

Solid Tumor Strategy



Giving the right medicine, to the right patient, at the right time

- **ICP-723 (Zurletrectinib)**
  80-90% ORR observed in patients with various type of solid tumors carrying **NTRK fusion** at dosages of **8 mg and above**
- **ICP-192 (Gunagratinib)**
  20 mg showed **efficacy in cholangiocarcinoma patients** with **52.9% ORR, 94.1% DCR**

RTKi	EGFRi	VEGFi	KRASi	RAFi
MEKi	CDK4/6i	PD-1/PD-L1	ICI	

ICP-189
SHP-2

ICP-B05
CCR8

Cornerstone of Combination Therapy

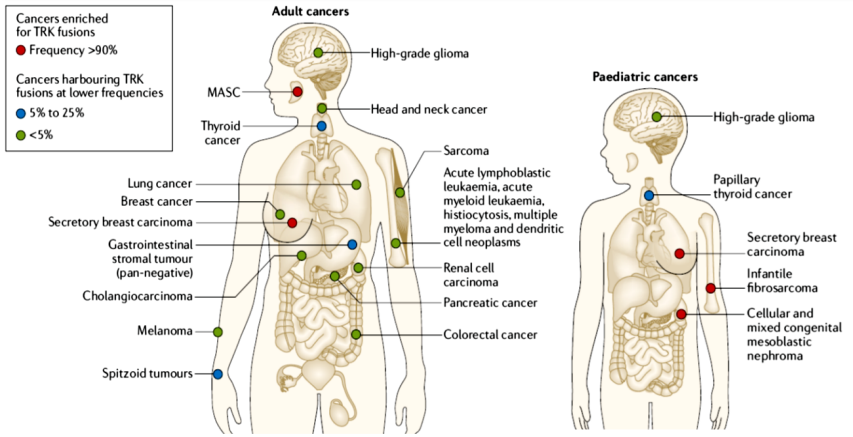
Major Program Update

ICP-723: Favorable Clinical Results with Potential Best-in-Class Profile

ICP-723 (Zurletrectinib,TRK)

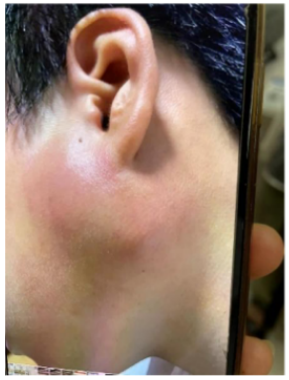
- **2nd generation TRKi overcomes acquired resistance to 1st generation TRKi**
- Phase I study demonstrated favorable PK profile and excellent anti-tumor activity
- **No DLTs** observed in Phase I dose escalation study (1-20 mg)
- **Phase II registration trial** for NTRK gene abnormalities ongoing, **80-90% ORR, NDA submission expected by end of 2024**
- **1 PR in larotrectinib-resistant patient**
- IND for **pediatric patients** approved
- Exploring in patients with ROS1 mutations

NTRK Gene Fusion Mutation is an Oncogenic Driver for a Variety of Cancer Types

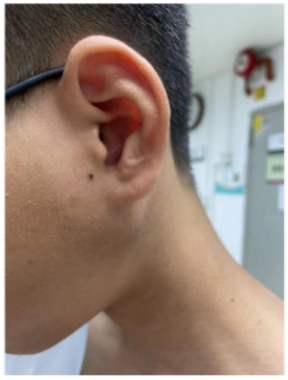


A Case in the Adolescent Arm

Before the treatment of ICP-723



15 days after dosing ICP-723



Major Program Update

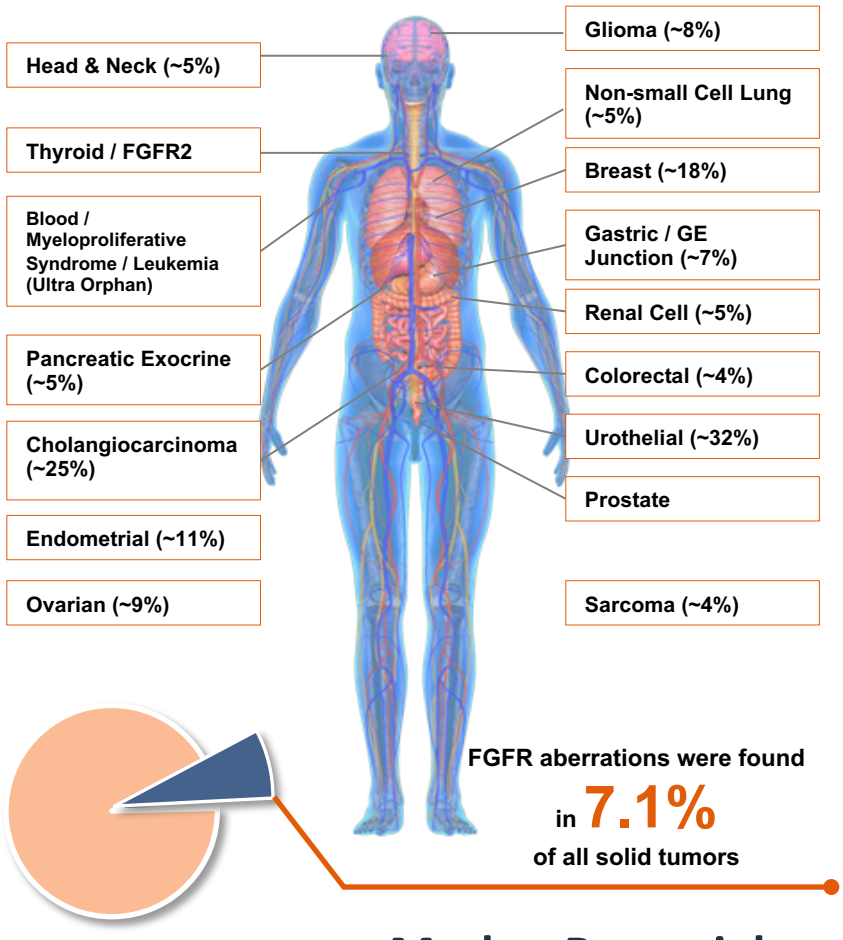
ICP-192: Promising Safety and Efficacy in Phase II Trials

INNOCARE 诺诚健华

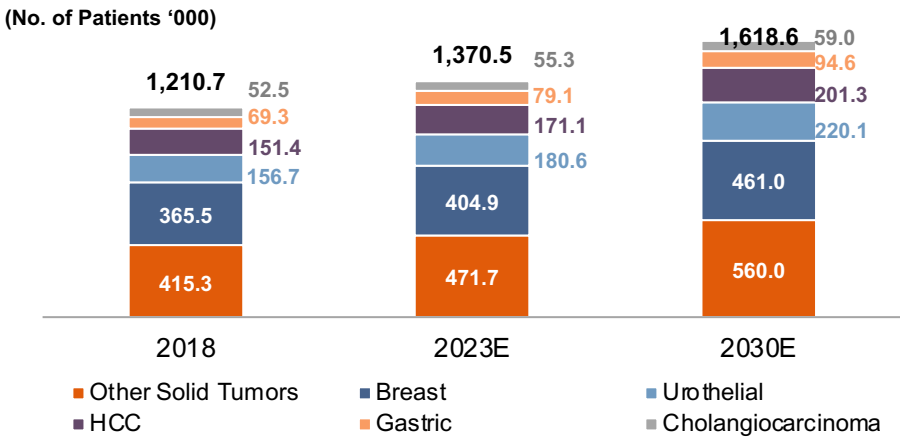
ICP-192 (Gunagratinib, FGFR)

- Finished phase I dose-escalation **2 mg to 26 mg, no DLT observed**
- Safe and well-tolerated in patients with advanced solid tumors
- **Registrational trial is ongoing at 20 mg in cholangiocarcinoma**
- Exploring multiple other indications in solid tumor

Frequency of All Currently Known FGFR 1, 2, 3 and 4 Aberrations



A Glance at FGFR Mutation by Solid Tumor Types Worldwide



Market Potential

Source: Frost & Sullivan Analysis
Source: Helsten et al., 2015, Clinical Cancer Research

Major Program Update

ICP-189: Potentially Best-in-Class and First-in-Class SHP2 Inhibitor with Large Potential in Combinational Treatments

INNOCARE 诺诚健华

ICP-189 Phase I in Advanced Solid Tumors

- Phase I does escalation to 120 mg QD cohort with no DLT observed
- **1 Confirmed PR** observed in a cervical cancer patient at 20 mg QD dose
- Potential class leading safety profile
- **IND accepted for combo with EGFRi in NSCLC**
- Demonstrated robust single agent activity in multiple xenograft models with strong PK/PD correlation and synergistic anti-tumor effects in combination with multiple targeted therapies targeting RAF/MEK/ERK, EGFR, CDK4/6, FGFR and anti-PD-1 *in vitro* and *in vivo*

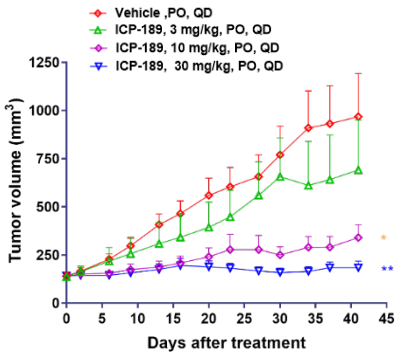
INNOCARE 诺诚健华 | ARRIVENT

ICP-189
SHP2 inhibitor

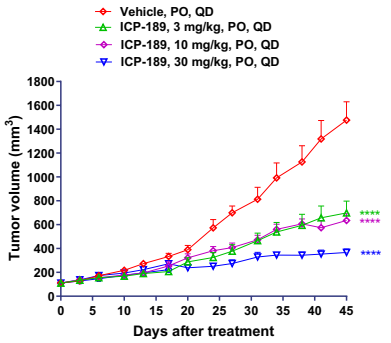
Furmonertinib
EGFR inhibitor

Significant Anti-Tumor Effect in Tumor Models Driven by $KRAS^{G12C}$ Mutation and EGFR Over-expression

NCI-H358 ($KRAS^{G12C}$)



KYSE520 (EGFR)



Research & Development

Product Pipeline – Autoimmune & Solid Tumor

INNOCARE 诺诚健华

Listed drug | Registrational Trial | NDA | Commercial Product

Company 2.0 Objective: Provide More Innovative Drugs to Patients

- ✓ **≥ 6 commercial products**
  - Marketed: Orela-Hema① , Tafa* (Hainan, HK, GBA)
  - 2025-6: Tafa② (China mainland) , ICP-723③, ICP-192④

    2027-8: Orela-AID⑤ (*ITP, SLE, MS*); ICP-248⑥, ICP-332⑦, ICP-488⑧, ICP-490, ICP-189, ICP-B02, ICP-B05…..
- ✓ **A recognized leader in hematology**
- ✓ A strong competitor in **autoimmune diseases** and solid tumor
- ✓ Additional 5-10 **well-positioned assets** in R&D, unique research platforms
- ✓ Powerful engine in R&D, BD, manufacturing and commercialization platforms, operational excellence
- ✓ **3-4 products globalization (*out-license, partnership, etc.*)**
- ✓ **Annual revenue reaches significant numbers**