InnoCare Pharma (9969 HK)

Biopharmaceutical company developing global innovative therapies in oncology and autoimmune areas

- **Fully-integrated platform with high operating efficiency**. Led by a world-class management team, InnoCare has built a fully integrated biopharmaceutical platform with strong in-house R&D capabilities. InnoCare's fully-integrated platform covers the entire spectrum of drug discovery and development functionalities, including drug target identification and verification, pre-clinical evaluation, clinical trial design and execution, drug manufacturing and quality control, and commercialization. During the last two years, InnoCare initiated seven clinical trials, including two registrational trials.
- **Strong ties with world-class scientists.** InnoCare's in-house R&D capability is supplemented by globally renowned structural biologist Dr. Yigong Shi (施一公), the Company's co-founder and President of Scientific Advisory Board, and cancer genomics expert Dr. Zemin Zhang (张泽民), the Company's Scientific Advisor. InnoCare has entered into exclusive strategic collaboration agreements with Dr. Shi and Dr. Zhang, respectively.
- **Orelabrutinib is a potential best-in-class BTK inhibitor.** Orelabrutinib (ICP-022) is a potential best-in-class, highly selective and irreversible BTK inhibitor under clinical trials in China and US for the treatment of various B-cell malignancies and autoimmune diseases. The NMPA has accepted the new drug application (NDA) of orelabrutinib for the treatment of patients with r/r CLL/SLL and r/r MCL and granted priority review status for these two applications. We expect orelabrutinib to receive approvals from NMPA for treatment of r/r CLL/SLL and r/r MCL in 2H20E.
- **Drug sales to start from 2021E.** We forecast drug sales to start from 2021E and expect risk-adjusted revenue of RMB106mn/ RMB274mn/ RMB553mn in FY2021E/22E/23E. The most advanced drug is orelabrutinib which may be approved by NMPA in 2H20E, in our view. We also forecast ICP-192 and ICP-105 to receive NMPA's approval in 2023E and 2024E, respectively. Considering that InnoCare owns the global rights in these above-mentioned drug candidates, we expect meaningful sales from the US market from 2024E. By applying different probability of success (PoS) to drug candidates, we forecast a net loss of RMB373mn/RMB286mn/RMB128mn in FY2020E/21E/22E and expect net profit to breakeven in 2023E.
- **Initiate BUY with TP of HK$16.21.** The most advanced drug is Orelabrutinib, which we expect to receive approval from NMPA by 2H20E. Innocare's future cash flows will rely on the successful commercialization of pipeline drugs. We see DCF as appropriate in valuing the Company. We derive a TP of HK$16.21 based on an 11-year DCF valuation (WACC: 9.7%, terminal growth rate: 5.0%).

Earnings Summary

(YE 31 Dec)	FY18A	FY19A	FY20E	FY21E	FY22E
Revenue (RMB mn)	2	1	2	106	274
YoY growth (%)	N/A	(23)	60	5,220	157
Attributable net profit (RMB mn)	(550)	(2,141)	(373)	(286)	(128)
YoY growth (%)	N/A	N/A	N/A	N/A	N/A
ROE (%)	N/A	N/A	N/A	N/A	N/A
ROA (%)	(25)	(82)	(8)	(6)	(3)
Net gearing (%)	Net cash	Net cash	Net cash	Net cash	Net cash
Current ratio (x)	29	37	271	181	129

Source: Company data, CMBIS estimates

BUY (Initiation)

Target Price	HK$16.21
Up/Downside	+14.3%
Current Price	HK$14.18

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Mkt. Cap. (HK$ mn)	18,280
Avg. 3mths t/o (HK$ mn)	N/A
52W High/Low (HK$)	15.40/9.31
Total Issued Shares (mn)	1,289

Source: Bloomberg

Shareholding Structure

Management	36.39%
Pre-IPO and Cornerstone investors	43.95%
Free float	19.67%

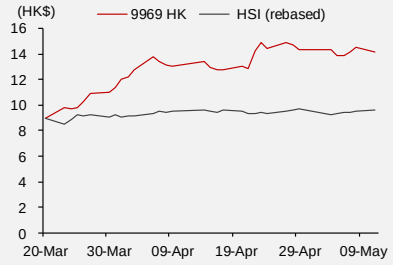
Source: Bloomberg

Share performance

	Absolute	Relative
1-mth	11.2%	11.5%
3-mth	N/A	N/A
6-mth	N/A	N/A

Source: Bloomberg

12-mth price performance



Source: Bloomberg

Auditor: Ernst & Young
Web-site: www.innocarepharma.com

Contents

Investment Thesis

Founded in Nov 2015 by Dr. Jisong Cui and Prof. Yigong Shi, InnoCare Pharma Limited (InnoCare) is a clinical-stage biopharmaceutical company committed to develop best-in-class and/or first-in-class drugs for treatment of cancer and autoimmune diseases.

Fully-integrated platform with high operating efficiency

Led by a world-class management team, InnoCare has built a fully integrated biopharmaceutical platform with strong in-house R&D capabilities. InnoCare's fully-integrated platform covers the entire spectrum of drug discovery and development functionalities, including drug target identification and verification, pre-clinical evaluation, clinical trial design and execution, drug manufacturing and quality control, and commercialization.

InnoCare has an R&D team with over 150 members, including a drug discovery team of approximately 100 employees and a clinical development team of approximately 50 employees. During the last two years, InnoCare initiated seven clinical trials, including two registrational trials. The Company advanced the orelabrutinib r/r CLL/SLL and r/r MCL registrational trials from ethics committee approvals to completion of the enrolment of 80 r/r CLL/SLL patients and 106 r/r MCL patients within one year.

Strong ties with world-class scientists

InnoCare's in-house R&D capability is supplemented by globally renowned structural biologist Dr. Yigong Shi (施一公), the Company's co-founder and President of Scientific Advisory Board, and cancer genomics expert Dr. Zemin Zhang (张泽民), the Company's Scientific Advisor. InnoCare has entered into exclusive strategic collaboration agreements with Dr. Shi and Dr. Zhang, respectively.

InnoCare has also established a Scientific Advisory Board comprising top-notch professors and key opinion leaders, including Dr. Zemin Zhang, Dr. Zhanguo Li, a world-class specialist in rheumatoid immunotherapy and former director of the Clinical Immunology Center/Rheumatism Immunology Department at Peking University People's Hospital, and Professor Arnold Levine, a globally recognized leader in cancer research and professor emeritus at the Institute of Advanced Study.

Orelabrutinib is a potential best-in-class BTK inhibitor

Orelabrutinib (ICP-022) is a potential best-in-class, highly selective and irreversible BTK inhibitor under clinical trials in China and US for the treatment of various B-cell malignancies and autoimmune diseases.

The Company has submitted two NDAs to the NMPA for Orelabrutinib: one for r/r CLL/SLL that was accepted in Nov 2019 and granted priority review in Jan 2020, the other for r/r MCL that was accepted and granted priority review in Mar 2020. We expect orelabrutinib to receive approvals from NMPA for treatment of r/r CLL/SLL and r/r MCL in 2H20E.

InnoCare is also evaluating orelabrutinib in three Phase II trials for patients with r/r marginal zone lymphoma (MZL), r/r central nervous system lymphoma (CNSL) and r/r Waldenstrom's Macroglobulinemia (WM) in China. We expect patient enrolment of these three trials to be completed by end-2020E and corresponding indications will receive NMPA approvals in 2022E.

Potentially due to its high selectivity, orelabrutinib demonstrated a favorable safety profile and was found to be well-tolerated by patients with r/r MCL and r/r CLL/SLL in two separate ongoing registrational studies. For TEAEs occurred in these two trials, all diarrheas were Grade 1 or 2 except for one Grade 3 (0.5%) and no atrial fibrillation was observed. The favorable safety profile as compared with approved BTK inhibitors may correlate with the higher selectivity of orelabrutinib.

Orelabrutinib's favorable safety profile and convenient QD dosing regimen make it a potential best-in-class therapeutic option for patients with B-cell malignancies. In addition, orelabrutinib has shown a robust efficacy profile in advanced-stage r/r MCL and r/r CLL/SLL patients.

ICP-192 is a potential first-to-market pan-FGFR inhibitor in China

ICP-192 is a potent, highly selective, irreversible small-molecule pan-FGFR inhibitor in clinical studies for the treatment of patients with various types of solid tumors in China. InnoCare plans to initially develop ICP-192 for the treatment of urothelial cancer and cholangiocarcinoma.

As of Apr 2020, the US FDA has approved two pan-FGFR inhibitors, including Johnson & Johnson's erdafitinib (厄达替尼; brand name Balversa) approved by the FDA in Apr 2019 for advanced urothelial cancer and Incyte's pemigatinib (brand name Pemazyre) approved in Apr 2020 for the treatment of cholangiocarcinoma. While there are multiple candidates under development, currently there is no marketed pan-FGFR inhibitor in China.

InnoCare is currently conducting a Phase I/IIa study of ICP-192 to define its MTD and/or OBD and PK/PD in patients with solid tumors. Preliminary data from the study reveal a favorable safety profile for ICP-192 and show the compound to be well tolerated by treated patients.

After MTD and/or OBD is identified, InnoCare will advance the current Phase I/IIa study from the dose escalation stage (Phase I) to its Phase IIa stage with the selected regimen. During this Phase IIa study, InnoCare will mainly focus on evaluating the safety and efficacy of ICP-192 in patients with cholangiocarcinoma with FGFR2 fusions. Meanwhile, InnoCare is initiating a separate Phase II trial in parallel with urothelial cancer with FGFR2/3 genetic alterations. InnoCare is actively seeking ways to investigate ICP-192 in combination with therapeutic agents such as immune checkpoint inhibitors. In addition, the Company plans to initiate several open-label, Phase II studies to evaluate the safety and efficacy of ICP-192 for additional indications, including gastric cancer and HCC.

ICP-105 is a potential first-to-market FGFR4 inhibitor in China

ICP-105 is a highly selective FGFR4 inhibitor that can effectively bind to FGFR4, inhibit FGF19-overexpression mediated activation of FGFR4 signaling in HCC and exert its anti-neoplastic effect by blocking the activation of the downstream ERK signaling pathway. While several FGFR4 inhibitors are under clinical development, there are currently no marketed FGFR4 inhibitors globally. We think ICP-105 has potential to become the first-to-market FGFR4 inhibitor in China.

ICP-105 is primarily being developed for the treatment of advanced HCC with FGFR4 pathway overactivation. InnoCare is currently assessing the safety and tolerability of ICP-105 in the dose escalation portion of a Phase I study in solid tumor patients. We expect the dose escalation trial to be completed in 4Q20E. Preliminary data from the study demonstrate a favorable safety profile for ICP-105 and show the compound to be well tolerated. We believe ICP-105 is potentially a first-in-class FGFR4 inhibitor in China for the treatment of HCC patients with FGFR4 pathway overactivation.

Addressing the large oncology and auto-immune disease market

The global oncology drug market has expanded significantly in the past, and will further expand at an accelerated pace. Growth in the global oncology drug market is primarily driven by the growing patient pool, increased affordability of healthcare service and the emergence of innovative and advanced therapies, such as molecularly-targeted and immuno-oncology therapies. Frost & Sullivan (F&S) forecasts global oncology drug market to grow from US$128.1bn in 2018 to US$390.4bn in 2030E.

China's oncology drug market experienced rapid growth in the past and will continue to grow. Growth in China's oncology drug market is primarily driven by an aging population and growing cancer incidence, increased awareness of cancer and paradigm shift of cancer treatment from chemotherapy

to molecularly-targeted and immuno-oncology therapies. F&S forecasts China oncology drug market to grow from US$24.2bn in 2018 to US$101.6bn in 2030E.

Bruton's Tyrosine Kinase ("BTK") is a key component of the B-cell receptor signaling pathway, which is an important regulator of cell proliferation and cell survival in various lymphomas (mainly NHL). In addition, BTK is an important enzyme for macrophage function, which is crucial to the pathogenesis of systemic lupus erythematosus (SLE) and other B-cell mediated autoimmune diseases. Such pivotal roles indicate that BTK could potentially be a valuable therapeutic target in various autoimmune diseases, including SLE, rheumatoid Arthritis (RA), multiple sclerosis (MS), pemphigus, psoriasis vulgaris (PV) and lupus nephritis (LN).

According to F&S, the global sales of BTK inhibitors reached US$4.5bn in 2018, and is expected to reach US$12.9bn in 2023E and US$23.5bn in 2030E. Meanwhile, F&S forecasts sales of BTK inhibitors in China to reach US$1.0bn in 2023E and US$2.6bn in 2030E.

Drug sales to start from 2021E

We forecast drug sales to start from 2021E and expect risk-adjusted revenue of RMB106mn/ RMB274mn/ RMB553mn in FY2021E/22E/23E. The most advanced drug is orelabrutinib which we believe will be approved by NMPA in 2H20E. We also forecast ICP-192 and ICP-105 to receive NMPA's approval in 2023E and 2024E, respectively. Considering that InnoCare owns the global rights in these above-mentioned drug candidates, we expect meaningful sales from the US market. We apply different probability of success (PoS) to drug candidates. We forecast a net loss of RMB373mn/RMB286mn/RMB128mn in FY2020E/21E/22E and expect net profit to break even in 2023E.

Initiate BUY with TP HK$16.21

Innocare's future cash flows will rely on the successful commercialization of pipeline drugs. We see DCF as appropriate in valuing the Company. We derive a TP of HK$16.21 based on an 11-year DCF valuation (WACC: 9.7%, terminal growth rate: 5.0%).

Investment risks

1) Having incurred net losses in the past and will continue to incur losses for the foreseeable future;
2) Failure in obtaining regulatory approval for drug candidates;
3) Competition from peers with more competing and successful drugs;
4) Failure in protecting intellectual property rights throughout the world.

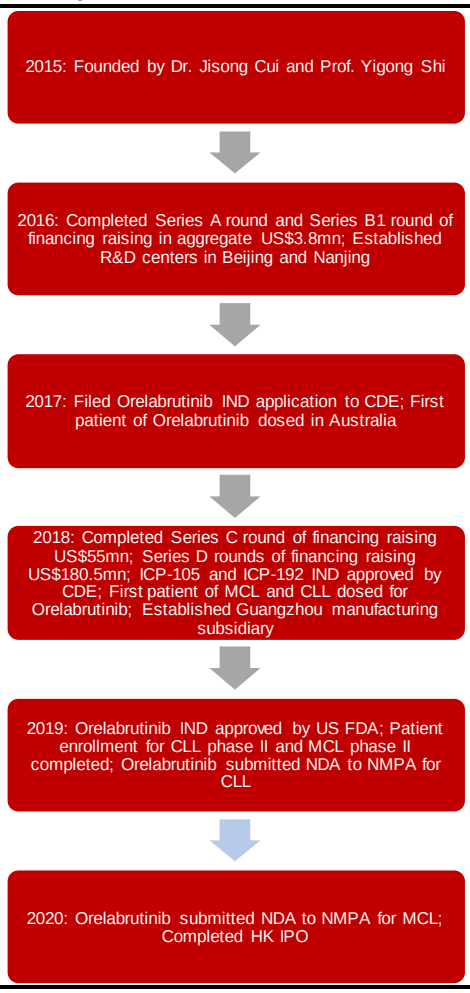
Company Overview

Clinial-stage biopharmaceutical company focusing on innovative therapies

Founded in Nov 2015 by Dr. Jisong Cui and Prof. Yigong Shi, InnoCare Pharma Limited (InnoCare) is a clinical-stage biopharmaceutical company committed to develop best-in-class and/or first-in-class drugs for treatment of cancer and autoimmune diseases.

Led by a world-class management team, InnoCare has built a fully integrated biopharmaceutical platform with strong in-house R&D capabilities. InnoCare's fully-integrated platform covers the entire spectrum of drug discovery and development functionalities, including drug target identification and verification, pre-clinical evaluation, clinical trial design and execution, drug manufacturing and quality control, and commercialization.

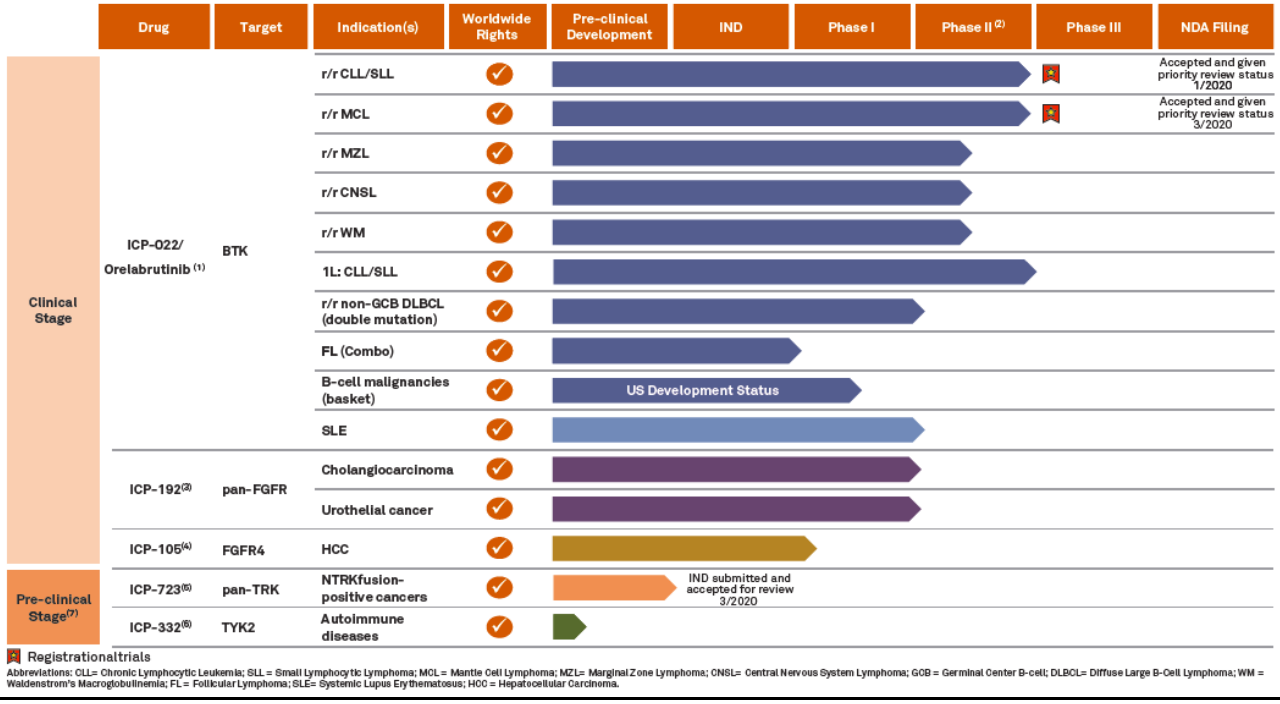
Figure 1: Development history of InnoCare



Source: Company data, CMBIS

In less than four years, InnoCare has discovered and developed a pipeline of nine drug candidates, including orelabrutinib (ICP-022, BTK inhibitor) with two NDAs for r/r CLL/SLL and r/r MCL accepted by NMPA and granted priority review status, ICP-192 (pan-FGFR inhibitor) and ICP-105 (FGFR4 inhibitor) in Phase I/II trials, ICP-723 (pan-TRK) submitted IND and five candidates at the IND-enabling stage.

Figure 2: Key pipeline drugs of InnoCare (As of Mar 2020)



Source: Company data, CMBIS

CLL = Chronic Lymphocytic Leukemia; SLL = Small Lymphocytic Lymphoma; MCL = Mantle Cell Lymphoma; MZL = Marginal Zone Lymphoma; CNSL = Central Nervous System Lymphoma; GCB = Germinal Center B-cell; DLBCL = Diffuse Large B-Cell Lymphoma; WM = Waldenstrom's Macroglobulinemia; FL = Follicular Lymphoma; SLE = Systemic Lupus Erythematosus; HCC = Hepatocellular Carcinoma.

1. Denotes the Company's Core Product Candidate, Orelabrutinib (ICP-022);
2. For indications of r/r CLL/SLL and r/r MCL, the registrational trial for NDA submission is the Phase II clinical trial based on the communications with the NMPA. Confirmatory Phase III clinical trials will be required after the Company receives conditional approvals from the NMPA based on the results of these two registrational Phase I and Phase II clinical trials;
3. Initiation of Phase II trials for cholangiocarcinoma have begun, patient screening is expected to begin in 2Q20;
4. Expect to complete the Phase I trial for HCC in 4Q20;
5. IND application for NTRK fusion-positive cancers submitted to the NMPA in 1Q20;
6. Expect to submit an IND application for autoimmune diseases to the NMPA in 2H20;
7. The Company also has four undisclosed IND-enabling stage candidates currently under development.

Fully-integrated platform with high operating efficiency

Led by Dr. Jisong Cui, the Company's co-founder and CEO, InnoCare has an R&D team with over 150 members, including a drug discovery team of approximately 100 employees and a clinical development team of approximately 50 employees. InnoCare has also established state-of-the-art research facilities with an approximately 8,300 m^2 laboratory in Beijing and a 3,350 m^2 laboratory in Nanjing to support chemistry, biology, *in vivo* pharmacology, DMPK, and CMC studies.

The Company's discovery capability is supplemented by support from globally renowned biophysicist Dr. Yigong Shi, the Company's co-founder and President of the Scientific Advisory Board, and cancer genomics expert Dr. Zemin Zhang, the Company's Scientific Advisor. InnoCare has entered into exclusive strategic collaboration agreements with Dr. Shi and Dr. Zhang and their laboratories to further strengthen the Company's internal target identification capability by leveraging their expertise in structural biology, single cell sequencing and big data analysis.

InnoCare has a clinical development team of 50 members in China led by Dr. Zhixin Rick Xu, the Chief Medical Officer. The Company has advanced three drug candidates into clinical trials in less than four years. During the last two years, InnoCare initiated seven clinical trials, including two registrational trials. The Company advanced the orelabrutinib r/r CLL/SLL and r/r MCL registrational trials from ethics

committee approvals to completion of the enrollment of 80 r/r CLL/SLL patients and 106 r/r MCL patients within one year.

InnoCare is currently building a 50,000 m^2 manufacturing facility in Guangzhou for commercial scale production with an annual production capacity of one billion pills. The facility is designed to comply with good-manufacturing practice (GMP) requirements of the US, Europe, Japan and China. InnoCare plans to obtain a manufacturing license for the facility in 2H20E.

Dr. Robin Lu, Vice President of InnoCare Guangzhou, oversees the manufacturing activities and brings over 10 years of drug manufacturing experience from the Yangtze River Pharmaceutical Group. As at 10 Oct 2019, the Company's manufacturing team in Guangzhou consisted of 30 employees.

To support the near-term product launches, InnoCare has assembled sales and marketing leadership team and is ramping up commercialization team, which is expected to have 80 to 90 sales representatives by the end of 2020E, covering over 300 hospitals. If orelabrutinib is included in the NRDL, InnoCare plans to expand the commercialization team to approximately 150 sales representatives and cover over 800 top hospitals to support the market expansion of orelabrutinib. The commercialization team will be led by Mr. Yi Zhang and Dr. Zhichao Si, who bring extensive sales and marketing experience in China's hematologic market from Janssen.

Figure 3: InnoCare's integrated biopharmaceutical platform

Source: Company data, CMBIS

Strong ties with world class scientists

InnoCare's in-house R&D capability is supplemented by globally renowned structural biologist Dr. Yigong Shi (施一公), the Company's co-founder and President of Scientific Advisory Board, and cancer genomics expert Dr. Zemin Zhang (张泽民), the Company's Scientific Advisor. InnoCare has entered into exclusive strategic collaboration agreements with Dr. Shi and Dr. Zhang, respectively.

Figure 4: InnoCare's exclusive strategic cooperation with Dr. Shi and Dr. Zhang

Source: Company data, CMBIS

Dr. Shi is a globally renowned structural biologist whose research has advanced scientific understanding in the molecular mechanisms behind cell apoptosis. From 1998 to 2008, Dr. Shi served in a number of positions, including as an assistant, associate and full professor at Princeton University. Since Nov 2007, he has served in a number of positions at Tsinghua University, including as the dean of the School of Life Sciences, vice president of Tsinghua University and university professor. He was a founder of Westlake University, at which he has served as the first president since Apr 2018. Dr. Shi has memberships or qualifications from Academician of the Chinese Academy of Sciences (中国科学院院士), Honorary Foreign Member of the American Academy of Arts and Sciences (美国艺术与科学院外籍院士), Foreign Associate of National Academy of Sciences of the US (美国国家科学院外籍院士) and Foreign Associate of European Molecular Biology Organisation (欧洲分子生物学组织外籍成员). Dr. Shi is the spouse of Dr. Renbin Zhao, InnoCare's Executive Director of Clinical Development and Regulatory Affairs.

Dr. Zhang has been serving as a scientific advisor to the Company's Scientific Advisory Board since Nov 2015. Dr. Zhang received his Bachelor of Science degree in genetics from Nankai University in 1988 and obtained his Doctor's degree in biochemistry and molecular biology from Pennsylvania State University in 1995. From Jan 1998 to 2014, Dr. Zhang served as a principal scientist at Genentech Inc. Since May 2014, Dr. Zhang has served as a tenured professor at the life sciences department of Peking University. He has pioneered multiple research directions in computational cancer biology and cancer genomics including the first ever whole genome tumor sequencing. He is also an inventor for 60 issued US patents and has directly contributed to the initial finding of the molecular targets of multiple cancer therapeutic agents in clinical trials. Dr. Zhang is the founder of Analytical Biosciences Limited (百奥智汇科技有限公司) which aims to create and harness the human disease precision atlas through cutting-edge single-cell genomics and bioinformatics.

InnoCare renewed an exclusive strategic collaboration agreement (the "Professor Shi Collaboration Agreement") with Dr. Yigong Shi in Aug 2018. Dr. Shi will provide assistance and guidance in issues presented in new drug discovery for a fee, including crystallization screening for proteins, protein structural analysis, protein functional analysis, and optimized binding of target proteins and candidate compounds, as well as selection of drug targets, especially with respect to precursor messenger RNA splicing regulatory targets and related family drug targets.

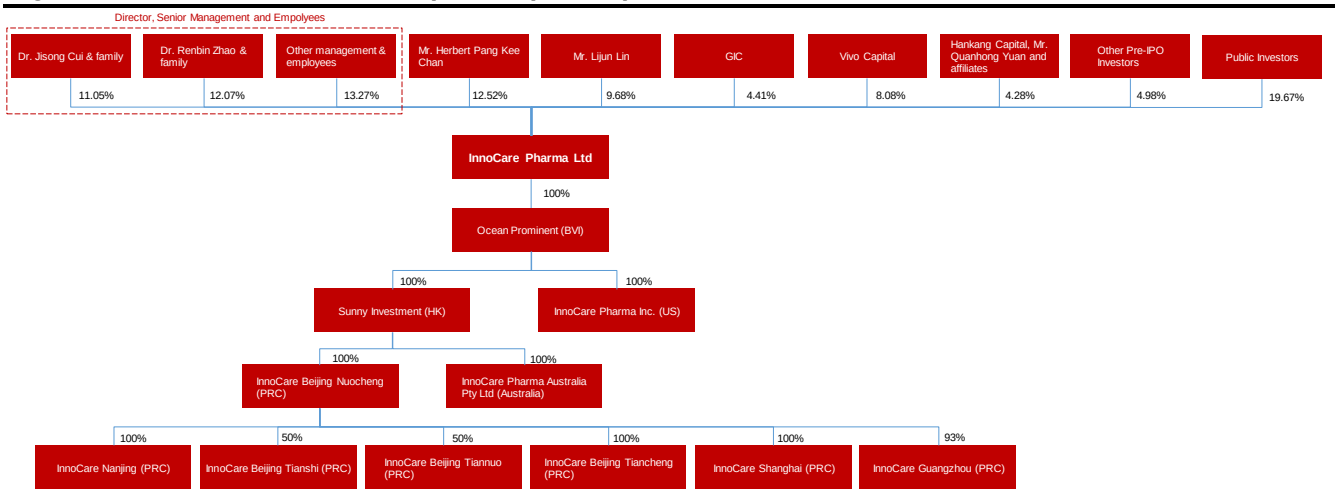
InnoCare also renewed an exclusive strategic collaboration agreement with Dr. Zhang (the “Professor Zhang Collaboration Agreement”) in Aug 2019. Dr. Zhang will provide assistance to InnoCare in exploring the relationship between cancer and cancer-specific driver genes and researching of tumor heterogeneity and resistance. Specific resources and efforts to be contributed by Dr. Zhang include, but are not limited to, access to his technical platform, technical support and seminars aiming to solve problems presented during the research.

InnoCare has also established a Scientific Advisory Board comprising top-notch professors and key opinion leaders, including Dr. Zemin Zhang, Dr. Zhanguo Li, a world-class specialist in rheumatoid immunotherapy and former director of the Clinical Immunology Center/Rheumatism Immunology Department at Peking University People’s Hospital, and Professor Arnold Levine, a globally recognized leader in cancer research and professor emeritus at the Institute of Advanced Study. In addition, InnoCare has recruited James Deng, general manager of Becton Dickinson’s Greater China business and the former chief executive officer and president of Novartis Pharmaceuticals China, as its Sales & Marketing Advisor.

Supported by top-tier investors

As of Apr 2020, Dr. Jisong Cui and Dr. Renbin Zhao own 11.05% and 12.07% of stake in the Company, respectively. Other management and employees (including Dr. Zemin Zhang) hold a combined 13.27% stake. Meanwhile, GIC and Vivo Capital have 4.41% and 8.08% stake, respectively.

Figure 5: Shareholders structure (As of Apr 2020)



Source: Company data, CMBIS

Core asset, Orelabrutinib, is a potential best-in-class BTK inhibitor

Orelabrutinib (ICP-022) has multiple clinical trials ongoing

Orelabrutinib (ICP-022) is a potential best-in-class, highly selective and irreversible BTK inhibitor under clinical trials in China and US for the treatment of various B-cell malignancies and autoimmune diseases.

In Nov 2019, the NMPA has accepted the new drug application (NDA) of orelabrutinib for the treatment of patients with r/r CLL/SLL. In Jan 2020, NMPA granted priority review status to orelabrutinib, indicating potential accelerated approval for orelabrutinib. The NDA is based on data from a Phase I/II clinical study investigating the safety, tolerability and pharmacokinetics/ pharmacodynamics of ICP-022 in Chinese patients with r/r CLL/SLL (registration No. CTR20180263). In Mar 2019, the Company has submitted the NDA of orelabrutinib for r/r MCL and obtained priority review status from the NMPA. The NDA is based on data from a Phase II clinical study (CTR20180196). We expect orelabrutinib to receive approvals from NMPA for treatment of r/r CLL/SLL and r/r MCL in 2H20E.

InnoCare is also evaluating orelabrutinib in three Phase II trials for patients with r/r marginal zone lymphoma (MZL), r/r central nervous system lymphoma (CNSL) and r/r Waldenstrom's Macroglobulinemia (WM) in China. We expect patient enrolment of these three trials to be completed by end-2020E and corresponding indications will receive NMPA approvals in 2022E.

InnoCare is currently communicating with the relevant authority to finalize study protocols for orelabrutinib as a first-line therapy for CLL/SLL patients in a Phase III study in China. The Company also plans to initiate a Phase II study to investigate orelabrutinib as a monotherapy in patients with r/r non-GCB diffuse large B-cell lymphoma (DLBCL) sub-population with MYD88 and CD79B double mutations in China. In addition, the Company has initiated a Phase I study of orelabrutinib in combination with a next-generation CD20 antibody (MIL62) for follicular lymphoma (FL) patients in China.

To explore orelabrutinib's potential for treatment of auto-immune diseases, InnoCare is currently obtaining approval from the relevant authority to start patient enrollment for a Phase Ib/IIa trial of orelabrutinib in combination with standard of care treatment for SLE in China and patient enrollment will begin in 2Q20E.

Separately, InnoCare has initiated a Phase I basket trial for B-cell malignancies in the US.

Figure 6: Clinical trials of Orelabrutinib (as of May 2020)

Trial name	Phase	Indication	Dose	Study design	Primary endpoint	Location	Patient enrollment No.	Progress	Time of First-patient in	Time of enrollment completion
ICP-CL-00102	Phase II	r/r MCL	100mg BID/150mg QD	single arm	ORR	China	106	Completed, NDA filed in Mar 2020	19/3/2018	28/5/2019
ICP-CL-00103	Phase II	r/r CLL/SLL	150mg QD	single arm	ORR	China	80	Completed, NDA filed in Nov 2019	3/4/2018	30/5/2019
ICP-CL-00104	Phase II	r/r MZL	150mg QD	single arm	ORR	China	80	Enrollment ongoing	1/4/2019	
ICP-CL-00105	Phase II	r/r WM	150mg QD	single arm	MRR (major response rate)	China	44	Enrollment ongoing	11/7/2019	
ICP-CL-00106	Phase II	r/r CNSL	150mg QD	single arm	ORR	China	39	Enrollment ongoing	18/6/2019	
ICP-CL-00108	Phase I	r/r non-GCB DLBCL	150mg QD	single arm	ORR	China	85	Trial initiation		

ICP-CL-00111	Phase III	1L CLL/SLL	150mg /100mg QD	randomized, Orelabrutinib vs SoC	PFS and ORR (17p del)	China	389	Trial initiation	
MIL62-CT03	Phase I	r/r FL	Orelabrutinib + MIL62 (next-generation CD20 antibody)	single arm	MTD and RP2D	China	35~50	Enrollment ongoing	
ICP-CL-00107	Phase I	r/r B-cell malignancies	150mg /100mg QD	single arm	MTD	US	15	Enrollment ongoing	31/10/2019
ICP-CL-00109	Phase Ib/IIa	SLE	50/80/100mg QD	randomized, placebo-controlled, double blinded	MTD and RP2D	China	60	Trial initiation	

Source: Company data, insight, CMBIS

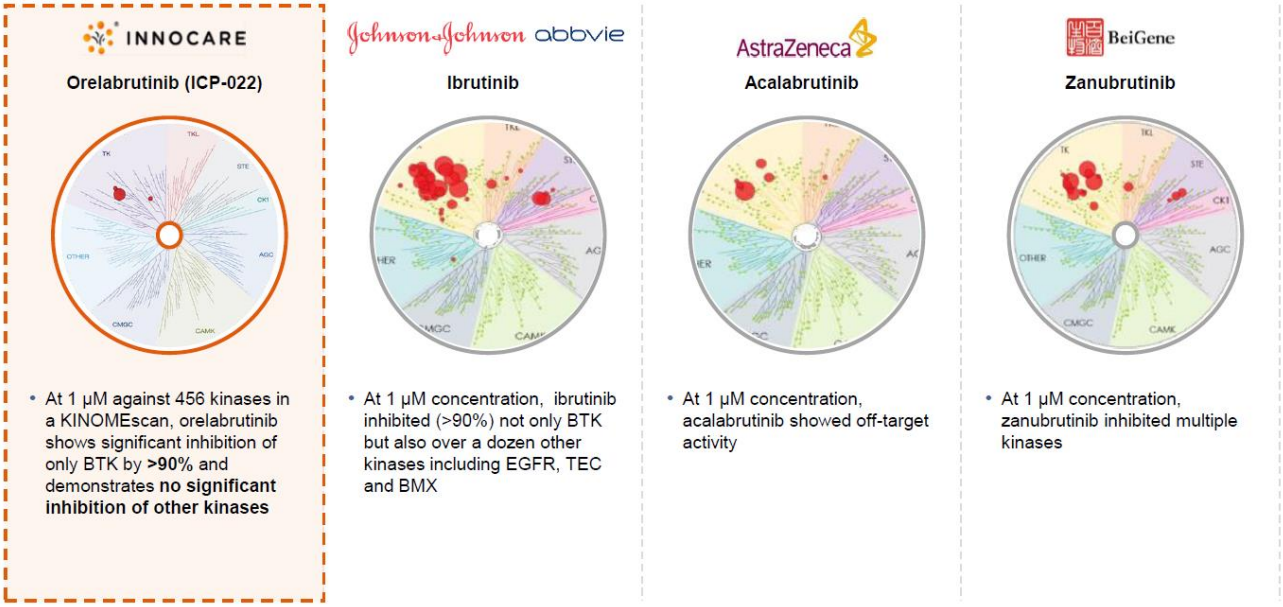
Orelabrutinib demonstrated improved target selectivity

Orelabrutinib has demonstrated higher selectivity against BTK based on data from pre-clinical studies and the reported data of ibrutinib (Imbruvica), acalabrutinib (Calquence) and zanubrutinib (Brukinsa). The better bioavailability of orelabrutinib tablet enables once-daily administration at low dosage and near 100% 24-hour BTK occupancy in blood. This combination of high selectivity and sustained BTK occupancy at low dosage reduces off-target activities and potentially results in a superior safety profile for orelabrutinib.

A KINOMEscan assay is an active site-directed competitive binding assay that quantitatively measures the interactions between test molecules and kinases. In a KINOMEscan assay against 456 kinases, orelabrutinib at 1 μM shows significant inhibition of only BTK by >90% AND demonstrates no significant inhibition of other kinases. Each branch of the dendrogram represents an individual human kinase. Kinases bound by orelabrutinib are indicated by red circles on the kinome tree.

At a concentration of 1 μM, acalabrutinib and ibrutinib showed off-target activity. Ibrutinib, in particular, inhibited (>90%) not only BTK but also over a dozen other kinases including epidermal growth factor receptor (EGFR), cytoplasmic tyrosine-protein kinase BMX and tyrosine kinase expressed in HCC (TEC), which are often associated with adverse events such as diarrhea, bleeding and atrial fibrillation, respectively.

Figure 7: Target selectivity comparison between orelabrutinib, ibrutinib, acalabrutinib and zanubrutinib



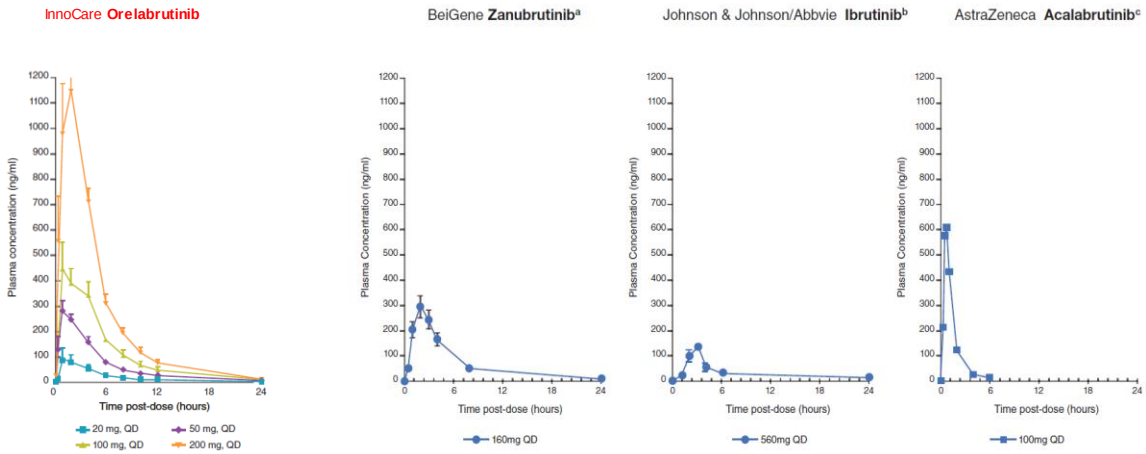
Source: Company data, CMBIS

Orelabrutinib shows favorable PK/PD profile and better target occupancy

Orelabrutinib has demonstrated sustained BTK occupancy at low dosage. Orelabrutinib's unique bioavailability enables a dosage regimen of 150 mg once-daily, as compared to 100 mg twice daily for acalabrutinib, 420mg/560mg daily for ibrutinib and 320 mg daily or 160 mg twice daily for zanubrutinib.

Available clinical data have demonstrated a favorable pharmacokinetic (PK) profile of orelabrutinib. After a single dose of orelabrutinib at 20 mg, 50 mg, 100 mg and 200 mg, Cmax of the drug was dose proportional, indicating that orelabrutinib has good bioavailability and a linear PK. While there is no head-to-head comparative study, the reported data of zanubrutinib, ibrutinib and acalabrutinib suggest a lower bioavailability at their respective dosage compared to orelabrutinib.

Figure 8: Comparison of post-dosing plasma exposure profile

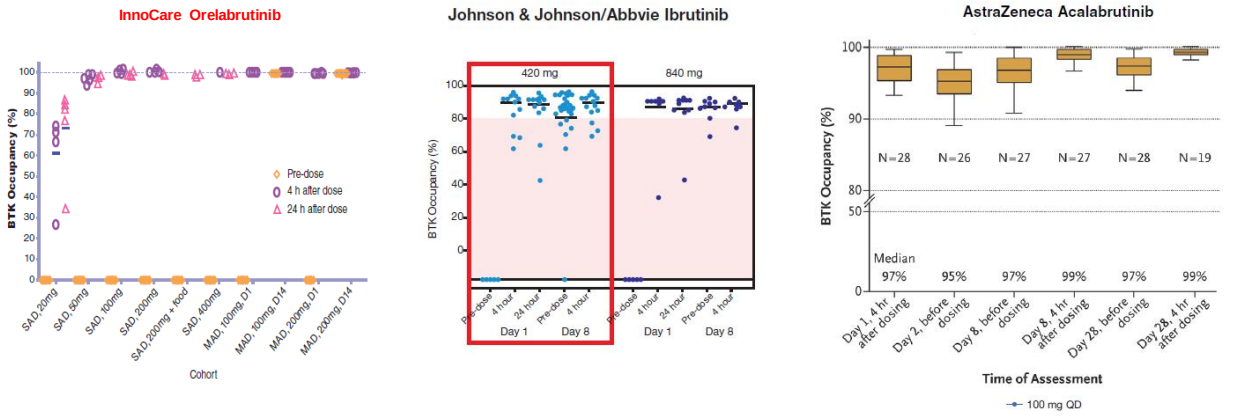


Source: Company data, CMBIS

While there is no head-to-head comparative study, orelabrutinib demonstrates better target occupancy than the reported data of ibrutinib and acalabrutinib. Prolonged pharmacodynamic effects were

observed after orelabrutinib had been cleared from circulation (up to 24 hours after a single dose). Sustained and near-100% BTK occupancy was achieved at a dosage level of 50 mg or higher and no decrease in BTK occupancy between 4- and 24-hour post-dosing was observed. At a dosage level of 420 mg for ibrutinib, instances of BTK occupancy below 80% and a decrease in BTK occupancy between 4- and 24-hour post-dosing were observed. At a dosage level of 100 mg twice daily for acalabrutinib, instances of BTK occupancy below 90% and a decrease in BTK occupancy between 4- and 24-hour post-dosing were observed.

Figure 9: Comparison of BTK occupancy



Source: Company data, CMBIS

Orelabrutinib has superior safety and potent efficacy profile

The safety, tolerability and efficacy profiles of orelabrutinib are being evaluated in seven ongoing clinical trials including two registrational trials. As of 30 Sep 2019, orelabrutinib has been administered to 254 subjects.

Currently approved BTK inhibitors have demonstrated common toxicities. Some of such toxicities may be attributable to the currently approved BTK inhibitors' off-target effects, such as diarrhea, bleeding and atrial fibrillation. These toxicities have caused intolerability and limited their clinical use.

Potentially due to its high selectivity, orelabrutinib demonstrated a favorable safety profile and was found to be well-tolerated by patients with r/r MCL and r/r CLL/SLL in two separate ongoing registrational studies. Both studies demonstrate orelabrutinib was well tolerated by treated patients. For TEAEs observed in these two studies, we consider diarrhea, bleeding and atrial fibrillation to be off-target related. Among these off-target TEAEs, all diarrheas were Grade 1 or 2 except for one Grade 3 (0.5%) and no atrial fibrillation was observed. The favorable safety profile as compared with approved BTK inhibitors may correlate with the higher selectivity of orelabrutinib.

According to the pooled safety data from orelabrutinib's registrational trials for r/r MCL and r/r CLL/SLL, adverse events of special interest are less frequent than other BTK inhibitors, although it's not head-to-head comparison.

Figure 10: Adverse events of special interest

Index	Orelabrutinib N=200	Zanubrutinib N=671	Acalabrutinib N=612	Ibrutinib N=1,124
Major bleeding	0.5%	2.7%	2.0%	3.0%
Atrial fibrillation (Grade 3 or Grade 4)	0.0%	0.6%	1.0%	4.0%
Hypertension (Grade 3 or Grade 4)	2.5%	3.1%	2.5%	5.0%
Infection (>=Grade 3)	16.0%	21.3%	18.0%	24.0%
Secondary malignancy	0.5%	7.9%	10.6%	10.0%
Diarrhea	7.0%	18.2%	38.4%	39.0%

Source: Company data, CMBIS; Note: Data showed above are not from head-to-head comparative studies but extracted from some pooled analyses. Orelabrutinib as of the data cut-off date of 30 Sep 2019 for ICP-CL-00102 trial, 9 Aug 2019 for ICP-CL-00103 trial and 31 Aug 2019 for ICP-CL-00104, ICP-CL-00105 and ICP-CL-00106 trial.

Study ICP-CL-00102 registrational study in patients with r/r MCL

Study ICP-CL-00102 is an open label, multi-center, two-stage, registrational study in r/r MCL patients to evaluate the safety, efficacy and tolerability of orelabrutinib at the RP2D. The primary endpoint is to determine objective response rate (ORR by IRC) of orelabrutinib in patients with r/r MCL. Secondary endpoints include: ORR (evaluated by investigator), duration of response (DOR evaluated by IRC), progression-free survival (PFS), overall survival (OS) and safety. Treatment response was assessed using Lugano criteria.

A total of 106 patients were enrolled and treated at 22 centers across China in this study. The trial was carried out in two stages. Stage I was designed for regimen selection where the patients were divided into two groups receiving 100 mg BID or 150 mg QD orally to determine the RP2D. Stage II was designed to evaluate efficacy in which patients were dosed at the RP2D (150 mg QD).

40 patients were enrolled and divided into two cohorts (n=20 each) for Stage I and an additional 66 patients were enrolled for Stage II of the study. The 150 mg QD regimen, was selected as RP2D because of its favorable safety profile, a better ORR and the convenience of once daily dosing. All patients who were enrolled in Stage I continued their treatment.

As of the data cut-off date of 30 Sep 2019, a total of 106 patients received orelabrutinib treatment, among them 99 patients had response assessments. The response rate was assessed by traditional CT imaging technology. The ORR (evaluated by IRC) for the evaluable patients was 85.9%, the complete response (CR) rate assessed by CT was 27.3% (among the 28 patients who had pre- and post-PET CT evaluation, the corresponding complete response rate was 53.6%), partial response (PR) rate was 58.6%. Stable disease rate was 5.1%. The total disease control rate was 90.9%. The median DOR has not yet been reached.

As of the data cut-off date of 30 Sep 2019, all 106 patients in this study ICP-CL-00102 had safety assessments. Among the 106 patients treated with orelabrutinib, the most frequent (15%) AEs of any cause were hematological toxicities, including thrombocytopenia, neutropenia, white blood cell count decrease, anaemia, and respiratory system infections, as well as rash. The most commonly reported (>10%) Grade 3 or higher AEs of any cause were thrombocytopenia (11.3%). No clinically relevant atrial fibrillation or flutter and no treatment related secondary malignancy was observed. No Grade 3 or higher hemorrhage was reported. No treatment-related Grade 3 or higher diarrhea or cardio toxicity was observed. Of the 106 patients, 29 experienced serious AEs, of which 15 were considered treatment-related, mostly relating to hematologic toxicities and/or infections; 46 Grade 3 or higher TEAEs were observed of which 33 were treatment-related.

Full data on the effectiveness and safety of orelabrutinib was presented at the 61st American Society of Hematology (ASH) Annual Meeting in Dec 2019.

We compared clinical trial data of major BTK inhibitors on r/r MCL and noticed that orelabrutinib had demonstrated potent efficacy with high ORR and superior safety with low rate of treatment discontinuation due to AEs (1.9%).

Figure 11: Comparison of BTK inhibitors' clinical trial data on MCL

	Orelabrutinib	Ibrutinib	Acalabrutinib	Zanubrutinib	
Source	2019 ASH	2015 ASH	2018 ASH	US approved label	
Trial ID	ICP-CL-00102/ NCT03494179	PCYC-1104-CA /NCT01236391	ACE-LY-004/ NCT02213926	BGB-3111-206/ NCT03206970	BGB-3111-AU-003/ NCT 02343120
Indication	r/r MCL	r/r MCL	r/r MCL	r/r MCL	r/r MCL
N	106	111	124	86	32
Phase	I/II	II	II	II	I/II
Line of treatment	≥2L	≥2L	⩾2L	⩾2L	⩾2L
Regimen	150mg QD	560mg QD	100mg BID	160mg BID	160mg BID or 320 QD
Median follow-up	10.5m	26.7m	26m	NA	NA
DoR	NA	17.5m	25.7m	19.5m	18.5m
ORR	85.9% (CT)	67.0% (IWGC)	81.0% (2014 Lugano)	84.0% (2014 Lugano)	84.0% (2014 Lugano)
CR	*27.3%*	*23.0%*	*43.0%*	*59.0%*	*22.0%*
PR	*58.6%*	*42.0%*	*38.0%*	*24.0%*	*62.0%*
SD	5.1%	NA	9.0%	NA	NA
DCR	90.9%	NA	90.0%	NA	NA
PFS	NA	13m	20m	19.1m	NA
OS	NA	22.5m	NA	NA	NA
Discontinue due to AEs	1.90%	11%	8%	7%	
Common AEs	The most common AE (>15%): *thrombocytopenia, neutropenia, respiratory system infections, and rash.* The most common SAE (>10%): *thrombocytopenia (12.3%)*	The most common AE (>30%): *diarrhea (54%), fatigue (50%), nausea (33%), and dyspnea (32%).* The most common SAE: *pneumonia (8%), urinary tract infection (4%), cellulitis (3%), hematuria (2%) and subdural hematoma (2%).*	The most common AE: *headache (38%), diarrhoea (36%), fatigue (28%), cough (22%) and myalgia (21%).* The most common SAE (⩾5%): *anaemia (10%), neutropenia (10%) and pneumonia (6%).*	The most common AE (>20%): *decreased neutrophil count, decreased platelet count, upper respiratory tract infection, decreased white blood cell count, decreased hemoglobin, rash, bruising, diarrhea,and cough.* The most common SAE: *pneumonia (11%), and hemorrhage (5%).*	

Source: Company data, ASH, US FDA, CMBIS

Study ICP-CL-00103 registrational study in patients with r/r CLL/SLL

Study ICP-CL-00103 is an open-label, multi-center, two stage, registrational study in r/r CLL/SLL patients to evaluate the safety, efficacy and tolerability of orelabrutinib at the RP2D. The primary endpoint is ORR (evaluated by IRC) of orelabrutinib in patients with r/r CLL/SLL. Secondary endpoints were ORR (evaluated by investigator), DOR, progression free survival (PFS) and safety. Treatment response was assessed using 2008 IWCLL criteria (with modification for PRL). The study was carried out in two stages. Stage I was designed to assess the DLT, safety and tolerability of orelabrutinib at 150mg QD in the first six patients with r/r CLL/SLL. Stage II was designed to evaluate the therapeutic benefits of orelabrutinib in patients that received the RP2D of 150mg QD.

Study enrollment has been completed and a total of 80 patients were enrolled and treated in this study. Six patients were enrolled in Stage I of the study and an additional 74 patients were enrolled in Stage II of the study.

Among the 80 total enrolled r/r CLL/SLL patients treated with orelabrutinib in study ICP-CL-00103, as of the data cut-off date of 9 Aug 2019, the IRC assessed objective response rate was 88.8% (IRC assessed), two patients achieved complete response (CR), one patient achieved CR with incomplete marrow recovery (CRi), partial response was 57.5%, partial response rate with lymphocytosis was 27.5% and the disease control rate was 93.8%. The median DOR has not yet been reached and 6-month DOR rate was 88.4%.

A total of 80 patients were enrolled and treated in this study. As of the data cut-off date of 9 Aug 2019, all 80 patients had safety assessments. Among the 80 patients treated, the most frequent (⩾20%) AEs of any cause were hematological toxicities, including thrombocytopenia, neutropenia, upper respiratory tract infection, lung infection, increased weight and blood urine present. No cases of clinically relevant atrial fibrillation or treatment related secondary malignancy was observed. Only one major bleeding and one grade 3 diarrhea was reported. The most frequently (⩾10%) reported ⩾Grade 3 AEs of any cause were neutropenia, thrombocytopenia and lung infection. Among all patients treated, 16 patients experienced at least one serious TRAE with two patients leading to dose reduction and three patients leading to death.

At the 61st American Society of Hematology (ASH) Annual Meeting in Dec 2019, InnoCare disclosed this updated clinical data on Study ICP-CL-00103.

Figure 12: Comparison of BTK inhibitors' clinical trial data on CLL/SLL

	Orelabrutinib	Ibrutinib	Acalabrutinib	Zanubrutinib
Source	2019 ASH	2019 ASCO	2019 EHA	2019 ICML
Trial ID	ICP-CL-00103/ NCT03493217	RESONATE (PCYC-1112)/ NCT01578707	ACE-CL-309 (ASCEND)/ NCT02970318	BGB-3111-205/ NCT03206918
Indication	r/r CLL/SLL	r/r CLL/SLL	r/r CLL	r/r CLL/SLL
N (patients on BTK)	80	195	155	91
Phase	I/II	III	III	II
Line of treatment	≥2L	≥2L	⩾2L	⩾2L
Regimen	150mg BID	420mg QD	100mg BID	160mg BID
Median follow-up	8.7m	65.3m	16.1m	15.1m
ORR	88.8% (2008 IWCLL)	88.0% (2008 IWCLL)	81.0% (2008 IWCLL)	84.6% (2008 IWCLL, 2014 Lugano)
CR	*3.8%*	*11.0%*	-	*3.3%*
PR	*85.0%*	*77.0%*	-	*81.3%*
SD	5.0%	-	-	4.4%
DCR	93.8%	-	-	89.0%
PFS	-	44.1m	NR	NR
OS	-	67.7m	12m-OS: 94% vs 91%	-
Discontinue due to AEs	3.8%	16%	11%	8.8%
Common AEs	The most common AE: *thrombocytopenia, neutropenia, anemia, respiratory system infections, and purpura* The most common SAE: *neutropenia, thrombocytopenia, lung infection*	The most common AE (>20%): *diarrhea, fatigue, pyrexia, and nausea* The most common SAE: *neutropenia, pneumoni, Atrial fibrillation, Pyrexia*	The most common AE: *headache (22%), neutropenia (19%), diarrhea (18%), anemia (15%), and cough (15%)* The most common SAE: *neutropenia (16%), anemia (12%), and pneumonia (5%); with rituximab/idelalisib, neutropenia (40%) and diarrhea (24%)*	The most common AE: *decrease (68.1%), upper respiratory tract infection (45.1%), purpura (34.1%), and platelet count decreased (33.0%)* The most common SAE: *neutrophil count decrease (44.0%), lung infection (9.9%), upper respiratory tract infection (9.9%), platelet count decrease (8.8%), and anemia (8.8%)*

Source: Company data, ASH, ASCO, EHA, ICML, CMBIS

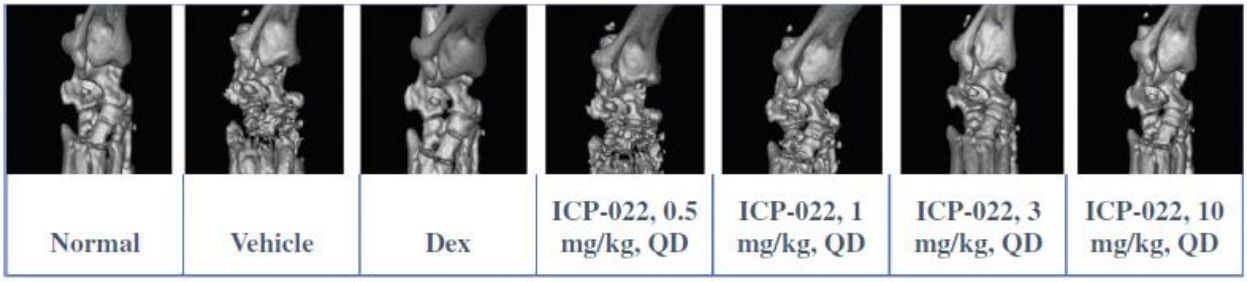
Orelabrutinib shows promising preclinical data on SLE

BTK is a promising target for the treatment of autoimmune diseases such as RA and SLE due to its role in mediating both B-cell and Fc receptor signaling. In autoimmune diseases like RA and SLE, the strong B-cell component is paired with activation of innate immune cells. Specifically, BTK plays key roles in both B-cells and macrophages, which are the two major cell types contributing to SLE pathogenesis.

Available data from animal models reveal a robust efficacy profile for orelabrutinib in both SLE and RA. Histological morphology of rat ankle joints demonstrated a dose-dependent protection from joint damage, including ankle inflammation, pannus formation, cartilage degradation and bone resorption. The bone-protective effect was further confirmed by micro-computed tomography analysis, which

showed orelabrutinib markedly reduced erosive bone changes and prevented bone loss, whereas the vehicle-treated group showed severe and widespread bone loss.

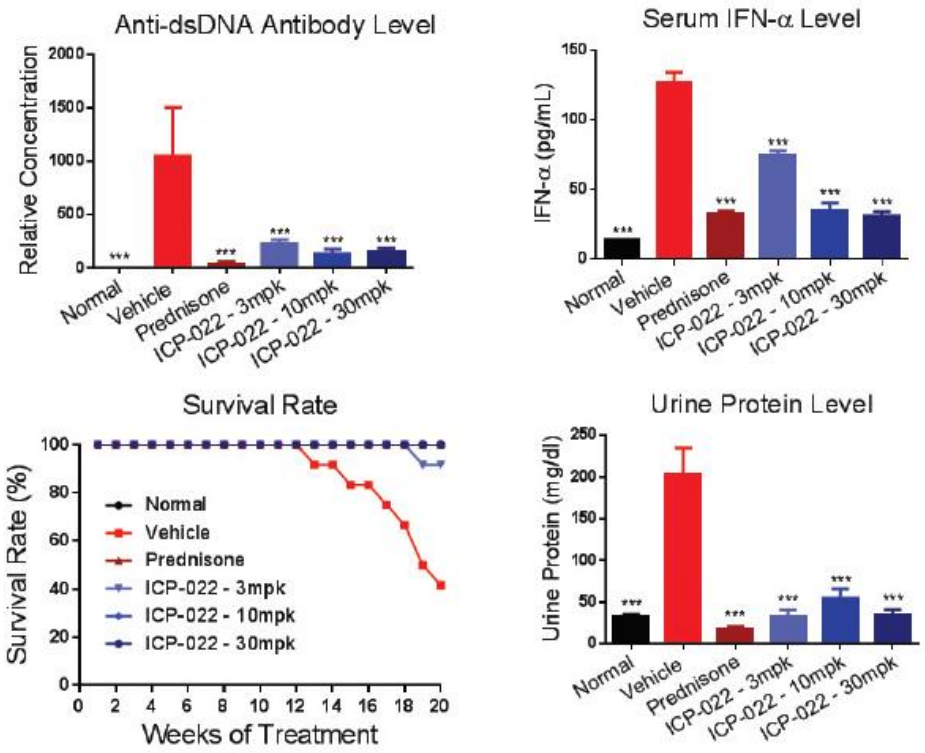
Figure 13: Representative micro-computed tomography images of rat ankle joints



Source: Company data, CMBIS

The MRL/lpr mouse is one of the best-studied mouse models for spontaneous SLE where lpr mutation accelerates the predisposition of MRL mice for developing autoimmunity with many of the SLE features observed in humans. In a 6-month study, orelabrutinib dramatically reduced inflammation and improved survival rate and kidney function of treated MRL/lpr animals. Efficacy was demonstrated at doses as low as 3 mg/kg QD, and complete disease protection was achieved at 10 mg/kg QD and 30 mg/kg QD. Survival protection in treated animals was observed in a dose-dependent manner. Correspondingly, anti-dsDNA and pro-inflammatory cytokine interferon (IFN)-α levels were also reduced in a dose-dependent manner.

Figure 14: Orelabrutinib efficacy in SLE mouse model

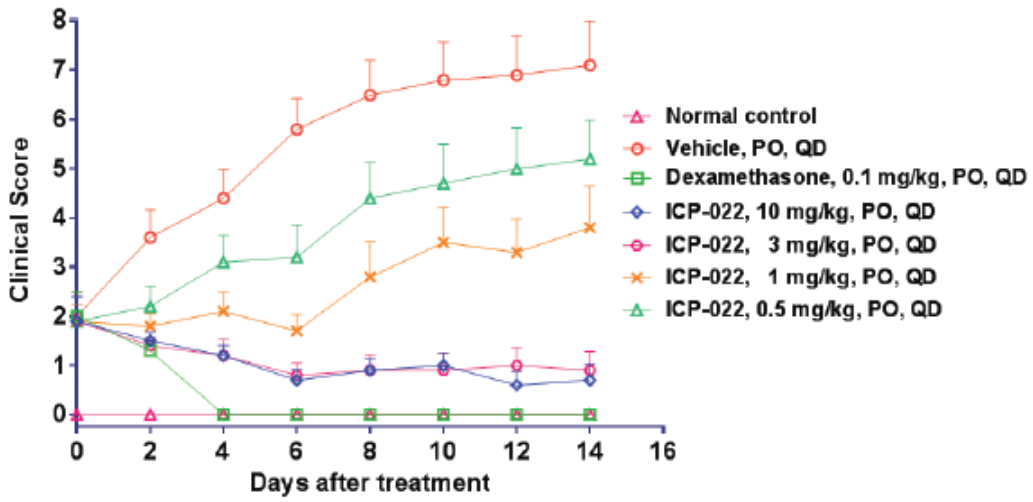


Source: Company data, CMBIS

A similar effect was observed in a pristane-induced SLE mouse model with dose-dependent inhibition of lupus-related arthritis and improved kidney function. The pristane-induced SLE mouse model is one of the most widely used murine models for induced lupus-like disease with immune complex glomerulonephritis, mild erosive arthritis and many lupus-associated autoantibodies. The efficacy of orelabrutinib at 3 mg/kg QD and 10 mg/kg QD was comparable to ibrutinib at 30 mg/kg QD measured by arthritis score. Orelabrutinib at 10 mg/kg QD and 30 mg/kg QD demonstrated a better efficacy profile than ibrutinib 30 mg/kg QD as measured by histopathology scores. Mouse kidneys were collected to assess renal pathology following completion of the study. Immunohistochemical staining was conducted to determine the intensity of IgG expression in the kidney basement membrane and the mesangial compartment. Histopathologic analysis of kidneys obtained from vehicle-treated animals revealed extensive IgG staining, whereas orelabrutinib-treated animals exhibited significantly reduced IgG staining.

In a rat Collagen-Induced Arthritis (CIA) model, one of the most commonly studied autoimmune models of RA, orelabrutinib also showed dose-dependent reduction of proinflammatory cytokines, ameliorated arthritis histopathology scores and prevented joint destruction.

Figure 15: Effect of orelabrutinib on clinical scores of arthritis in CIA rat model



Source: Company data, CMBIS

InnoCare is currently obtaining approval from the relevant authority to start patient enrolment for a Phase Ib/IIa study of orelabrutinib in combination with standard of care treatment for SLE in China and patient enrollment will begin in 2Q20E. Study ICP-CL-00109 is a randomized, placebo-controlled, double-blinded, dose-ranging, Phase Ib/IIa study to identify the optimal dosing regimen and evaluate the safety, tolerability and the biomarker readout of orelabrutinib at 50 mg, 80 mg and 100 mg QD in patients with SLE in China. The primary endpoint is safety and tolerability, the secondary endpoints are efficacy and PK/PD.

Expect RMB2.83bn risk-adjusted peak sales from Orelabrutinib

We think the majority of orelabrutinib's sales will come from China thanks to the favourable competition environment in China and InnoCare's strong expertise in the domestic market. Meanwhile, we think orelabrutinib will have meaningful sales from CNSL, MZL, DLBCL, FL and SLE indications in the US market given that competition in these indications are relatively mild in the US.

Orelabrutinib's patent will be valid till 2034E, while ibrutinib's patent will expire in 2027E. Considering the potential competition from ibrutinib generics, we conservatively forecast that orelabrutinib's market share in several indications, including CLL/SLL, MCL, MZL, WM, DLBCL and FL, will gradually decrease from 2027E. Meanwhile, we think orelabrutinib will enjoy market share gain in its unique indications such as CNSL and SLE beyond 2027E.

In May 2015, InnoCare Beijing Nuocheng, the Company's wholly-owned subsidiary, entered into an intellectual property assignment agreement (the "BioDuro Agreement") with BioDuro Shanghai, concerning the transfer of worldwide intellectual property rights related to orelabrutinib. Under the BioDuro Agreement, BioDuro Shanghai is entitled to receive an upfront payment and milestone payments, which InnoCare have paid in full to BioDuro Shanghai. In addition, InnoCare will be obligated to share with BioDuro Shanghai a single-digit percentage of any licensing fee if InnoCare out-licenses any intellectual property rights under the BioDuro Agreement outside of Greater China. InnoCare will also be obligated to share with BioDuro Shanghai a single-digit percentage of the annual net after-tax sales outside of Greater China of orelabrutinib.

As of Jan 2020, ibrutinib is priced at RMB189 per 140mg, indicating RMB17,010-22,680 treatment cost per month. We assume orelabrutinib to be priced at RMB12,000 per month when it is initially commercialized in China in 2H20E. Adjusted by possibility of success and sales royalties paid to

BioDuro Shanghai, we expect orelabrutinib's risk-adjusted peak sales will reach RMB2.83bn by 2030E, including RMB1.99bn risk-adjusted sales from China and RMB0.84bn risk-adjusted peak sales from the US.

Figure 16: Orelabrutinib China sales forecasts

Orelabrutinib sales projection (China market)	Expected Year of approval	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Orelabrutinib sales in CLL/SLL (RMB mn)	2020 (1L approval in 2023)	38	95	168	264	386	530	616	674	708	726
Probability of success for CLL/SLL		*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*
Orelabrutinib sales in MCL (RMB mn)	2020	38	78	124	182	248	306	323	328	325	319
Probability of success for MCL		*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*	*90%*
Orelabrutinib sales in MZL (RMB mn)	2022	17	51	104	177	259	353	397	423	438	447
Probability of success for MZL		*85%*	*85%*	*85%*	*85%*	*85%*	*85%*	*85%*	*85%*	*85%*	*85%*
Orelabrutinib sales in CNSL (RMB mn)	2022	10	40	59	81	100	115	116	115	114	112
Probability of success for CNSL		*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
Orelabrutinib sales in WM (RMB mn)	2022	3	8	16	28	42	58	68	75	79	80
Probability of success for WM		*85%*	*85%*	*85%*	*85%*	*85%*	*85%*	*85%*	*85%*	*85%*	*85%*
Orelabrutinib sales in non-GCB DLBCL (RMB mn)	2024	43	128	262	448	686	925	1,019	1,082	1,120	1,137
Probability of success for non-GCB DLBCL		*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
Orelabrutinib sales in FL (RMB mn)	2024	5	20	45	83	136	197	239	272	296	313
Probability of success for FL		*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
Orelabrutinib sales in SLE (RMB mn)	2024	14	30	50	125	216	327	506	585	661	732
Probability of success for SLE		*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
Risk-adjusted Orelabrutinib sales in China (RMB mn)		**106**	**274**	**494**	**794**	**1,155**	**1,545**	**1,751**	**1,875**	**1,950**	**1,989**

Source: Company data, CMBIS

Figure 17: Orelabrutinib US sales forecasts

Orelabrutinib sales projection (US market)	Expected year of approval	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Orelabrutinib sales in CNSL (RMB mn)	2024	20	40	65	94	128	166	207
Probability of success for CNSL		*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
Orelabrutinib sales in MZL (RMB mn)	2024	86	271	506	579	586	566	531
Probability of success for MZL		*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*
Orelabrutinib sales in non-GCB DLBCL (RMB mn)	2025	0	124	393	396	383	353	309
Probability of success for non-GCB DLBCL		*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
Orelabrutinib sales in FL (RMB mn)	2025	0	51	198	300	364	396	400
Probability of success for FL		*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
Orelabrutinib sales in SLE (RMB mn)	2026			246	456	709	1,002	1,333
Probability of success for SLE				*15%*	*15%*	*15%*	*15%*	*15%*
Riskt-adjusted Orelabrutinib sales (RMB mn)		**70**	**262**	**600**	**730**	**805**	**854**	**888**
% of royalties paid		*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
Attributable risk-adjusted Orelabrutinib sales (RMB mn)		**67**	**249**	**570**	**693**	**765**	**811**	**844**

Source: Company data, CMBIS

ICP-192 is a potential first-to-market pan-FGFR inhibitor in China

ICP-192 is a highly selective pan-FGFR inhibitor

ICP-192 is a potent, highly selective, irreversible small-molecule pan-FGFR inhibitor in clinical studies for the treatment of patients with various types of solid tumors in China. InnoCare is currently conducting a Phase I/IIa study of ICP-192 to define its MTD and/or OBD and PK/PD in patients with solid tumors. Preliminary data from the study reveal a favorable safety profile for ICP-192 and show the compound to be well tolerated by treated patients. The plasma exposure of ICP-192 after a single dose of 8 mg was fourfold of that after a single dose of 2 mg, which suggests the increase of exposure was dose-proportional. The plasma exposure of ICP-192 at 8 mg QD has exceeded the therapeutic exposure of ICP-192 in pre-clinical efficacy studies in xenograft models. Hyperphosphatemia, a PD marker for FGFR inhibition, was consistently observed in treated patients at dose 8 mg QD.

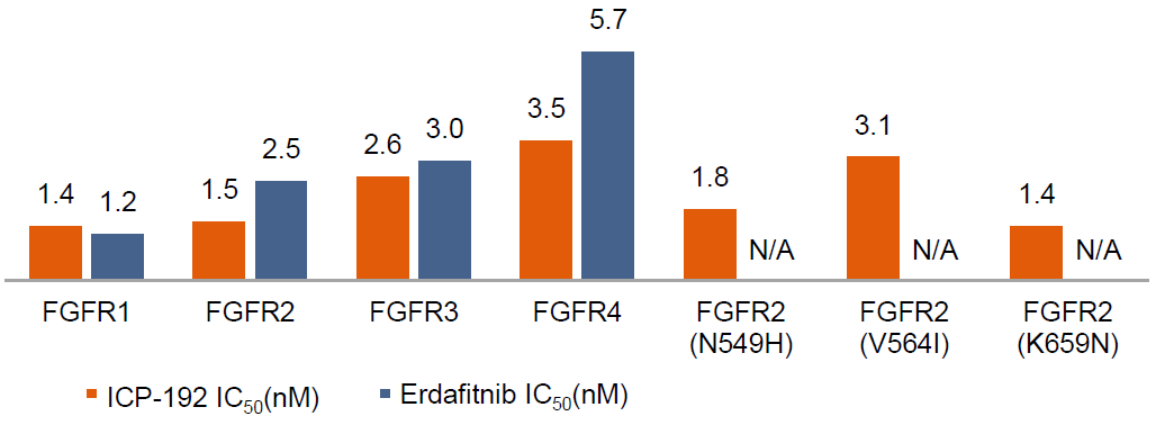
As preliminary results show that ICP-192 was well-tolerated with no DLTs reached, the Company has initiated two Phase II studies targeting cholangiocarcinoma and urothelial cancer, two indications with high incidence of FGFR aberrations and significant market opportunity in China. InnoCare is also expanding ICP-192's clinical program globally and has received IND approval from the US FDA in Apr 2020.

As of Apr 2020, the US FDA has approved two pan-FGFR inhibitors, including Johnson & Johnson's erdafitinib (brand name Balversa) approved by the FDA in Apr 2019 for advanced urothelial cancer and Incyte's pemigatinib (brand name Pemazyre) approved in Apr 2020 for the treatment of cholangiocarcinoma.

While there are multiple candidates under development, currently there is no marketed pan-FGFR inhibitor in China.

ICP-192 is a highly selective pan-FGFR inhibitor that can bind to FGFR1-4 with IC_{50} of 1.4nM, 1.5nM, 2.6nM and 3.5nM, respectively. Furthermore, ICP-192 demonstrated selective inhibition of FGFR2 (N549H)/(V564I)/(K659N) with IC_{50} of 1.8nM, 3.1nM and 1.4nM, respectively. While there is no head-to-head comparative study, ICP-192 showed similar inhibitory potency toward FGFR1-4 when compared to the reported data of erdafitinib.

Figure 18: ICP-192 has similar inhibitory potency when compared to erdafitinib

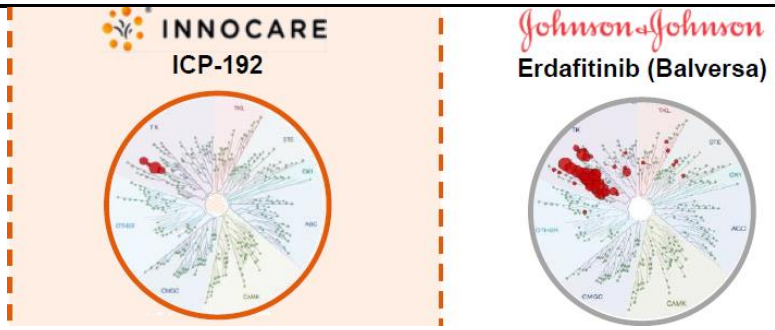


Source: Company data, CMBIS

At 1 μM concentration against 468 kinases in a KINOMEscan assay, ICP-192 inhibited only FGFR1-4 by >90% and showed no obvious inhibition of other kinases. While there is no head-to-head

comparative study, ICP-192 showed greater target selectivity than the reported data of erdafitinib, which inhibited not only FGFR1-4 but also over a dozen other kinases at 1 μM concentration.

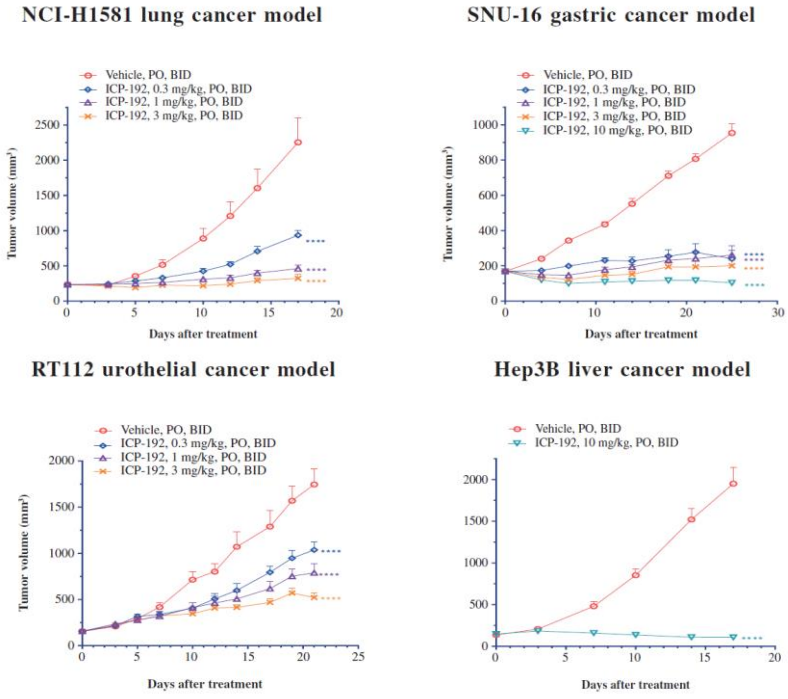
Figure 19: Kinase dendrogram shows improved target selectivity for ICP-192 versus erdafitinib



Source: Company data, CMBIS

ICP-192 also demonstrated a favorable safety profile in xenograft models. Not only was the MTD shown to be substantially higher than the effective dose, a 14-day continuous administration to rats also demonstrated no apparent toxicity. Efficacy was observed in lung, gastric, urothelial and liver cancer models where animals were treated with ICP-192. In an SNU-16 xenograft tumor model, ICP-192 demonstrated significant anti-tumor response at the dosage level from 0.3 mg/kg BID. An Hep3B xenograft model, a decrease in tumor volume was observed at the dosage level of 10 mg/kg BID.

Figure 20: ICP-192's efficacy shown in multiple tumor models harboring FGFR abnormalities



Source: Company data, CMBIS

ICP-192 has good preliminary clinical trial data

InnoCare is currently conducting a Phase I/IIa study of ICP-192 to define its MTD and/or OBD and PK/PD in patients with solid tumors. Study ICP-CL-00301 is an open-label, multi-center two-stage Phase I/IIa study in China. Stage I of the study is the dose escalation portion for defining the MTD

and/or OBD and PK/PD in patients with solid tumors. Stage II of the study is the dose expansion portion for investigating the safety, tolerability and preliminary efficacy of ICP-192 in patients with cholangiocarcinoma with FGFR2 fusions.

Patients were enrolled into sequentially escalating dose cohorts (2, 4, 8, 10 and 12 mg) with a daily dosing schedule of 21-day cycles. As of the data cut-off date of 3 Dec 2019, 15 patients with solid tumors have been treated with ICP-192 at dosage levels ranging from 2 mg to 12 mg, QD. The plasma exposure of ICP-192 increased with dose and suggests the pharmacokinetics of ICP-192 is linear. The plasma exposure of ICP-192, at 8 mg QD, has exceeded the therapeutic exposure of ICP-192 in pre-clinical efficacy studies in xenograft models. Hyperphosphatemia, a PD marker for FGFR inhibition, was consistently observed in patients treated with 8 mg QD or higher. The majority of AEs reported by investigators were Grade 1 or 2 and no treatment-related DLT was reported. Dose escalation remains ongoing.

After MTD and/or OBD is identified, InnoCare will advance the current Phase I/IIa study from the dose escalation stage (Phase I) to its Phase IIa stage with the selected regimen. During this Phase IIa study, InnoCare will mainly focus on evaluating the safety and efficacy of ICP-192 in patients with cholangiocarcinoma with FGFR2 fusions.

Meanwhile, InnoCare is initiating a separate Phase II trial in parallel with urothelial cancer with FGFR2/3 genetic alterations. InnoCare is actively seeking ways to investigate ICP-192 in combination with therapeutic agents such as immune checkpoint inhibitors. In addition, the Company plans to initiate several open-label, Phase II studies to evaluate the safety and efficacy of ICP-192 for additional indications, including gastric cancer and HCC.

In April 2020, the US FDA approved ICP-192 for initiation of clinical investigations. Following the IND approval, InnoCare will soon initiate clinical studies in the US for ICP-192. InnoCare will also actively explore collaboration opportunities with innovative biotech and pharmaceutical companies in these areas.

Expect RMB876mn risk-adjusted peak sales from ICP-192

InnoCare owns the global rights in ICP-192. We think ICP-192 will have promising market potential in both China and the US. Major pan-FGFR inhibitors under development in the global market are erdafitinib, pemigatinib, infigratinib, TAS-120, rogaratinib, ICP-192, etc.

Erdafitinib received the approval from US FDA in Apr 2019 for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma that has susceptible FGFR3 or FGFR2 genetic alterations and progressed during or following at least one line of prior platinum-containing chemotherapy including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

In Apr 2020, the US FDA has approved pemigatinib for treatment of previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or other rearrangement as detected by a FDA-approved test. The FDA granted pemigatinib Breakthrough Therapy designation for the treatment of patients with previously treated advanced/metastatic or unresectable FGFR2 translocated cholangiocarcinoma and Orphan Drug designation for the treatment of cholangiocarcinoma in Feb 2019 and Mar 2018, respectively. Study results demonstrated that in patients harboring FGFR2 fusions or rearrangements (Cohort A), pemigatinib monotherapy resulted in an ORR of 36%, and median DOR of 7.5 months with a median follow-up of 15 months.

Given that the earliest patent expiration of competing pan-FGFR inhibitors will be erdafitinib in 2031, we expect ICP-192 will realize RMB876mn risk-adjusted peak sales in 2030E with RMB465mn sales from China and RMB410mn sales from the US.

Figure 21: ICP-192 China sales forecasts

ICP-192 sales projection (China market)	Expected year of approval	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
ICP-192 sales in UC (RMB mn)	2023	57	107	154	210	275	349	414	490
Probability of success for UC		*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
ICP-192 sales in CAA (RMB mn)	2023	60	112	159	213	274	343	390	441
Probability of success for CAA		*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
Risk-adjusted ICP-192 sales in China (RMB mn)		**59**	**109**	**157**	**212**	**275**	**346**	**402**	**465**

Source: Company data, CMBIS

Figure 22: ICP-192 US sales forecasts

ICP-192 sales projection (US)	Expected year of approval	2024E	2025E	2026E	2027E	2028E	2029E	2030E
ICP-192 sales in UC (RMB mn)	2024	122	219	332	427	531	643	763
Probability of success for UC		*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
ICP-192 sales in CAA (RMB mn)	2024	9	17	25	32	40	49	58
Probability of success for CAA		*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
Risk-adjusted ICP-192 sales in US (RMB mn)		**66**	**118**	**178**	**230**	**286**	**346**	**410**

Source: Company data, CMBIS

ICP-105 is a potential first-to-market FGFR4 inhibitor in China

ICP-105 is a highly selective FGFR4 inhibitor

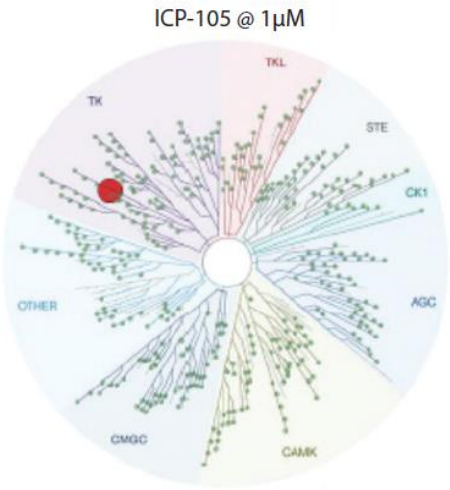
ICP-105 is a highly selective FGFR4 inhibitor that can effectively bind to FGFR4, inhibit FGF19-overexpression mediated activation of FGFR4 signaling in HCC and exert its anti-neoplastic effect by blocking the activation of the downstream ERK signaling pathway.

ICP-105 is primarily being developed for the treatment of advanced HCC with FGFR4 pathway overactivation. InnoCare is currently assessing the safety and tolerability of ICP-105 in the dose escalation portion of a Phase I study in solid tumor patients. Preliminary data from the study demonstrate a favorable safety profile for ICP-105 and show the compound to be well tolerated. We expect the dose escalation trial to be completed in 4Q20E. We believe ICP-105 is potentially a first-in-class FGFR4 inhibitor in China for the treatment of HCC patients with FGFR4 pathway overactivation.

While several FGFR4 inhibitors are under clinical development, there are currently no marketed FGFR4 inhibitors globally.

ICP-105 inhibits the activity of the FGFR4 kinase with an IC_{50} of 0.93nM, and the inhibitory effects of ICP-105 on other subtypes of FGFR family, including FGFR1, FGFR2 and FGFR3, are several thousand times weaker than that on FGFR4. As illustrated in the dendrogram below, in a KINOMEscan assay against 468 kinases, ICP-105 at a concentration of 1 μM inhibited FGFR4 only by >90% and showed no obvious inhibitions of other kinases.

Figure 23: Kinase dendrogram of ICP-105

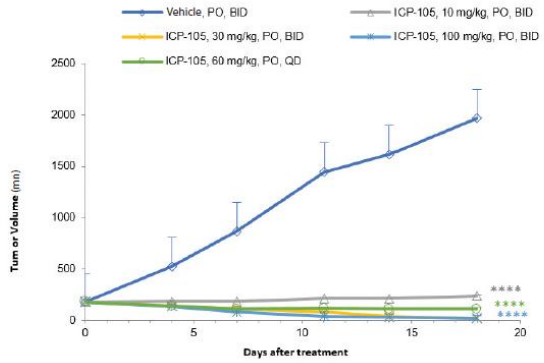


Source: Company data, CMBIS

ICP-105 also demonstrated a favorable tolerability profile in animal studies in SD rats and beagles, two of the most common animal models for toxicity assessment. ICP-105 showed no significant toxicity at 360 mg/kg (HED: 4064 mg/day) and no significant increase in AST/ALT in SD rats. ICP-105 showed no significant toxicity at 180 mg/kg (HED: 7000mg/day), or significant increase in AST/ALT in beagles.

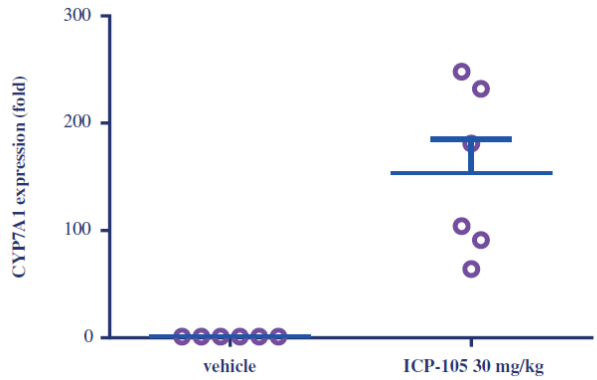
Anti-tumor efficacy of ICP-105 was evaluated in HCC xenograft models where tumor growth is driven by FGFR4 signaling. At a dose of 10 mg/kg, BID, ICP-105 induced CRs in a subset of mice for at least 18 days after cessation of treatment. At a dose of 30mg/kg and beyond, BID, ICP-105 inhibited tumor growth completely. At the dose of 30 mg/kg, significant induction of CYP7A1 expression was seen. As FGFR4 and its ligand, FGF19, down-regulate the expression of CYP7A1, induction of CYP7A1 expression suggests inhibition of FGFR4 signaling. A correlation between the concentration of ICP-105 in mouse plasma and the level of expression of CYP7A1 was also observed in an HCC xenograft model in the same study. The correlation between ICP-105 plasma concentration, level of induction of CYP7A1 expression and anti-tumor efficacy suggests that the observed anti-tumor response is due to the inhibition of FGFR4 signaling.

Figure 24: Tumor size reduction in HCC mouse model after ICP-105 administration



Source: Company data, CMBIS

Figure 25: CYP7A1 gene expression induced by ICP-105 in HCC mouse model



Source: Company data, CMBIS

InnoCare is conducting a Phase I study in patients with solid tumors. Study ICP-CL-00201 is a Phase I open-label, dose escalation study to characterize the MTD and/or OBD in patients with solid tumors

in China. The dose escalation stage was conducted in patients with solid tumors. The primary endpoints are safety and tolerability of ICP-105. The trial plans to enrol a total of 54 patients. The first patient was enrolled on 31 Aug 2018.

As of the data cut-off date of 3 Dec 2019, 19 patients had been treated with ICP-105 following a 3+3 dose escalation design. Eight cohorts of patients with solid tumor were evaluated at dosage levels ranging from 20 mg to 450 mg BID. The study is still at dose escalation stage. The majority of AEs reported by investigators were Grade 1 or 2. No treatment-related DLT, nor treatment-related SAE, was reported. InnoCare targets to complete the dose escalation trial by 4Q20E.

InnoCare plans to initiate an open-label, potential registration-enabling study to evaluate the safety and efficacy of ICP-105 if the results generated from early clinical studies are positive. Depending on the data, the Company will explore the potential of ICP-105 in combination therapies. InnoCare will also consider initiating a two-stage study in the US to further explore its market and therapeutic potential. Stage I will be an abbreviated bridging dose escalation portion to define RP2D and stage II will be a dose expansion portion in HCC patients with FGFR4 pathway overactivation.

Expect RMB148mn peak sales from ICP-105

We conservatively only figure in sales potential of ICP-2015 from China market. Assuming the drug to receive approval from NMPA in 2024E, we forecast ICP-015's risk-adjusted sales to reach RMB148mn by 2030E.

Figure 26: ICP-105 sales forecasts

ICP-105 sales projection (China market)	Expected year of approval	2024E	2025E	2026E	2027E	2028E	2029E	2030E
ICP-105 sales in HCC (RMB mn)	2024	32	79	143	223	319	403	493
Probability of success for HCC		*30%*	*30%*	*30%*	*30%*	*30%*	*30%*	*30%*
Risk-adjusted ICP-105 sales in China (RMB mn)		**10**	**24**	**43**	**67**	**96**	**121**	**148**

Source: Company data, CMBIS

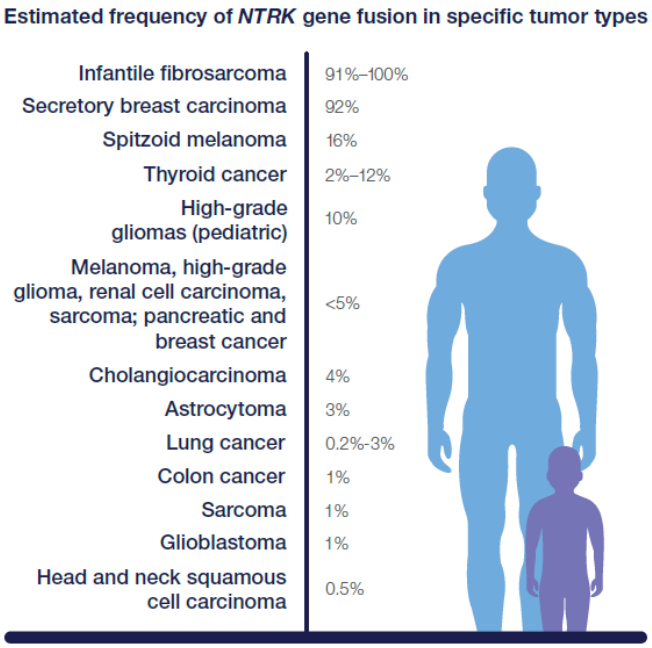
Other pre-clinical drug candidates

ICP-723 (pan-TRK inhibitor)

ICP-723 is a second-generation small-molecule pan-TRK inhibitor designed to treat patients with neurotrophic receptor tyrosine kinase (NTRK) fusion-positive cancers, as well as those refractory to the first-generation TRK inhibitors due to resistant TRK mutations, regardless of tumor types. The IND application for ICP-723 was submitted and accepted by the NMPA in Mar 2020.

NTRK fusion is quite rare, accounting for only up to about 1% of all solid cancers. However, it is implicated in up to 20 different cancer types, albeit in low frequencies of NTRK-fusion occurrence (less than 5%), with many cancer types being quite common - eg, lung adenocarcinoma, large cell neuroendocrine cancer of the lung, colorectal cancer, pancreatic cancer, cholangiocarcinoma, breast cancer, sarcoma, melanoma and brain cancers. NTRK fusions can also be found highly enriched (more than 75%) in some rare cancer types - eg, infantile fibrosarcoma, mammary analog secretory carcinoma of the salivary gland and secretory breast cancer.

Figure 27: Estimated frequency of NTRK gene fusion in specific tumor types



Source: Thermo Fisher, CMBIS

In Nov 2018, the US FDA approved the first pan-TRK inhibitor, larotrectinib (brand name Vitrakvi), which is developed by Bayer and Loxo Oncology (which was acquired by Eli Lily). Larotrectinib is approved for treatment of solid tumors that have a NTRK gene fusion without a known acquired resistance mutation, are metastatic or where surgical resection is likely to result in severe morbidity, and have no satisfactory alternative treatments or that have progressed following treatment. This is the second tissue-agnostic FDA approval for the treatment of cancer.

Larotrectinib has shown a dramatic and durable activity against solid tumors with NTRK fusions. Approval of larotrectinib was based on data from three multicenter, open-label, single-arm clinical trials: LOXO-TRK-14001 (NCT02122913), SCOUT (NCT02637687), and NAVIGATE (NCT02576431). Efficacy was evaluated in the first 55 patients with unresectable or metastatic solid tumors harboring an NTRK gene fusion enrolled across the three trials. A total of 12 cancer types were represented, with the most common being salivary gland tumors (22%), soft tissue sarcoma (20%), infantile

fibrosarcoma (13%), and thyroid cancer (9%). ORR was 75%, including 22% complete responses and 53% partial responses.

In Aug 2019, the US approved the second pan-TRK inhibitor, entrectinib (brand name Rozlytrek), developed by Roche. Entrectinib does not only target pan-TRK, but also ALK and ROS1. Entrectinib is approved for the treatment of 1) ROS1-positive metastatic non-small cell lung cancer (NSCLC), 2) solid tumors that have a NTRK gene fusion without a known acquired resistance mutation, are metastatic or where surgical resection is likely to result in severe morbidity, and have progressed following treatment or have no satisfactory alternative therapy.

Despite durable disease control in many patients, advanced stage NTRK fusion-positive cancers eventually become refractory to TRK inhibition. Next-generation TRK inhibitors, such as LOXO-195, TPX-0005, that overcome acquired resistance to first-generation TKIs are in development.

ICP-332 (TYK2 inhibitor)

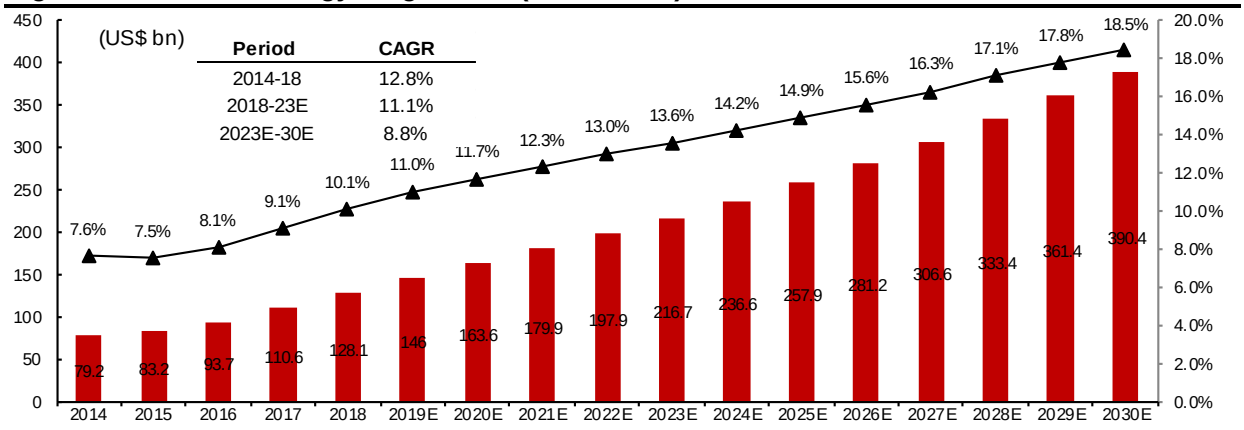
ICP-332 is a small-molecule inhibitor of tyrosine kinase 2 (TYK2), a non-receptor tyrosine kinase that mediates immune signaling. InnoCare plans to develop ICP-332 for the treatment of various T-cell mediated autoimmune disorders, such as psoriasis, inflammatory bowel disease (IBD) and SLE. The Company plans to submit the IND application for ICP-332 to the NMPA by early 2021E.

Industry overview

Global oncology drug market

The global oncology drug market has expanded significantly in the past, and is projected to further expand at an accelerated pace. Growth in the global oncology drug market is primarily driven by the growing patient pool, increased affordability of healthcare service and the emergence of innovative and advanced therapies, such as molecularly-targeted and immuno-oncology therapies. F&S forecasts global oncology drug market to grow from US$128.1bn in 2018 to US$390.4bn in 2030E.

Figure 28: Global oncology drug market (2014-2030E)



Source: F&S, CMBIS

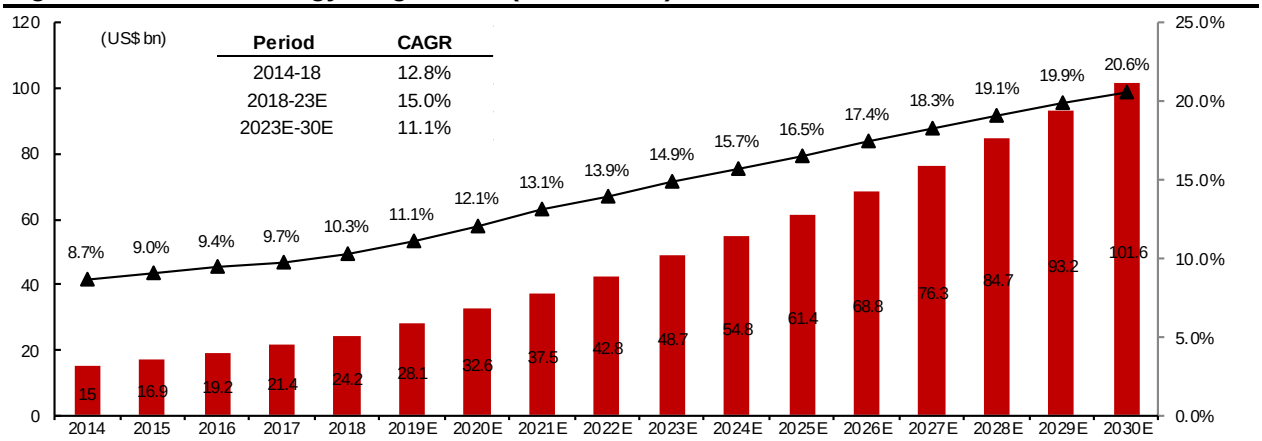
The field of cancer treatment has developed significantly in the past century, progressing from surgery to immunotherapy. Main treatment methods today include surgery, radiotherapy, chemotherapy, molecularly-targeted therapy, and immuno-oncology therapy. Molecularly-targeted therapy and immuno-oncology therapy have revolutionized cancer treatment and are expected to further propel the growth of global oncology drug markets.

Molecularly-targeted therapy is an important pillar of cancer treatment. By targeting specific biologic pathways for the purpose of inhibiting the growth of cancer cells, molecularly-targeted therapy is generally less harmful to normal cells than conventional chemotherapy. Therefore, molecularly-targeted oncology drugs often have fewer side effects and are better tolerated than chemotherapy drugs. The global molecularly-targeted oncology drug market is expected to grow due to identification of new targets, better accessibility to diagnostic tools and the emergence of combination therapies.

China oncology drug market

China's oncology drug market experienced rapid growth in the past and is expected to continue to grow. Growth in China's oncology drug market is primarily driven by an aging population and growing cancer incidence, increased awareness of cancer and paradigm shift of cancer treatment from chemotherapy to molecularly-targeted and immuno-oncology therapies. F&S forecasts China oncology drug market to grow from US$24.2bn in 2018 to US$101.6bn in 2030E.

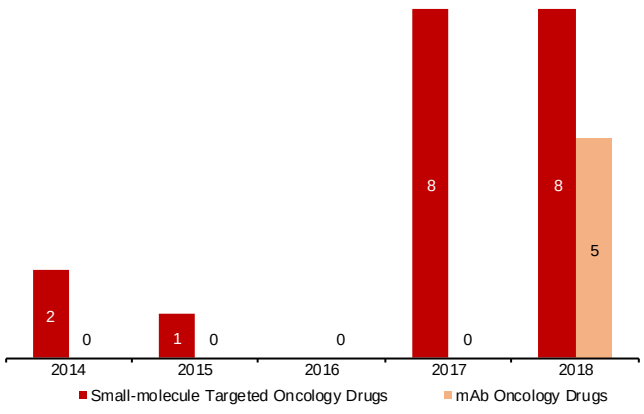
Figure 29: China oncology drug market (2014-2030E)



Source: F&S, CMBIS

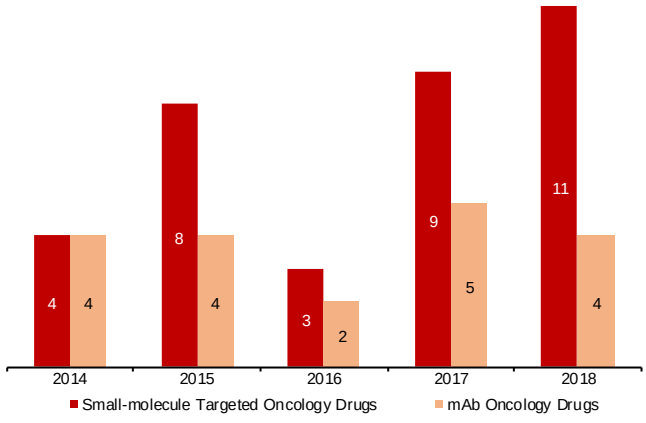
There is significant potential for growth in China's small-molecule targeted oncology drug market and immuno-oncology drug market. There were 35 small-molecule targeted oncology drugs and 19 monoclonal antibody ("mAbs") oncology drugs approved in the US from 2014 to 2018, with the number of small-molecule targeted oncology drug showing an upward trend since 2016, suggesting small-molecule targeted oncology drugs to remain an important pillar of cancer treatment. In comparison, there were only 19 small-molecule targeted oncology drugs and 5 mAb oncology drugs approved in China from 2014 to 2018. The difference in the number of marketed small-molecule targeted oncology drugs and mAb oncology drugs between the US and China suggests significant room for growth in these markets in China. Top oncology drugs globally such as pembrolizumab, ibrutinib, palbociclib and osimeritinib, were recently approved in China, indicating China is at its early stage of adopting small-molecule targeted oncology drugs and immuno-oncology drugs. According to F&S, China's small-molecule targeted oncology drug market reached US$1.8bn in 2018, and is expected to reach US$4.2bn in 2023E and further to US$10.3bn in 2030E.

Figure 30: Number of NMPA Approved Small-molecule Targeted Oncology Drugs and mAb Oncology Drugs, 2014-2018



Source: F&S, CMBIS

Figure 31: Number of FDA Approved Small-molecule Oncology Targeted Drugs and mAb Oncology Drugs, 2014-2018



Source: F&S, CMBIS

Large and Increasing Patient Pool

Cancer incidence in China has increased steadily in the past five years, climbing from 3.8mn in 2014 to 4.3mn in 2018. The incidence number is expected to grow at an accelerated pace, and is projected

to reach 4.9mn by 2023 and 5.7mn in 2030E, which is primarily attributable to the change of life style, stress, and an aging population in China. The large and growing cancer patient pool in China not only generates substantial market demand for cancer treatments, but also provides a favourable clinical trial environment.

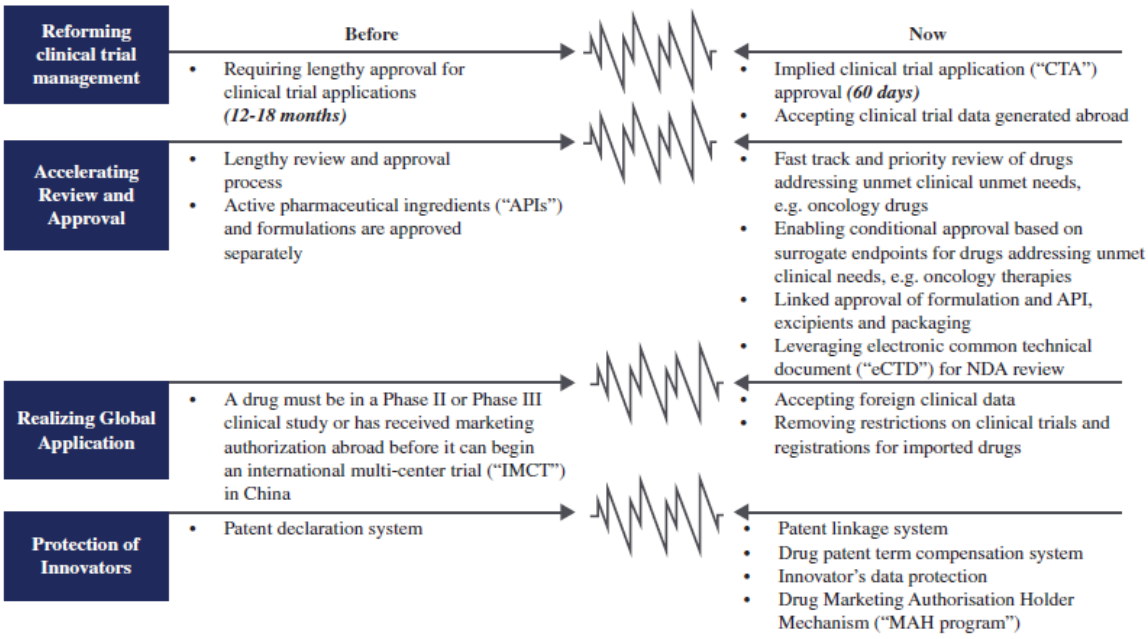
Increasing Healthcare Expenditure and Affordability

Healthcare expenditure in China is expected to grow due to continued urbanization and strong governmental support. In addition, the expansion of the National Reimbursement Drug List ("NRDL") is expected to make oncology treatments more accessible, contributing to an increasing market size of oncology drugs. The NRDL sets forth a list of reimbursable drugs for patients covered by the urban employee and resident basic medical insurance schemes, both of which are managed and/or subsidized by the Chinese government. Since 2000, five versions of the NRDL have been published, and each new version added more drugs to the list.

Transformation of Drug Approval Process in China

On 8 Oct 2017, the General Office of the State Council released the Opinions on Reform of the Drug and Medical Device Review and Approval (“关于深化审评审批制度改革鼓励药品医疗器械创新的意见”) (the "Opinions"), which has shifted the regulatory landscape of China's pharmaceutical market. The Opinions aim to accelerate drug development and approval process in China, and to encourage the innovation of drugs and medical devices.

Figure 32: China's regulatory shifts encouraging innovation of drugs and medical devices



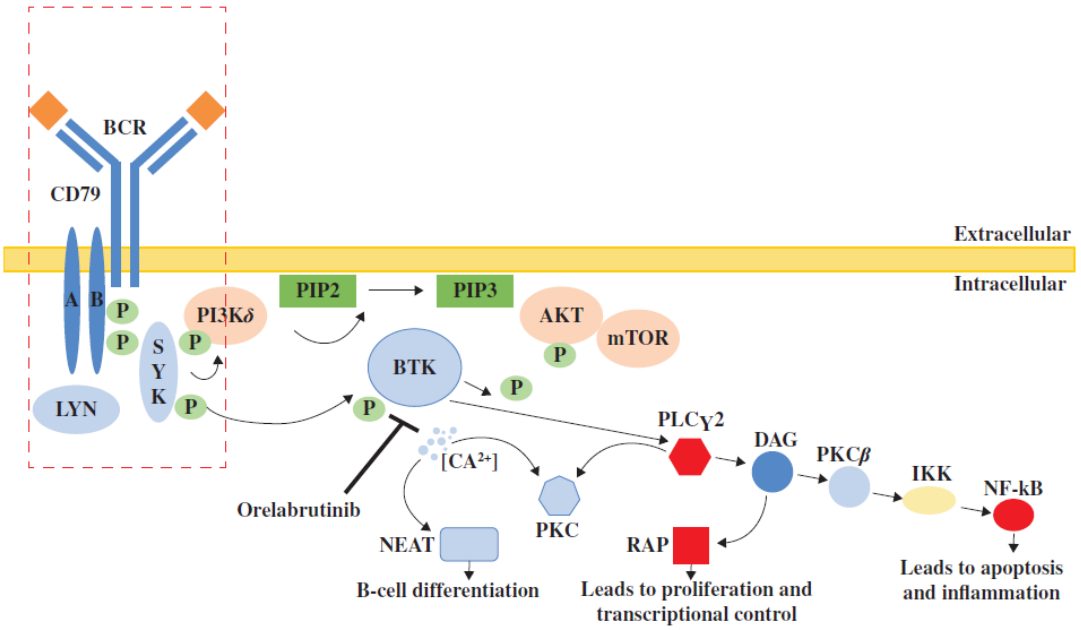
Source: F&S, CMBIS

BTK inhibitors address NHL and auto-immune disease market

BTK inhibitors have promising market size

Bruton's Tyrosine Kinase ("BTK") is a key component of the B-cell receptor signalling pathway, which is an important regulator of cell proliferation and cell survival in various lymphomas (mainly NHL). BTK inhibitors block B-cell receptor ("BCR") induced BTK activation and its downstream signaling. Successful blockage of BTK activation would result in growth inhibition and cell death of B-cells. Orelabrutinib is an orally available potent BTK inhibitor that irreversibly binds to BTK to induce downstream kinase inactivation and cell death.

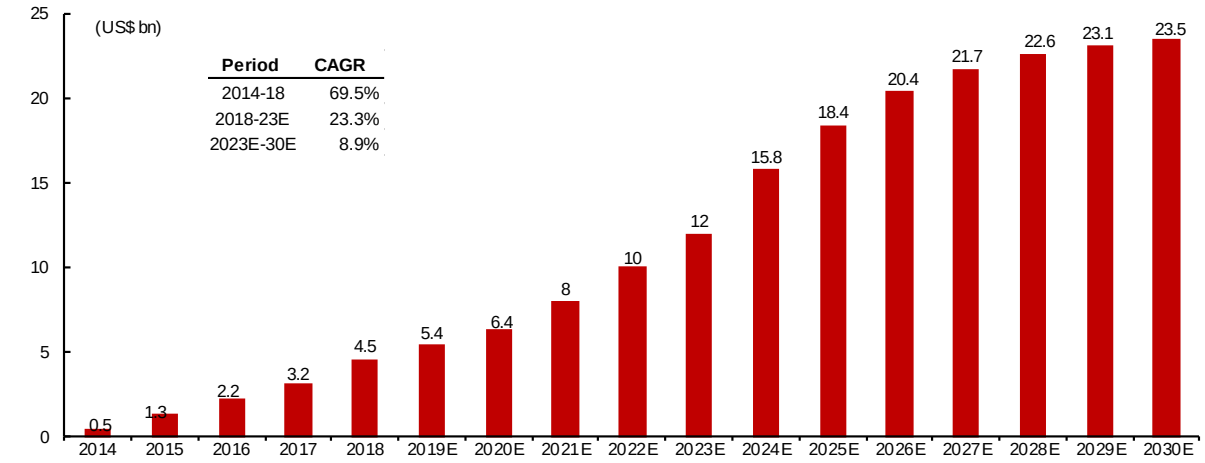
Figure 33: Mechanism of action of orelabrutinib in B-cell malignancies



Source: Company, CMBIS

According to F&S, the global sales of BTK inhibitors reached US$4.5bn in 2018, and is expected to reach US$12.9bn in 2023E and US$23.5bn in 2030E.

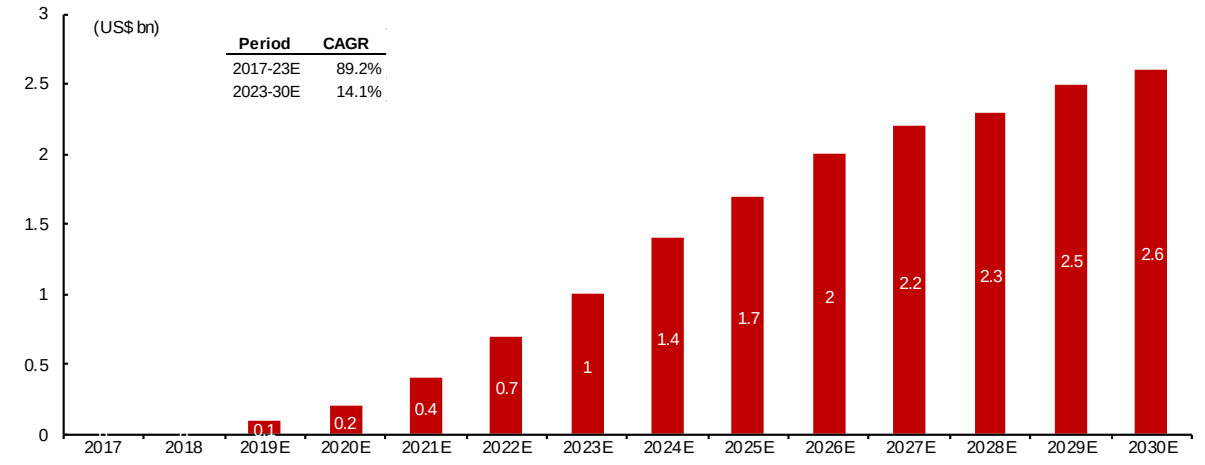
Figure 34: Market Size of Global BTK Inhibitors Market (2014-2030E)



Source: F&S, CMBIS

Meanwhile, F&S forecasts sales of BTK inhibitors in China to reach US$1.0bn in 2023E and US$2.6bn in 2030E.

Figure 35: Market Size of China BTK Inhibitors Market (2017-2030E)



Source: F&S, CMBIS

Strong sales from commercialzed BTK inhibitors

Johnson & Johnson/Abbvie's Imbruvica (ibrutinib) and AstraZeneca's Calquence (acalabrutinib) and Beigene's Brukinsa (zanubrutinib) are currently the only three BTK inhibitors approved globally. Ibrutinib was first approved by the US FDA in 2013 for the second-line treatment of patients with MCL. Since 2013, ibrutinib has received supplemental US FDA approvals for the treatment of patients with CLL/SLL, WM (2L), MZL (2L) and cGVHD (2L). Acalabrutinib is a second-generation BTK inhibitor which received the US FDA approval in Oct 2017 for the second-line treatment of MCL and is yet to be approved by the NMPA for commercial launch in China. Ibrutinib was launched in China in 2017 for the treatment of r/r CLL/SLL, r/r MCL and WM, and was included in the NRDL in late 2018. As of 31 Dec 2019, ibrutinib was the only BTK inhibitor marketed in China. Zanubrutinib received accelerated approval from the US FDA as a treatment for MCL (2L) in Nov 2019 and may receive approval from NMPA for r/r MCL and r/r CLL/SLL in 1H20E.

Ibrutinib recorded US$4,130mn sales worldwide in 9M19, up 28% YoY. Meanwhile, global sales of acalabrutinib reached US$108mn in 9M19, up 185% YoY, vs US$62mn sales in full-year 2018.

Figure 36: Globally commercialized BTK Inhibitors (as of Dec 2019)

	Ibrutinib (Imbruvica)	Acalabrutinib (Calquence)	Zanubrutinib / BGB-3111 (Brukinsa)
Company	Abbvie / JNJ	AstraZeneca	BeiGene
US FDA approval time	2013.11	2017.10	2019.11
US FDA approved indications	MCL, CLL/SLL, WM, MZL, cGVHD	MCL, CLL/SLL	MCL
NMPA approval time	2017.08		
NMPA approved indications	MCL, CLL/SLL, WM		
List price per year in US	$179,026(2)	$178,753(3)	$157,375.8(4)
Worldwide sales(1) in 9M19	$4,130mn	$108mn	NA

Source: Company data, CMBIS; Notes: (1) The worldwide sales of IMBRUVICA (ibrutinib) refers to the sum of Johnson & Johnson's sales revenue outside of the US and Abbvie's sales revenue in the US. (2) The price of IMBRUVICA is around $12,612 per bottle (90 capsules) in the US. (3) The price of CALQUENCE (acalabrutinib) is around $14,692 per bottle (60 capsules) in the US. The list price per year for CALQUENCE in the US is calculated on a 365-day-basis based on the recommended dosage for each patient. (4) The price of BRUKINSA (zanubrutinib) is around $12,935 for a 30-day supply in the US. The list price per year for BRUKINSA in the US is calculated on a 365-day-basis based on the recommended dosage for each patient.

As of 31 Dec 2019, ibrutinib was the only commercialized BTK inhibitor in China. Ibrutinib was included into the National Reimbursement Drug List (NRDL) in Oct 2018 while reimbursement is limited to second line treatment of MCL or treatment of CLL/SLL. According to data from PDB, sales of ibrutinib in sample hospitals in China reached RMB250mn in 2019. We estimate the total retail sales of ibrutinib in China should exceed RMB1bn in 2019.

Overview of lymphomas

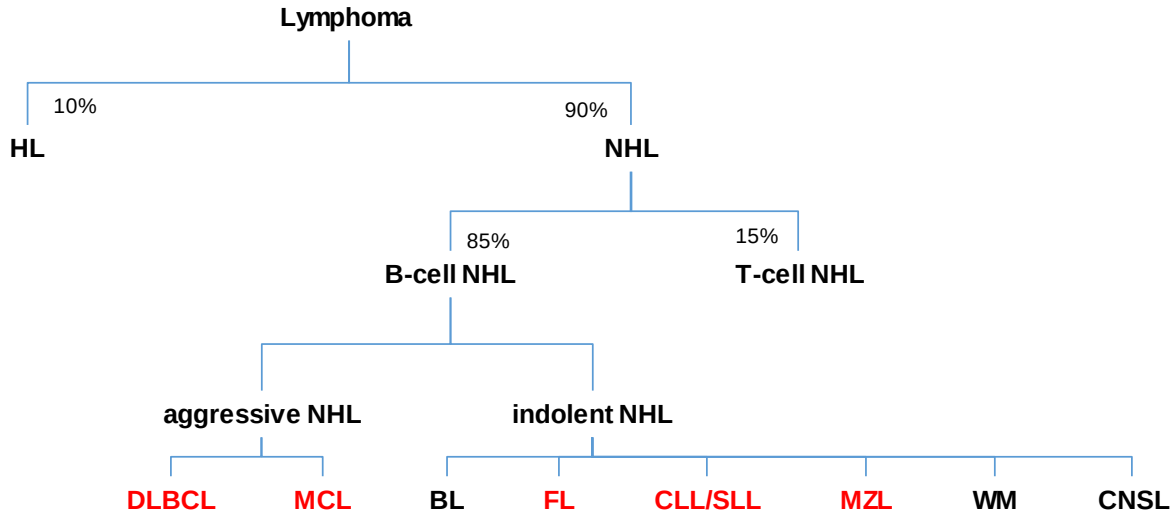
Lymphomas are hematologic cancers involving lymphoceles of the immune system. They can be broadly categorized into non-Hodgkin's lymphomas (NHL), and Hodgkin Lymphoma (HL). NHL consists of a heterogeneous group of malignancies arising from lymphoid tissues, and accounts for around 90% of lymphoma.

Depending on the origin of the cancer cells, NHL can be characterized as either B-cell, T-cell or other types of lymphomas. B-cell lymphomas account for approximately 85% of NHLs and consist of various distinct diseases involving B-cells at different stages of maturation or differentiation.

B-cell lymphomas can also be categorized into aggressive NHL, such as Diffuse Large B-Cell Lymphoma (DLBCL), Mantle Cell Lymphoma (MCL), and Burkitt's Lymphoma (BL), and indolent NHL, such as Chronic Lymphocytic Leukemia (CLL), Small Lymphocytic Lymphoma (SLL), Follicular Lymphoma (FL), Marginal Zone Lymphoma (MZL), CNSL and WM.

The most common NHL subtypes, both globally and in China, are DLBCL, FL, MZL, CLL/SLL and MCL. Among all subtypes of NHL, DLBCL, MZL and FL are the top three subtypes in China, and DLBCL alone accounts for around 40% of NHL incidence.

Figure 37: Classification of Lymphomas



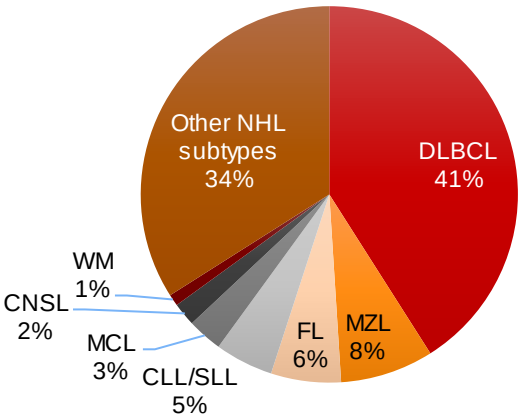
Note: Diseases highlighted in RED are common NHL subtypes

Source: F&S, CMBIS

According to F&S, global NHL prevalence reached 2.42mn in 2018 and is expected to increase to 2.79mn in 2023E at a CAGR of 2.8% from 2018, and 3.3mn in 2030E at a CAGR of 2.4% from 2023E. Global new cases of NHL have grown from 486,145 in 2014 to 530,622 in 2018, and are projected to reach approximately 592,000 in 2023E at a CAGR of 2.2% from 2018, and to reach approximately 687,000 in 2030E at a CAGR of 2.1% from 2023E.

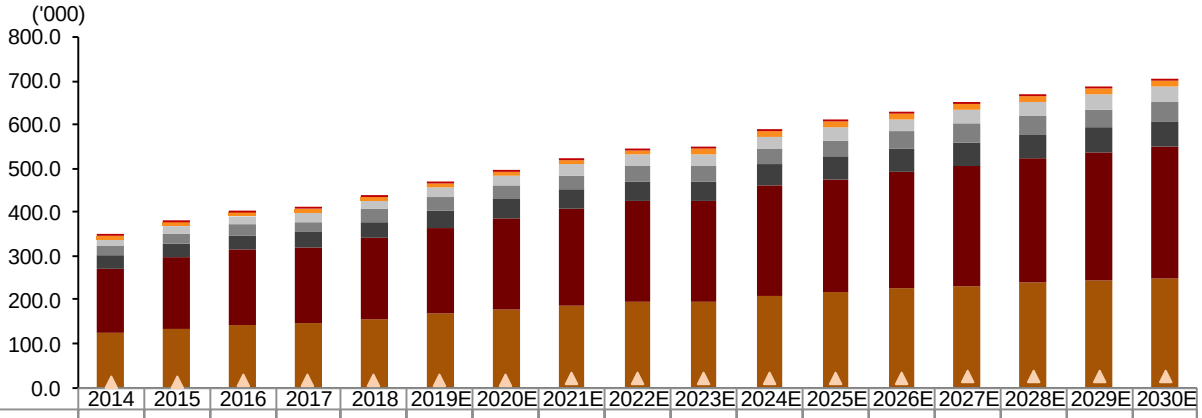
In China, NHL prevalence reached 454,982 in 2018 and is projected to reach approximately 589,000 in 2023E, representing a CAGR of 2.3% from 2018, and approximately 730,000 in 2030E, representing a CAGR of 3.1% from 2023E.

Figure 38: Prevalence of NHL Subtypes in China (2018)



Source: F&S, CMBIS

Figure 39: Prevalence of NHL Subtypes in China (2014-2030E)

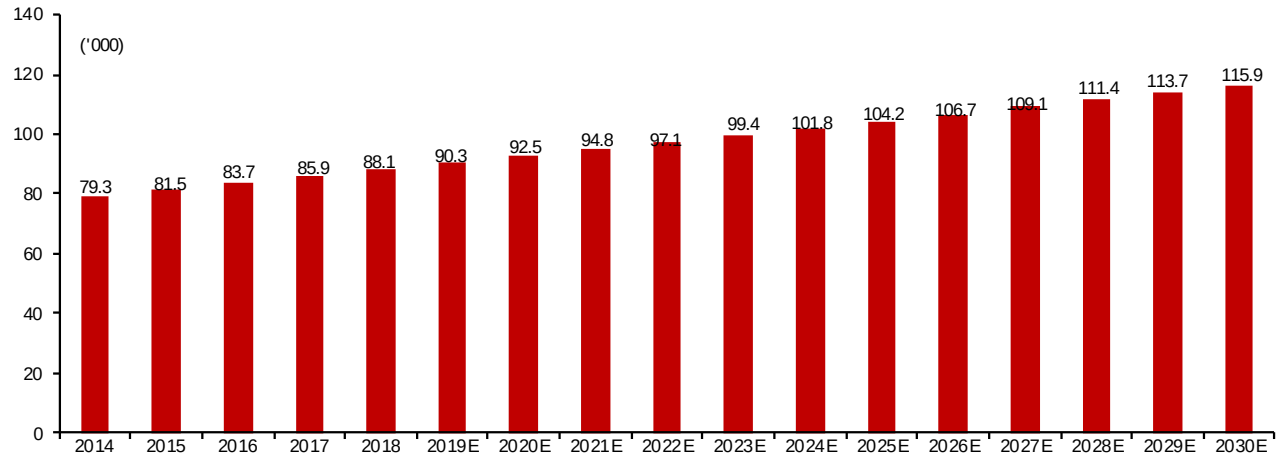


	2014	2015	2016	2017	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
WM	2.5	2.7	2.9	3.0	3.2	3.4	3.6	3.8	4.0	4.1	4.3	4.4	4.6	4.7	4.9	5.0	5.1
CNSL	7.2	7.9	8.3	8.5	9.1	9.7	10.3	10.8	11.3	11.8	12.2	12.6	13.1	13.5	13.9	14.2	14.6
CLL/SLL	16.6	18.1	19.2	19.5	20.9	22.3	23.7	24.9	26.0	27.1	28.1	29.1	30.0	31.0	31.9	32.7	33.6
FL	22.0	24.0	25.4	25.9	27.8	29.6	31.4	33.0	34.5	35.9	37.3	38.6	39.8	41.1	42.3	43.4	44.5
MZL	28.5	31.0	32.9	33.5	35.9	38.4	40.6	42.7	44.7	44.7	48.3	50.0	51.6	53.2	54.7	56.2	57.5
DLBCL	148.0	161.0	170.9	173.9	186.5	199.1	210.8	221.8	232.0	232.0	250.5	259.2	267.8	276.1	284.1	291.8	299.3
Others	123.9	134.7	143.0	145.5	156.1	166.5	176.4	185.5	194.1	194.0	209.5	216.9	224.0	231.0	237.7	244.1	250.4
MCL	12.3	13.4	14.2	14.4	15.5	16.5	17.5	18.4	19.2	20.0	20.8	21.5	22.2	22.9	23.6	24.2	24.8

Source: F&S, CMBIS

According to F&S, the new cases of NHL in China have reached 88,090 in 2018, and are expected to increase to approximately 99,000 in 2023E, representing a CAGR of 2.4% from 2018, and to approximately 116,000 in 2030E at a CAGR of 2.2% from 2023E.

Figure 40: NHL new cases in China (2014-2030E)



Source: F&S, CMBIS

Conventional methods of treating lymphomas vary subject to the specific type or histology, but generally comprise chemotherapy, CD20 antibody therapy, and, less frequently, radiation. Significant progress has been accomplished in the development of new therapies for lymphomas, including BTK inhibitors, PI3K inhibitors (idelalisib and copanlisib) and Bcl-2 inhibitor (venetoclax). There is significant potential for molecularly-targeted drug candidates as compared to conventional therapies, as they demonstrate improved efficacy, fewer side effects and better tolerability which lead to higher patient satisfaction. Despite their improvements as compared to conventional therapies, current small

molecularly-targeted therapies have shown adverse events, some of which are related to mechanism of action, such as cytopenias, pneumonitis and infection, while the others are believed to be attributable in part to the currently approved BTK inhibitors' off-target effects, such as diarrhea, bleeding and atrial fibrillation, indicating significant unmet medical needs. YESCARTA, a CD-19 directed genetically modified autologous T-cell immuno-oncology therapy, was recently approved for the treatment of DLBCL.

Given that there are already three BTK inhibitors approved by the US FDA for treatment of B-cell lymphoma, the bar is higher for other BTK inhibitor candidates targeting B-cell lymphoma indications. We think competitions in indications such as DLBCL, FL, MZL and CNSL are relatively moderate among other B-cell lymphomas. Meanwhile, several reversible BTK inhibitors are being developed to address the issues of ibrutinib-acquired resistance, such as LOXO-305, SNS-062 and ARQ 531.

Figure 41: BTK inhibitors under development for NHL diseases in global market (ex-China, as of Jan 2020)

Candidates	Binding properties	Company	NHL indications					
			CLL/SLL	MCL	WM	MZL	FL	DLBCL
Ibrutinib	Irreversible	Abbvie / JNJ	Marketed (1L)	Marketed (2L)	Marketed (1L)	Marketed (2L)	Ph1 (combo, 1L)	Ph3 (Combo, 1L)
Acalabrutinib	Irreversible	AstraZeneca	Marketed (1L)	Marketed (2L)	Ph2 (2L)	Ph2 (2L) Ph2 (combo, 2L)	-	Ph2 (combo, 1L)
Zanubrutinib / BGB-3111	Irreversible	BeiGene	Ph2 (2L)	Marketed (2L)	Ph3 (1L)	-	-	-
Orelabrutinib / ICP-022	**Irreversible**	**Innocare**	**Ph1 (2L)**	**Ph1 (2L)**		**Ph1 (2L)**	**Ph1 (2L)**	**-**
ONO-4059 /GS-4059/ Tirabrutinib	Irreversible	Gilead/ Ono	Ph2 (2L) Ph2 (combo, 2L)	Ph2 (2L)	Ph2 (2L)	Ph2 (2L)	-	-
M7583 / Evobrutinib	Irreversible	Merck KGaA	-	Ph2 (2L)	-	-	-	Ph2 (2L)
LOXO-305	Reversible	Eli Lilly	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)	-	-
SNS-062 / Vecabrutinib	Reversible	Sunesis	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)
ARQ 531	Reversible	ArQule	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)	Ph2 (3L)
TG-1701	-	TG Therapeutics / Hengrui	Ph1	-	-	-	-	-

Source: clinicaltrials.gov, CMBIS

As of 31 Dec 2019, ibrutinib was the only BTK inhibitor marketed in China. Zanubrutinib may receive approval from NMPA for r/r MCL and r/r CLL/SLL in 1H20E. Orelabrutinib has potential to become the third to market BTK inhibitor in China.

Acalabrutinib is going through clinical trials for treatment of CLL/SLL and MCL in China. Several BTK inhibitors developed by domestic companies are under early phase clinical trials for treatment of NHL diseases, including DTRMWXHS-12, CT-1530 and SHR1459.

Figure 42: BTK inhibitors under development for NHL diseases in China (as of Jan 2020)

Candidates	Binding properties	Company	NHL indications						
			CLL/SLL	MCL	WM	MZL	FL	DLBCL	CNSL
Ibrutinib	Irreversible	Abbvie / JNJ	Marketed (1L)	Marketed (2L)	Marketed (2L)	-	-	Ph2 (combo, 1L)	-
Acalabrutinib	Irreversible	AstraZeneca	Ph2 (2L) Ph3 (1L)	Ph2 (2L)	-	-	-	-	-
Zanubrutinib / BGB-3111	Irreversible	BeiGene	NDA	NDA	Ph2 (2L)	Ph2 (2L)	Ph2 (combo, 2L)	Ph2 (2L)	-
Orelabrutinib / ICP-022	**Irreversible**	**Innocare**	**NDA (2L) P3 (1L)**	**NDA (2L)**	**Ph2 (2L)**	**Ph2 (2L)**	**P1 (combo, 2L)**	**Ph2 (2L)**	**Ph2 (2L)**
DTRMWXHS-12	-	DTRM	-	Ph1 (2L)	-	-	-	-	-
CT-1530	Irreversible	Centaurus	Ph1 (2L)	Ph1 (2L)	Ph1 (2L)	Ph1 (2L)	Ph1 (2L)	Ph1 (2L)	-
SHR1459	-	Hengrui	Ph1 (2L)	Ph1 (2L)	Ph1 (2L)	Ph1 (2L)	Ph1 (2L)	Ph1 (2L)	-

Source: chinadrugtrials.org.cn, insight, CMBIS

BTK inhibitors have potential to treat auto-immune diseases

Overview of auto-immune diseases

Autoimmune diseases involve a condition where the body's immune system mistakenly attacks the body itself. Currently, there are about 100 different types of autoimmune disorders, including systemic lupus erythematosus, rheumatoid arthritis and psoriasis. Studies have shown that autoimmune disorders arise due to the breakage of immune tolerance to self-antigens, which leads to unregulated immune activation and tissue damage, and eventually to autoimmune disease with B-cell and T-cell dysfunctions.

Most of the current therapies for autoimmune diseases can only alleviate symptoms such as pain and inflammatory responses but are not able to cure them. As a result, therapies for autoimmune diseases require high safety profile for chronic use. Treatments for autoimmune diseases include anti-inflammatory agents and targeted therapies. Targeted therapy is an emerging area for the treatment of the autoimmune diseases, and therapies targeting IL-1, IL-6, IL-17 and IL-23, antibodies targeting CD20 and CD22, and BTK inhibitors are under development.

BTK inhibitors block BCR induced BTK activation and downstream signaling, the abnormal activation of which induces B-cell dysfunction and transforms them into autoreactive B-cells. In addition, BTK is an important enzyme for macrophage function, which is crucial to the pathogenesis of systemic lupus erythematosus (SLE) and other B-cell mediated autoimmune diseases. Such pivotal roles indicate that BTK could potentially be a valuable therapeutic target in various autoimmune diseases, including SLE, rheumatoid Arthritis (RA), multiple sclerosis (MS), pemphigus, psoriasis vulgaris (PV) and lupus nephritis (LN).

As of 31 Dec 2019, there were no approved BTK inhibitors for autoimmune diseases globally, while clinical trials for SLE, RA, sjögren's syndrome, MS and pemphigus vulgaris were being conducted globally.

BTK inhibitors under development for autoimmune diseases in global market (except China) include fenebrutinib, evobrutinib, acalabrutinib, PRN1008, BMS-986142, ABBV-105, CC-292, TAS5315, tirabrutinib, etc.

Figure 43: BTK inhibitors under development for autoimmune diseases in global market (ex-China, as of Jan 2020)

Candidates	Binding properties	Company	Autoimmune indications						
			RA	SLE	MS	Pemphigus Vulgaris	ITP	Urticaria	Sjögren Syndrome
Acalabrutinib	Irreversible	AstraZeneca	Ph2	-	-	-	-	-	-
Fenebrutinib / RG7845	Reversible	Roche	Ph2	Ph2	-	-	-	Ph2 (terminated)	-
M7583 / Evobrutinib	Irreversible	Merck KGaA	Ph2 (2L)	Ph2	Ph3 (2L)	-	-	-	-
PRN1008	Irreversible	Principia Biopharma	-	-	-	Ph3 (1L)	Ph2 (2L)	-	-
BMS-986142	Reversible	BMS	Ph2 (combo)		-	-	-		Ph2
ABBV-105	-	AbbVie	Ph2 (mono/combo, 2L)	Ph2 (mono/combo, 2L)	-	-	-	-	-
TAS5315	-	Taiho Pharmaceutical	Ph2 (2L)	-	-	-	-	-	-
CC-292/ Spebrutinib	-	Celgene	Ph2 (2L)	-	-	-	-	-	-
ONO-4059 /GS-4059/ Tirabrutinib	Irreversible	Gilead/Ono	Ph1 (2L)	-	-	-	-	-	Ph2
BMS-986195 / Branebrutinib	Irreversible	BMS	Ph1 (combo)		-	-	-		
SAR442168 / PRN2246	Irreversible	Sanofi/ Principia Biopharma	-	-	Ph2 (2L)	-	-		
LOU064	-	Novartis	-	-	-	-	-	Ph2	Ph2
AC0058	-	ACEA	-	Ph1	-	-	-	-	-
BIIB-068	-	Biogen	-	Ph1	-	-	-	-	-

Source: clinicaltrials.gov, CMBIS

There are only three BTK inhibitors targeting auto-immune diseases in China, according to data from chinadrugtrials.org. InnoCare is currently obtaining approval from the relevant authority to start patient enrolment for a Phase Ib/IIa trial of orelabrutinib in combination with standard of care treatment for SLE in China. WXFL10230486/HWH486 and SHR1459 are developed by domestic companies and are under phase I trials for RA indication.

Figure 44: BTK inhibitors under development for autoimmune diseases in China (as of Jan 2020)

Candidates	Binding properties	Company	Autoimmune indications	
			RA	SLE
Orelabrutinib / ICP-022	**Irreversible**	**Innocare**	**-**	**Ph2a**
WXFL10230486/HWH486	-	Humanwell Healthcare	Ph1	-
SHR1459	-	Hengrui	Ph1	-

Source: chinadrugtrials.org.cn, CMBIS

Systemic Lupus Erythematosus

SLE is an autoimmune disease, in which the patient's immune system mistakenly attacks healthy tissues and organs in the body, potentially leading to serious organ complications and even death. SLE may evolve from initial symptoms such as joint pains, muscle pains and fatigue to organ damages, which may involve organs like eyes, skin, lung and kidney. The typical onset age for SLE patients is between 15 and 45, and the average life expectancy reduction is 12.4 years. The average life expectancy reduction for SLE patients with renal damage is up to 23.7 years. Studies show that young women are more frequently affected by SLE.

Global SLE prevalence reached 7.6mn in 2018, and is expected to increase to 8.6mn in 2030E at a CAGR of 1.0% from 2018. Primarily driven by an expanding patient pool and an increase in available

therapeutic options, the global SLE therapeutic market reached US$1.2bn in 2018, and is expected to further grow at an accelerated pace, potentially reaching US$12.0bn in 2030E at a CAGR of 21.2% from 2018.

The prevalence of SLE in China reached 1.0mn in 2018, and is projected to increase to 1.1mn in 2030E at a CAGR of 0.6% from 2018. China's SLE market reached RMB1.4bn in 2018, and is projected to increase to RMB14.9bn in 2030E at a CAGR of 21.7% from 2018.

The current treatment objective for SLE is to induce remission and suppress symptoms. Both the type and seriousness of the symptoms are taken into account when determining the treatment option for each patient. The most prevalent treatments include non-steroidal anti-inflammatory drugs ("NSAIDs"), corticosteroids, antimalarial drugs and biological therapies. The existing treatment options for SLE patients remain limited and are either ineffective, inconvenient or poorly tolerated in a sizeable group of patients. The use of corticosteroids and immunosuppressants is associated with severe side effects, such as increased risks of infection and osteoporosis for SLE patients. The only approved targeted therapy for SLE, belimumab, has also shown limited efficacy and needs to be administered by injection. Inhibition of BTK signaling pathways may be a promising treatment option for SLE patients.

Considering the high economic burden and the low treatment compliance rate of the current therapeutic options for SLE, there is an urgent need for new types of drugs with superior efficacy and more convenient administration regimen. Various BTK inhibitors are being developed at clinical stages for SLE, including orelabrutinib, GDC-0853, BIIB068, M2951 and ABBV-105.

Figure 45: Traditional and emerging therapies for SLE

Traditional Therapy	Therapy Categories	Common Drugs (FDA Approved)	Features
Early Stage	NSAIDS	• Ibuprofen • Naproxen	The drugs can be used to control the symptoms of SLE.
	Antimalarial drugs	• Hydroxychloroquine	
	Immunomodulatory drugs	• Thalidomide	
	Corticosteroids	• Prednisone	
Moderate Stage	Immunomodulatory drugs (Combined with Glucocorticoid)	• Methotrexate • Azathioprine	The drugs are used for remission induction and consolidation therapy. The conditions can be controlled rapidly.
Late Stage	Immunomodulatory drugs	• Cyclophosphamide • Ciclosporin • Mycophenolate mofetil	
Emerging Therapy	**Typical Product**	**Features**	
Biologics	• mAbs (Belimumab)	Belimumab is a BLyS inhibitor, which showed statistically significant, albeit modest, efficacy for the treatment of SLE. It also needs to be administered by injection. It represents a step forward in advance against SLE.	
Small Molecule	BTK Inhibitor	There is no approved BTK inhibitor for the treatment of SLE patients. BTK signaling significantly impacts multiple key effector pathways that contribute to the pathogenesis of SLE. Both B-cell activation and FcR signaling have important implications for the treatment of SLE patients.	

Source: F&S, CMBIS

As of 31 Dec 2019, there were no BTK inhibitors for SLE treatment approved in the global market. Besides orelabrutinib, other BTK inhibitor candidates are under clinical development for SLE treatment, including fenebrutinib, evobrutinib, ABBV-105, etc.

Figure 46: BTK inhibitors for SLE treatment at clinical stage

Drug Name	Company	Global clinical stage (except China)	China clinical stage
Fenebrutinib	Roche	Phase II	NA
Evobrutinib	Merck	Phase II	NA
ABBV-105	AbbVie	Phase II	NA
AC0058	ACEA Pharma	Phase I	NA
ICP-022	**InnoCare**	**NA**	**Phase IIa**
BIIB068	Biogen	Phase I	NA
SN1011	SinoMab	Phase I	NA

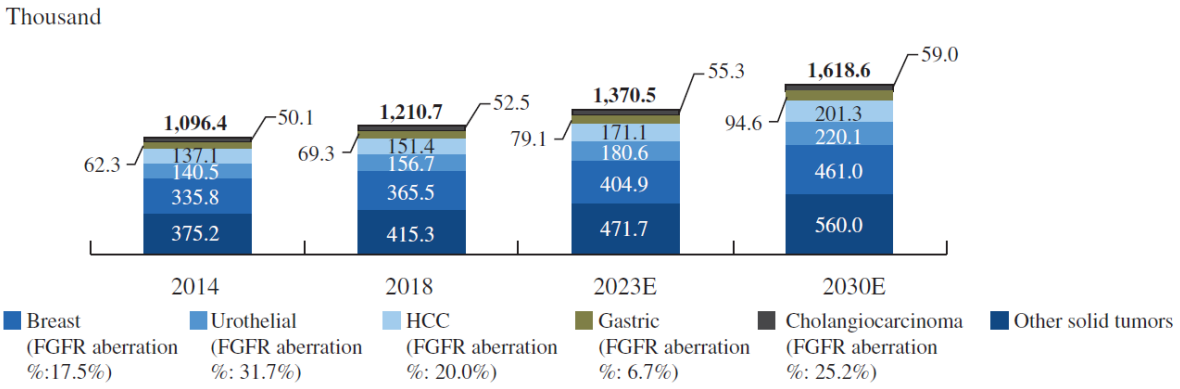
Source: F&S, CMBIS

FGFR inhibitors target various types of cancer

Overview of FGFR inhibitors

Fibroblast growth factor receptors (FGFRs) are transmembrane tyrosine kinase receptors that are highly conserved and widely expressed. FGFR is a family of highly homologous receptors, including FGFR1-4. FGFR aberration is prevalent in solid tumor patients, accounting for approximately 7.1% of all solid tumor patients. The cancers most commonly affected by FGFR aberration were urothelial carcinoma (31.7%), cholangiocarcinoma (25.2%), hepatocellular carcinoma (20.0%), breast carcinoma (17.5%) and gastric carcinoma (6.7%).

Figure 47: Number of New Cases of FGFR Mutation by Cancer Types Globally (2014-2030E)



Source: F&S, CMBIS

Specific FGFR aberrations have been observed more frequently in certain types of carcinoma: FGFR1 amplification is more common in breast, squamous cell lung, ovarian and urothelial cancers, FGFR2 fusions in endometrial and gastric cancers and cholangiocarcinoma, FGFR3 mutations in urothelial cancer, and FGFR4 pathway overactivation in hepatocellular carcinoma.

Pan-FGFR inhibitors

Fibroblast growth factor receptors (FGFRs) are transmembrane tyrosine kinase receptors that are highly conserved and widely expressed. FGFR is a family of highly homologous receptors, including FGFR1-4. FGFR aberration is prevalent in solid tumor patients, accounting for approximately 7.1% of all solid tumor patients. The cancers most commonly affected by FGFR aberration were urothelial carcinoma (31.7%), cholangiocarcinoma (25.2%), hepatocellular carcinoma (20.0%), breast carcinoma (17.5%) and gastric carcinoma (6.7%).

There is evidence that some specific FGFR aberrations may have different sensitivity or resistance to different FGFR inhibitors. As a result, pan-FGFR inhibitors that have the potential to inhibit the activity of FGFR1-4 may cover a wider range of indications as compared to inhibitors targeting a specific FGFR homolog.

As of 31 Dec 2019, there was no marketed pan-FGFR inhibitor in China. In 2019, the US FDA approved the first pan-FGFR inhibitor, Balversa (erdafitinib) to treat patients with metastatic urothelial carcinoma who are susceptible to FGFR3 or FGFR2 genetic alterations. In Apr 2020, the US FDA has approved pemigatinib for treatment of previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or other rearrangement as detected by a FDA-approved test.

Besides ICP-192, there are a few pan-FGFR inhibitors at clinical stage in China, including JNJ-42756493, pemigatinib, EOC317, HZB1006, HMPL-453, infigratinib, BPI-17509, HH-185/3D185, etc.

Figure 48: FGFR1-4 or FGFR1/2/3 inhibitors at clinical stage in China and global

Candidates	Target	Company	UC indication	CAA indication	Other indications
Erdafitinib (JNJ-42756493)	FGFR 1-4	JNJ	Marketed in US (2L) Ph 3 in China	-	solid tumors (Ph 1/2 in US)
Pemigatinib / INCB54828/ INCB-054828	FGFR 1-3	Incyte/ Innvoent	Ph2 in US	Marketed in US (2L) Ph2 in China	MPN (Ph2 in US) solid tumors (Ph 1 in China)
Infigratinib / BGJ398/ NVP-BGJ-398	FGFR 1-3	Novartis/ BridgeBio Pharma	-	Ph 3 in US	solid tumors (Ph 1 in China)
TAS-120	FGFR 1-4	Taiho Oncology	-	Ph 3 in US	-
Rogaratinib (BAY1163877)	FGFR 1-4	Bayer	Ph 2/3 in US Ph 2/3 in China (Terminated)	-	-
ICP-192	**FGFR 1-4**	**InnoCare**	**Ph 1 in China**	**Ph 1 in China**	
EOC317	FGFR 1-4	Bayer/ Edding Pharm	-	-	solid tumors (Ph 1 in China)
HZB1006	FGFR 1-4	Wuxi AppTec/ ZBO	-	-	HCC (Ph1 in China)
ODM-203	FGFR 1-4	Orion	-	-	solid tumors (Ph 1 in US)
PRN1371	FGFR 1-4	Principia Biopharma	-	-	solid tumors (Ph 1 in US)
LY2874455	FGFR 1-4	Eli Lilly	-	-	Advcanced cancers (Ph 1 in US)
HMPL-453	FGFR 1-3	Hutchison Medi Pharma	-	-	solid tumors (Ph 1 in US) solid tumors (Ph 1/2 in China)
3D185 / HH185	FGFR 1-3	HaiHe/ Medicilon	-	-	solid tumors (Ph 1 in China)
BPI-17509	FGFR 1-3	Betta	-	-	solid tumors (Ph 1 in China)
AZD4547	FGFR 1-3	AstraZeneca	-	-	Lung cancer (Ph 2/3 in US)
DEBIO-1347 / CH5183284/ FF-284	FGFR 1-3	Debiopharm/ Roche	-	-	solid tumors (Ph2 in US)
E7090	FGFR 1-3	Eisai	-	-	solid tumors (Ph1 in US) solid tumors (IND in China)

Source: clinicaltrials.gov, chinadrugtrials.org.cn, CMBIS

Urothelial Cancer

Urothelial cancer (UC) is a type of cancer that starts from the urothelial cells on the urinary tract. FGFR aberrations were found in 31.7% of UC cases. Though UC can be treated at an early stage, the treatment method depends on the clinical stage of the cancer and the degree of metastasis.

The global new cases of UC increased from 443,072 in 2014 to 494,454 in 2018, which is projected to reach approximately 570,000 in 2023E at a CAGR of 2.9% from 2018, and to approximately 694,000 in 2030E at a CAGR of 2.9% from 2023E.

In China, the new cases of UC grew from 64,806 in 2014 to 74,043 in 2018, and is expected to reach approximately 86,000 in 2023E at a CAGR of 3.2% from 2018, and to approximately 107,000 in 2030E at a CAGR of 3.0% from 2023E.

UC is the ninth most frequently diagnosed cancer and the seventh leading cause of male cancer incidence in China. UC imposes unique challenges as it is more common in adults aged over 50 years and recurs frequently. Muscle-invasive UC is also more difficult to treat and is associated with lower 5-year survival rate. Current treatment options for muscle-invasive UC include first-line treatment such as cystectomy, radiotherapy, chemotherapy and checkpoint inhibitors such as atezolizumab and pembrolizumab, and second-line treatment such as chemotherapy with gemcitabine and cisplatin. Chemotherapy remains the standard treatment for UC but is limited by its side effects.

Cholangiocarcinoma

Cholangiocarcinoma (CCA) is a type of cancer that forms along the bile ducts, which is an uncommon malignancy with a high rate of fatality. For patients with unresectable tumors or metastatic cancer cells, the median survival length is shorter than 12 months. Extrahepatic cholangiocarcinoma (肝外胆管癌) is one of the major sub-types of CCA, which develops outside the liver, accounting for 90% of CCA.

F&S forecasts that the new cases of CCA increased from 198,792 in 2014 to 208,150 in 2018 globally, and is projected to reach approximately 219,000 in 2023E at a CAGR of 1.1% from 2018 and to reach approximately 234,000 in 2030E at a CAGR of 0.9% from 2023E.

In China, the new cases of CCA reached 87,295 in 2018, which is expected to increase to approximately 94,000 in 2023E at a CAGR of 1.6% from 2018, and to approximately 104,000 in 2030E at a CAGR of 1.4% from 2023E. FGFR aberrations were found in 25.2% of CCA cases.

CCA is a very aggressive type of tumor and considered incurable unless fully resected during early stage through surgery. Stage IIIB – IV CCA is managed through a combination of chemotherapy, radiotherapy and palliative care. The use of chemotherapy drugs is associated with many side-effects, including a decrease in patients' white blood cell counts, strokes and even kidney failure. The efficiency of cytotoxic chemotherapy is also short-lived, and the patients will eventually develop drug resistance. For stage IIIB – IV CCA patients, current treatments have not shown significant improvement in overall survival rate. As a result, new therapies for CCA treatments are being studied, including targeted therapies and precision medicine. Some molecular targets for precision medicine have been identified, including tyrosine kinase receptors, metabolic enzymes, and transcription factors.

FGFR4 inhibitors

Fibroblast growth factor receptor 4 (FGFR4), coupled with its ligand, FGF19, regulates bile acid metabolism in hepatocytes and liver regeneration following injury. Aberrant activation of FGFR4 signaling is a major cause of a subset of hepatocellular carcinoma (HCC) patients. For these patients, FGF19 is overexpressed in hepatocytes, which results in autocrine signaling and tumor growth. FGFR4 inhibitors, by binding to the kinase domain of FGFR4, prevent downstream pathway activation and thereby hinder tumor growth. As of 31 Dec 2019, there was no marketed FGFR4 inhibitors globally.

Figure 49: FGFR4 inhibitors at clinical stage in China and global

Drug candidate	Company	Current NMPA status	Lead Indications (China)	Current Global status (expect China)	Lead Indications (Global)
ICP-105	InnoCare	Phase I	HCC	NA	NA
BLU-554, CS3008	Blueprint Medicines/ CStone	Phase I	HCC	Phase I	HCC
FGF-401	Novartis/ Everest Medicines	NA	NA	Phase I/II	HCC
H3B-6527	H3 Biomedicine	NA	NA	Phase I	Advanced HCC, Intrahepatic Cholangiocarcinoma, Bile Duct Cancer
INCB62079	Incyte	NA	NA	Phase I	HCC, Cholangiocarcinoma, Esophageal Cancer, Ovarian Cancer, Solid Tumors

Source: F&S, CMBIS

Hepatocellular Carcinoma

Liver cancer is the fourth most common cancer and the second leading cause of death from cancer in China in 2018, and hepatocellular carcinoma (HCC) is the most common type of liver cancer. HCC is one of the most lethal cancers, which is ranked as the third-mostcommon cause of cancer-related deaths worldwide.

FGFR4 signaling is aberrantly activated in approximately 20% of HCC patients. Global HCC patients with overexpression of FGF19/FGFR4 reached 151,394 in 2018, and is projected to increase to approximately 201,000 in 2030E, according to F&S.

HCC usually occurs in patients with chronic liver inflammation. The risk of HCC is higher for patients affected by hepatitis B or hepatitis C. As one of the major causes of liver cancer, hepatitis virus infection accounts for 80% of liver cancer and cirrhosis incidence in 2017 in China.

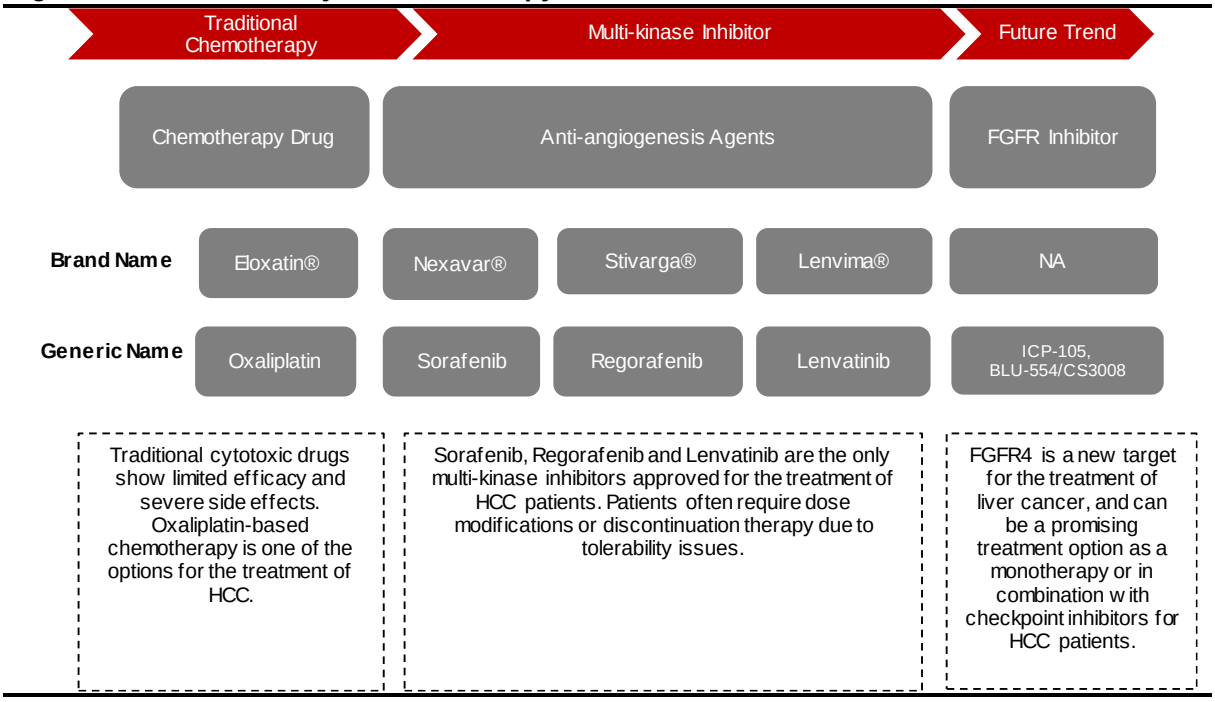
Global new cases of HCC reached 756,972 in 2018, and are expected to increase to approximately 856,000 in 2023E at a CAGR of 2.5% from 2018, and to 1.0 million in 2030E at a CAGR of 2.3% from 2023E. In China, the new cases of HCC reached 360,181 in 2018, and are projected to grow to approximately 407,000 in 2023E at a CAGR of 2.5% from 2018, and to approximately 473,000 in 2030E at a CAGR of 2.2% from 2023E.

As the understanding of liver cancer pathogenesis evolves, the treatment landscape of HCC has advanced significantly, progressing from traditional chemotherapy to multi-kinase inhibitors (including sorafenib and regorafenib), FGFR inhibitors and combination therapies with checkpoint inhibitors. HCC places a substantial economic burden upon a significant number of patients in China, which generates strong market demand for new types of treatment with higher accessibility and enhanced affordability.

Sorafenib, which is approved by the US FDA as a first-line treatment for advanced HCC, is a multi-kinase inhibitor that targets VEGFR and many other kinases and exhibits anti-angiogenic effects. Regorafenib is approved by the US FDA as a second-line treatment for advanced HCC based on data from a pivotal trial showing improved median overall survival of 2.8 months and an 11% ORR in patients with documented disease progression following sorafenib treatment.

In clinical practice, however, patients often require dose modifications or discontinue therapy with sorafenib and regorafenib due to tolerability issues. There is an unmet need for therapies with a favorable risk-benefit profile and the potential to be used alone or in combination with other approved or emerging therapies for advanced HCC.

Figure 50: Evolution of Systematic Therapy for HCC



Source: F&S, CMBIS

Financial analysis

Drugs sales to start from 2021E

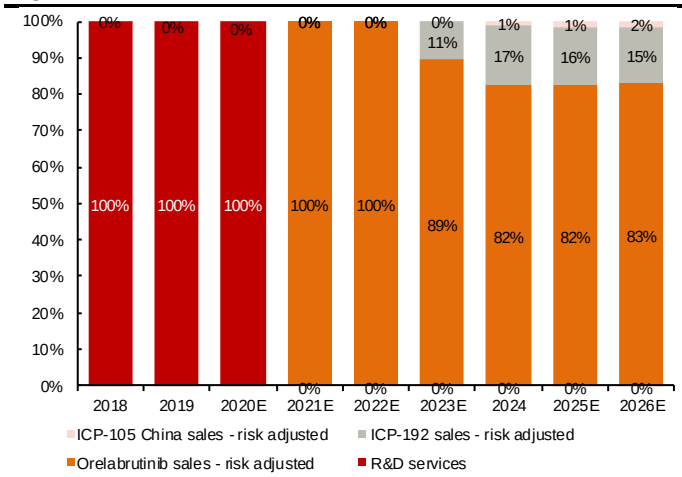
We forecast drug sales to start from 2021E and expect risk-adjusted revenue of RMB106mn/ RMB274mn/ RMB553mn in FY2021E/22E/23E. The most advanced drug is orelabrutinib which may be approved by NMPA in 2H20E. We also forecast ICP-192 and ICP-105 to receive NMPA's approval in 2023E and 2024E, respectively. Considering that InnoCare owns the global rights in these above-mentioned drug candidates, we expect meaningful sales from the US market from 2024E. Furthermore, to factor in the risk in drug development, we apply different probability of success (PoS) to our sales forecasts.

Figure 51: Revenue forecasts (2020-26E)

(YE 31 Dec) (RMB mn)	2020E	2021E	2022E	2023E	2024	2025E	2026E
R&D services	2	0	0	0	0	0	0
YoY	*24%*	*-100%*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
Orelabrutinib sales - risk adjusted	0	106	274	494	861	1,404	2,115
YoY			*157%*	*81%*	*74%*	*63%*	*51%*
Orelabrutinib China sales - risk adjusted	0	106	274	494	794	1,155	1,545
YoY			*157%*	*81%*	*61%*	*45%*	*34%*
Orelabrutinib US sales - risk adjusted	0	0	0	0	67	249	570
YoY						*274%*	*129%*
ICP-192 sales - risk adjusted	0	0	0	59	175	274	390
YoY					*199%*	*57%*	*42%*
ICP-192 China sales - risk adjusted	0	0	0	59	109	157	212
YoY growth					*87%*	*43%*	*35%*
ICP-192 US sales - risk adjusted	0	0	0	0	66	118	178
YoY growth						*79%*	*52%*
ICP-105 China sales - risk adjusted	0	0	0	0	10	24	43
YoY						*150%*	*80%*
Total Revenue	**2**	**106**	**274**	**553**	**1,045**	**1,702**	**2,548**
YoY	*24%*	*5220%*	*157%*	*102%*	*89%*	*63%*	*50%*

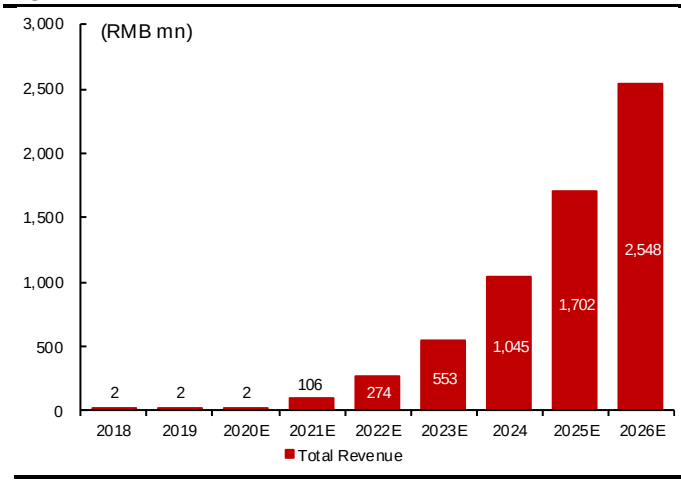
Source: Company data, CMBIS estimates

Figure 52: Revenue breakdown



Source: Company data, CMBIS estimates

Figure 53: Total revenue forecasts



Source: Company data, CMBIS estimates

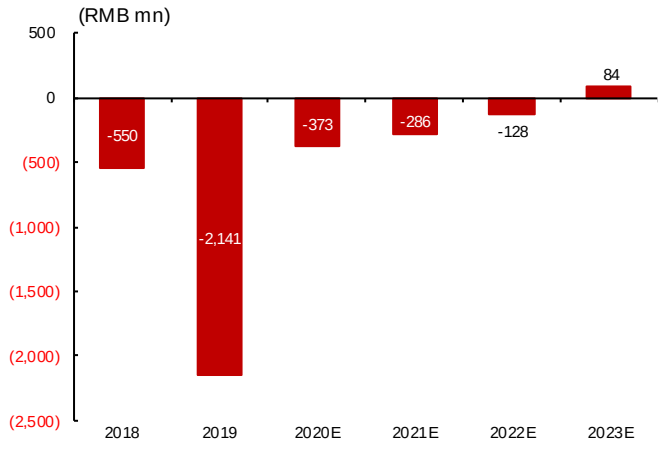
Innocare recorded net losses of RMB342mn/ RMB550mn/RMB2,141mn in FY17A/18A/19A. We expect it to continue incur net losses of RMB373mn/ RMB286mn/ RMB128mn in FY20E/21E/22E and expect net profit to breakeven in 2023E.

Figure 54: P&L forecasts

(YE 31 Dec) (RMB mn)	2018	2019	2020E	2021E	2022E	2023E
Revenue	**2**	**1**	**2**	**106**	**274**	**553**
YoY	*N/A*	*-23%*	*60%*	*5220%*	*157%*	*102%*
Cost of sales	0	0	(0)	(19)	(44)	(83)
% of revenue	*0%*	*0%*	*-20%*	*-18%*	*-16%*	*-15%*
Gross profit	**2**	**1**	**2**	**87**	**230**	**470**
GPM	*100%*	*100%*	*80%*	*82%*	*84%*	*85%*
Other income and gains	31	104	186	206	130	116
% of revenue	*1942%*	*8376%*	*9291%*	*194%*	*48%*	*21%*
Selling and distribution expenses	(1)	(3)	(80)	(120)	(137)	(155)
% of revenue	*-35%*	*-277%*	*-4000%*	*-113%*	*-50%*	*-28%*
Research and development costs	(150)	(213)	(350)	(350)	(219)	(221)
% of revenue	*-9259%*	*-17091%*	*-17500%*	*-329%*	*-80%*	*-40%*
Administrative expenses	(18)	(64)	(80)	(60)	(82)	(111)
% of revenue	*-1084%*	*-5102%*	*-4000%*	*-56%*	*-30%*	*-20%*
Other expenses	(28)	(160)	(50)	(50)	(50)	0
% of revenue	*-1730%*	*-12823%*	*-2500%*	*-47%*	*-18%*	*0%*
Profit from operations	(163)	(334)	(373)	(286)	(128)	99
% of revenue	*-10066%*	*-26818%*	*-18629%*	*-269%*	*-47%*	*18%*
Fair value changes of convertible redeemable preferred shares	(388)	(1,814)	0	0	0	0
% of revenue	*-23983%*	*-145471%*	*0%*	*0%*	*0%*	*0%*
Finance costs	(3)	(2)	0	0	0	0
% of revenue	*-213%*	*-154%*	*0%*	*0%*	*0%*	*0%*
Profit before taxation	(554)	(2,150)	(373)	(286)	(128)	99
% of revenue	*-34262%*	*-172442%*	*-18629%*	*-269%*	*-47%*	*18%*
Income tax expense	0	0	0	0	0	(15)
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*-15%*
Profit (loss) for the year	**(554)**	**(2,150)**	**(373)**	**(286)**	**(128)**	**84**
Non-controlling interests	4	9	0	0	0	0
Profit (loss) attributable to shareholders	**(550)**	**(2,141)**	**(373)**	**(286)**	**(128)**	**84**
NPM	*N/A*	*N/A*	*N/A*	*-269%*	*-47%*	*15%*

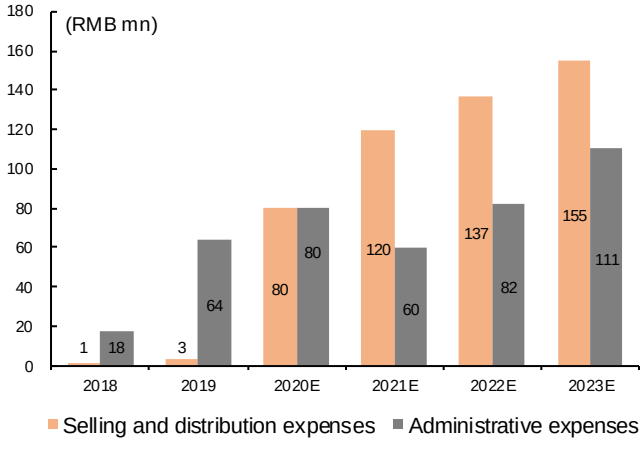
Source: Company data, CMBIS estimates

Figure 55: Net profit forecasts



Source: Company data, CMBIS estimates

Figure 56: SG&A expenses forecasts

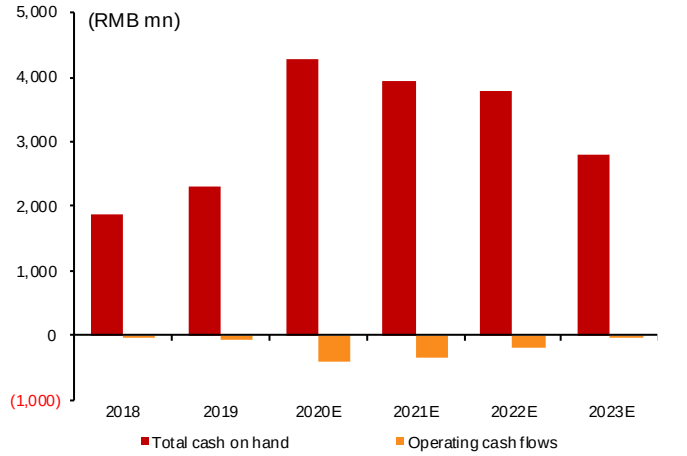


Source: Company data, CMBIS estimates

S&G spending to increase. We forecast selling expenses to be RMB80mn/ RMB120mn/ RMB137mn in FY20E/21E/22E. We expect admin expenses to reach RMB80mn/ RMB60mn/ RMB82mn in FY20E/21E/22E, including listing expenses.

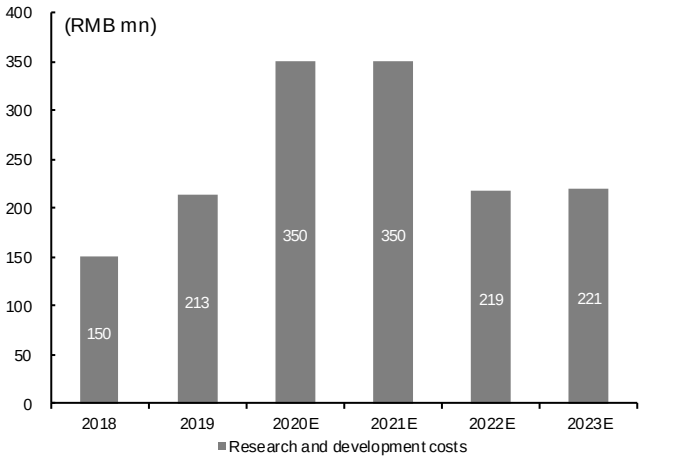
R&D spending to increase. We forecast R&D cost to climb from RMB150mn/ RMB213mn in FY18A/19A to RMB350mn/ RMB350mn/ RMB219mn in FY20E/21E/22E, mainly due to initiation of new clinical trials and progress of existing clinical trials.

Figure 57: Cash on hand and operating cash flows



Source: Company data, CMBIS estimates

Figure 58: R&D expenses



Source: Company data, CMBIS estimates

Financial Statments

Income statement

YE 31 Dec (RMB mn)	FY18A	FY19A	FY20E	FY21E	FY22E
Revenue	**2**	**1**	**2**	**106**	**274**
Orelabrutinib - risk adjusted	0	0	0	106	274
ICP-192 - risk adjusted	0	0	0	0	0
ICP-105 - risk adjusted	0	0	0	0	0
R&D services	2	2	2	0	0
Cost of sales	0	0	(0)	(19)	(44)
Gross profit	**2**	**1**	**2**	**87**	**230**
Other income	31	104	186	206	130
Selling & distribution expenses	(1)	(3)	(80)	(120)	(137)
R&D expenses	(150)	(213)	(350)	(350)	(219)
Administrative expenses	(18)	(64)	(80)	(60)	(82)
Other expenses	(28)	(160)	(50)	(50)	(50)
Operating profit (loss)	**(163)**	**(334)**	**(373)**	**(286)**	**(128)**
Fair value changes of convertible redeemable preferred shares	(388)	(1,814)	0	0	0
Finance costs	(3)	(2)	0	0	0
Pre-tax profit (loss)	**(554)**	**(2,150)**	**(373)**	**(286)**	**(128)**
Income tax	0	0	0	0	0
Minority interests	4	9	0	0	0
Attributable net profit (loss)	**(550)**	**(2,141)**	**(373)**	**(286)**	**(128)**

Cash flow summary

YE 31 Dec (RMB mn)	FY18A	FY19A	FY20E	FY21E	FY22E
Profit before tax	**(554)**	**(2,150)**	**(373)**	**(286)**	**(128)**
Depreciation and amortization	5	9	4	4	4
Change in working capital	47	21	(13)	(12)	(20)
Others	484	2,040	(36)	(56)	(50)
Net income tax paid	0	0	0	0	0
Net operating cash flow	**(18)**	**(80)**	**(418)**	**(351)**	**(194)**
Interest received	0	0	82	103	96
Purchases of PP&E	(4)	(45)	(250)	(100)	(50)
Purchases of other intangible assets	(16)	(0)	0	0	0
Net purchases of financial assets	(160)	85	0	0	0
Others	(708)	8	4	4	4
Net investing cash flow	**(888)**	**47**	**(164)**	**6**	**50**
Net proceeds from shares issued	1,165	422	2,563	0	0
Bank borrowing, net	873	(50)	0	0	0
Acquisition of non-controlling interests	0	0	0	0	0
Others	63	(9)	0	0	0
Net financing cash flow	**2,101**	**363**	**2,563**	**0**	**0**
FX changes	13	18	0	0	0
Net change in cash	1,196	331	1,981	(344)	(143)
Cash at the beginning	37	1,245	2,292	4,273	3,929
Cash at the end	**1,245**	**1,594**	**4,273**	**3,929**	**3,785**

Balance sheet

YE 31 Dec (RMB mn)	FY18A	FY19A	FY20E	FY21E	FY22E
Non-current assets	**138**	**207**	**453**	**549**	**595**
PP&E	5	48	297	396	444
Goodwill	3	3	3	3	3
Other intangible assets	37	37	37	36	36
Right-of-use assets	13	86	84	82	80
Investment in JVs	1	1	1	1	1
Other non-current assets	78	31	31	31	31
Current assets	**2,064**	**2,409**	**4,354**	**4,027**	**3,912**
Inventories	0	0	0	4	8
Trade receivables	0	0	0	12	30
Prepayments, other receivables & other assets	18	37	0	3	7
Cash and cash equivalents	1,877	2,292	4,273	3,929	3,785
Others	169	80	80	80	80
Current liabilities	**72**	**66**	**16**	**22**	**30**
Trade payables	2	8	0	5	12
Loans and borrowings	50	0	0	0	0
Other payables and accruals	5	42	0	1	2
Lease liabilities	5	6	6	6	6
Loans from a related party	9	9	9	9	9
Others	0	1	1	1	1
Non-current liabilities	**2,967**	**5,498**	**5,548**	**5,598**	**5,648**
Convertible redeemable preferred shares	1,935	4,214	4,214	4,214	4,214
Convertible loan	957	1,117	1,167	1,217	1,267
Loans and borrowings	0	0	0	0	0
Others	75	167	167	167	167
Total net assets	**(838)**	**(2,948)**	**(757)**	**(1,044)**	**(1,172)**
Minority interest	66	57	57	57	57
Shareholders' equity	**(904)**	**(3,005)**	**(814)**	**(1,101)**	**(1,229)**

Key ratios

YE 31 Dec	FY18A	FY19A	FY20E	FY21E	FY22E
Sales mix (%)					
Orelabrutinib - risk adjusted	0	0	0	100	100
ICP-192 - risk adjusted	0	0	0	0	0
ICP-105 - risk adjusted	0	0	0	0	0
R&D services	100	100	100	0	0
Total	100	100	100	100	100
Profit & loss ratios (%)					
Gross margin	100	100	80	82	84
EBITDA margin	NA	NA	NA	NA	NA
Pre-tax margin	NA	NA	NA	NA	NA
Net margin	NA	NA	NA	NA	NA
Effective tax rate	0	0	0	0	0
Balance sheet ratios					
Current ratio (x)	29	37	271	181	129
Trade receivables turnover days	NA	NA	40	40	40
Trade payables turnover days	NA	NA	100	100	100
Net debt to total equity ratio (%)	Net cash	Net cash	Net cash	Net cash	Net cash
Returns (%)					
ROE	NA	NA	NA	NA	NA
ROA	-25	-82	-8	-6	-3

Source: Company data, CMBIS estimates

Valuation

TP HK$16.21 based on DCF model

We expect Innocare to commercialize the first product, Orelabrutinib, in 2H20E and its future cash flows will rely on the successful commercialization of pipeline drugs. We see DCF as appropriate in valuing the Company. We derive a TP of HK$16.21 based on an 11-year DCF valuation (WACC: 9.7%, terminal growth rate: 5.0%).

Figure 59: Base case risk-adjusted DCF valuation

DCF Valuation (in Rmb mn)	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
EBIT	(455)	(389)	(224)	17	337	766	1,333	1,602	1,802	1,940	2,051
Tax rate	0%	0%	0%	15%	15%	15%	15%	15%	15%	15%	15%
EBIT*(1-tax rate)	(455)	(389)	(224)	15	286	651	1,133	1,362	1,531	1,649	1,743
+ D&A	4	4	4	4	4	4	4	4	4	4	4
- Change in working capital	(13)	(12)	(20)	(33)	(59)	(80)	(104)	(52)	(37)	(26)	(21)
- Capex	(250)	(100)	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
FCFF	**(714)**	**(497)**	**(290)**	**(64)**	**182**	**525**	**983**	**1,263**	**1,448**	**1,577**	**1,676**
Terminal value											**37,646**
FCF + Terminal value	(714)	(497)	(290)	(64)	182	525	983	1,263	1,448	1,577	39,322

Present value of enterprise (RMB mn)	15,701
Net Debt	(3,106)
Minorities	57
Equity value (RMB mn)	18,750
Equity value (HK$ mn)	20,903
# of shares outstanding	1,289,165,235
TP per share (HK$)	**16.21**

Terminal growth rate	**5.0%**
WACC	**9.7%**
Cost of Equity	12.0%
Cost of Debt	5.0%
Equity Beta	0.9
Risk Free Rate	3.0%
Market Risk Premium	10.0%
Target Debt to Asset ratio	30.0%
Effective Corporate Tax Rate	15.0%

Source: CMBIS estimates

Investment risks

Having incurred net losses in the past and will continue to incur losses for the foreseeable future

Investment in pharmaceutical drug development is highly speculative. It entails substantial upfront capital expenditures and significant risk that a drug candidate will fail to gain regulatory approval or become commercially viable. InnoCare incurred losses in each period since its inception. In 2017 and 2018 and 9M19, InnoCare had a loss for the year/period of RMB341.7mn, RMB554.0mn and RMB653.2mn, respectively. If InnoCare is unable to maintain adequate working capital, it may default on payment obligations and may not be able to meet capital expenditure requirements.

Fail in obtaining regulatory approval for drug candidates

InnoCare's business will depend on the successful development, regulatory approval and commercialization of its drug candidates for the treatment of patients with cancer or autoimmune diseases, all of which are still in pre-clinical or clinical development. If InnoCare is unable to successfully complete clinical development, obtain regulatory approval and commercialize its drug candidates, or experience significant delays in doing so, its business will be materially harmed.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. If clinical trials of InnoCare's drug candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, the Company may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of drug candidates.

Competition from peers with more competing and successful drugs

The development and commercialization of new drugs is highly competitive. InnoCare faces competition from major pharmaceutical companies, specialty pharmaceutical companies and biopharmaceutical companies worldwide. InnoCare will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

Fail in protecting intellectual property rights throughout the world

If InnoCare is unable to obtain and maintain patent protection for its drug candidates and other intellectual property, or if the scope of such intellectual property rights obtained is not sufficiently broad, third parties could develop and commercialize products and technologies similar or identical to the Company's and compete directly against InnoCare, and the Company's ability to successfully commercialize any product or technology may be adversely affected.

Appendix: Company Profile

Figure 60: Management profile (as of Mar 2020)

Name	Age	Date of Joining	Date of Appointment	Position	Roles and Responsibilities
Dr. Jisong Cui	57	3 Nov 2015	3 Nov 2015	Executive Director, Chairperson and Chief Executive Officer	Overall strategic planning, business direction and operational management
Dr. Renbin Zhao	51	3 Nov 2015	3 Nov 2015	Executive Director	Overall strategic planning, business direction and operational management
Dr. Yigong Shi	52	3 Nov 2015	28 Nov 2018	Non-executive Director	Participating in decision-making in respect of major matters such as strategy
Dr. Zhixin Rick Xu	64	12 Jun 2018	12 Jun 2018	Chief Medical Officer	Leading clinical development and participating in overall strategic planning and business direction
Mr. Shaojing Tong	48	3 Jun 2019	3 Jun 2019	Chief Financial Officer	Financial and strategic planning, financing and investor relation activities
Dr. Xiangyang Chen	53	1 Oct 2015	1 Oct 2019	Chief Technology Officer	Drug discovery and development therapeutic areas of (immuno) oncology and autoimmune diseases

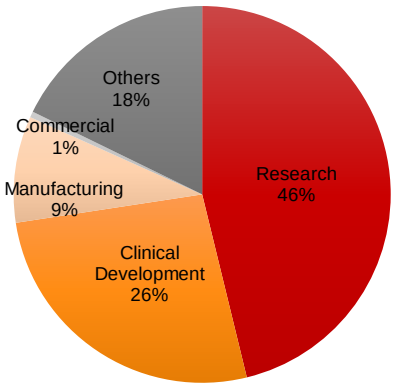
Source: Company data

Figure 61: Employee structure (as of Mar 2020)

Function	# of employees	% of Total
Research	97	44%
Clinical Development	60	27%
Manufacturing	21	10%
Commercial	7	3%
Others	36	16%
Total	221	100%

Source: Company data

Figure 62: Employee number split (as of Mar 2020)



Source: Company data

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