

# Innovent Biologics (1801 HK)

## Growing into a global biopharma company

- Rich innovative drug pipelines.** Innovent is a leading integrated biopharma company with comprehensive innovative pipelines including monoclonal antibodies (mAbs), bispecific antibodies (bsAbs), small molecules and CAR-T therapies, covering oncology, autoimmune and metabolic diseases. Besides five marketed products (sintilimab, three biosimilars and pemigatinib), Innovent has six innovative drugs in pivotal clinical stage, including IBI306 (PCSK9 antibody), IBI310 (CTLA-4 antibody), IBI376 (PI3K $\delta$  inhibitor), IBI326 (BCMA-CART), talrectinib (ROS1/NTRK inhibitor) and HQP1351 (olverembatinib, third-generation BCR-ABL TKI). In addition, Innovent has established a comprehensive innovative portfolio covering next-generation immuno-oncology (I/O) targets, including CD47/SIRP $\alpha$ , TIGIT, LAG3, 4-1BB, etc. It's worth noting that Innovent is an early mover in CD47-SIRP $\alpha$  pathway with three assets under development, including clinical-stage IBI188 (a CD47 antibody) and IBI322 (a PD-L1/CD47 bispecific antibody), and preclinical stage IBI397 (AL008, a SIRP $\alpha$  antibody).
- Tyvyt being an early mover in large indications.** After the approval for r/r-cHL in Dec 2018, Tyvyt has been approved by the NMPA for 1L ns-NSCLC, 1L s-NSCLC and 1L HCC in 2021. These three large indications may be included in the NRDLD during this year's negotiation. Innovent has also filed sNDA for Tyvyt for 2L s-NSCLC. With 7 clinical trials in phase 3 stage, we expect Tyvyt to further expand its labels in China to cover all major indications. Moreover, with the first BLA for 1L ns-NSCLC accepted by the US FDA in May 2021, Tyvyt will penetrate into overseas market.
- Proven commercial capability.** As of end-2020, Innovent had 1,300 commercialization employees which mainly focus on oncology area. With a sizable commercial team, Innovent has successfully promoted Tyvyt in Chinese market and achieved RMB2.29bn sales from Tyvyt in 2020, up 125% YoY. In 2020, Innovent received approvals for three biosimilars (IBI301, IBI303 and IBI305) from the NMPA. In Jun 2021, the Company received approval for IBI375 (Pemigatinib) by TFDA in Taiwan. With a comprehensive commercial product portfolio, Innovent will further strengthen its commercial capability, in our view.
- Initiate at BUY with TP of HK\$120.91.** We expect Tyvyt, Byvasda (bevacizumab biosimilar), Sulinno (adalimumab biosimilar) and Halpryza (rituximab biosimilar) will contribute the majority of revenue in the near future. We expect the Company to commercialize IBI375, IBI306, IBI310 and IBI376 in China during 2022-23E. To factor in the potential contribution from innovative drug pipelines, we use DCF model in valuing the Company. We derive our target price of HK\$120.91 based on a 15-year DCF valuation (WACC: 9.05%, terminal growth rate: 4.0%).

### Earnings Summary

(YE 31 Dec)	FY19A	FY20A	FY21E	FY22E	FY23E
Revenue (RMB mn)	1,048	3,844	3,579	5,747	8,192
YoY growth (%)	N/A	267%	-7%	61%	43%
Net loss (RMB mn)	(1,720)	(998)	(1,399)	(857)	(125)
EPS (RMB)	(1.46)	(0.74)	(0.96)	(0.59)	(0.09)
Consensus EPS (RMB)	N/A	N/A	(0.82)	(0.18)	0.43
R&D expenses (RMB mn)	(1,295)	(1,851)	(2,200)	(2,500)	(2,800)
Capex (RMB mn)	(366)	(489)	(200)	(200)	(200)

Source: Company data, CMBIS estimates

### BUY (Initiation)

Target Price	HK\$120.91
Up/Downside	+43.00%
Current Price	HK\$84.55

### China Healthcare Sector

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Mkt. Cap. (HK\$ mn)	123,312
Avg. 3mths t/o (HK\$ mn)	497.71
52W High/Low (HK\$)	107.1/45.6
Total Issued Shares (mn)	2,609

Source: Bloomberg

### Shareholding Structure

Temasek Holdings	8.23%
Yu De-Chao Michael	8.21%
Citigroup	5.63%
Eight Roads Investments	5.20%
Brown Brothers Harriman & Co.	5.02%
Free float	67.71%

Source: HKEx, Bloomberg

### Share performance

	Absolute	Relative
1-mth	0.6%	6.3%
3-mth	6.9%	14.2%
6-mth	-15.9%	-7.6%

Source: Bloomberg

### 12-mth price performance



Source: Bloomberg

**Auditor: Deloitte**  
**Web-site: www.innoventbio.cn**

Please cast your valuable vote for CMBIS research team in the 2021 Asiamoney Brokers Poll:  
<https://euromoney.com/brokers>

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## Investment Thesis

### Rich and highly innovative product pipelines

Leveraging strong R&D platforms, Innovent has built a robust pipeline of 25 clinical-stage assets in the fields of cancer, metabolic, autoimmune diseases and other major therapeutic areas, with 5 products, including Tyvyt (sintilimab injection, PD-1 antibody), Byvasda (bevacizumab injection), Sulinno (adalimumab injection) and Halpzyza (rituximab injection) approved by the National Medicine Products Administration (NMPA) for marketing in Mainland China and IBI375 (Pemigatinib, FGFR1/2/3 inhibitor) approved by Taiwan Food and Drug Administration (TFDA), 6 assets in pivotal clinical trials, and additional 14 molecules in early clinical stage.

Besides the five approved drugs mentioned above, Innovent has six innovative drugs in registrational clinical stage, including IBI306 (PCSK9 antibody), IBI310 (CTLA-4 antibody), IBI376 (PI3K $\delta$  inhibitor), IBI326 (BCMA-CART), taletrectinib (ROS1/NTRK inhibitor), and HQP1351 (olverembatinib, third-generation BCR-ABL TKI).

In addition, Innovent has built up a comprehensive innovative portfolio covering next-generation immuno-oncology (I/O) targets, including CD47/ SIRP $\alpha$ , TIGIT, LAG3, 4-1BB, etc. It's worth noting that Innovent is an early mover in CD47-SIRP $\alpha$  pathway with three assets under development, including clinical-stage IBI188 (a CD47 antibody) and IBI322 (a PD-L1/CD47 bispecific antibody), and preclinical stage IBI397 (AL008, a SIRP $\alpha$  antibody).

Tyvyt is the Company's major source of revenue during recent years. Tyvyt was approved by the NMPA in Dec 2018, and came to the market in 2019. Tyvyt was the first PD-1 inhibitor included in the NRDL in 2019 in China. Subsequently, Tyvyt was approved by the NMPA for first-line treatment of non-squamous non-small cell lung cancer (1L ns-NSCLC), first-line treatment of squamous non-small cell lung cancer (1L s-NSCLC) and first-line treatment of Hepatocellular Carcinoma (1L HCC) in 2021. In May 2021, the US FDA accepted for review a BLA for Tyvyt in combination with pemetrexed and platinum chemotherapy for 1L ns-NSCLC. We expect Tyvyt to realize RMB5,974mn peak sales in China and US\$1,565mn peak sales in overseas markets.

### Comprehensive R&D platform

Led by Dr. Yong Jun Liu (刘勇军), Innovent has approximately 950 R&D staff as of end-2020, covering functions such as drug discovery, translation medicine, product development, BD, IP, etc.

Innovent has developed state-of-the-art technology platforms in goal for potentially first-in-class drugs, including 1) a complete discovery platform for therapeutic monoclonal antibodies covering the various stages from antibody generation, antibody engineering, in vitro potency, in vivo efficacy to developed capabilities; 2) a comprehensive clinical trial operating platform for developing innovative drugs covering the full process for all study stages from Phase I through Phase III; 3) a complete and product-oriented platform that covers new drug lead candidates' entire development life cycle.

With steadily growing R&D expense, Innovent has become one of the leading R&D driven biopharmaceutical companies among domestic peers. In addition, Innovent is also building a laboratory in the US for further expansion and development of innovative candidates in overseas market.

### Sufficient manufacturing capacity

Innovent has built a high-end biopharmaceutical manufacturing facility in compliance with the current Good Manufacturing Practices (GMP) standards of the NMPA, FDA and EMA. In 2020, Innovent has expanded manufacturing capacity from 5,000L to a total of 24,000L to support the production needs for commercial product and clinical stage candidates in the pipeline. In 2020, the Company started the

construction of a new manufacturing facility (the M2 site) in Suzhou that is designed to house additional twelve 3,000L production capacities, which once completed, will expand the Company's production capacity to a total of 60,000L. Innovent plans to finish the M2 facility construction by the end of 2021.

### Wide global partnership enhances the R&D and commercialization capability

Innovent has strong track record in BD deals, including both in-licensing and out-licensing cooperation. Through in-license deals with Adimab, Eli Lilly, Hanmi, Incyte, Roche, Alector, AnHeart and Ascentage, Innovent has significantly expanded its R&D pipelines, which also proves the acknowledge of Innovent's capacity in R&D and commercialization by both MNC and biotech companies.

After co-developing and co-promoting Tyvyt with Eli Lilly in China, Innovent expanded its strategic collaboration with Eli Lilly in Aug 2020. Eli Lilly obtained an exclusive license for Tyvyt for geographies outside of China and plans to pursue registration of Tyvyt in the US and other markets. In May 2021, Eli Lilly submitted a BLA to the US FDA for Tyvyt for treatment of 1L ns-NSCLC.

### Proven commercial capability

As of end-2020, Innovent had 1,300 commercialization employees which mainly focus on oncology area. With a sizable commercial team, Innovent has successfully promoted Tyvyt in Chinese market and achieved RMB2.29bn sales from Tyvyt in 2020, up 125% YoY.

In 2020, Innovent received approvals for three biosimilars (IBI301, IBI303 and IBI305). In Jun 2021, the Company received approval for IBI375 (Pemigatinib, FGFR1/2/3 inhibitor) by TFDA in Taiwan. With more comprehensive commercial product portfolio, Innovent will further strengthen its commercial capability, in our view.

### Initiate at BUY with TP of HK\$120.91

We expect Tyvyt, Byvasda (bevacizumab biosimilar), Sulinno (adalimumab biosimilar) and Halpryza (rituximab biosimilar) will contribute the majority of revenue in the near future. We expect the Company to commercialize IBI375, IBI306, IBI310 and IBI376 in China during 2022-23E. To factor in the potential contribution from innovative drug pipelines, we use DCF model in valuing the Company. We derive our target price of HK\$120.91 based on a 15-year DCF valuation (WACC: 9.05%, terminal growth rate: 4.0%).

### Investment risks

- 1) Clinical risks: Any failure on Innovent's pipeline's ongoing trials on different indications might induce lead to failure on approval.
- 2) Regulatory approval risks: The Company's ability to generate revenue will depend primarily on the successful regulatory approvals of its pipeline assets.
- 3) Competition risk: The Company faces intense competition from competitors' PD-1/L1, both in mono therapies and combo therapies.

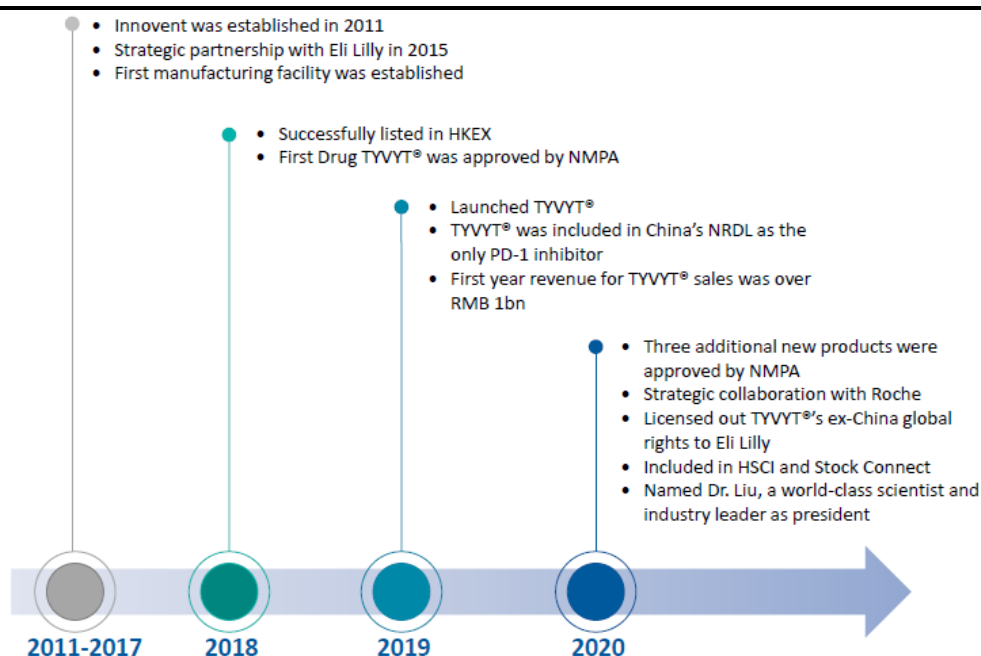
## A biopharmaceutical pioneer in China

Established in 2011, Innovent is committed to developing, manufacturing and commercializing high quality innovative medicines for the treatment of major diseases such as cancer. Innovent was listed on the HKEX in Oct 2018. In Jun 2020, the “B” marker was removed from the Company’s stock name, which marketed Innovent transforming from a biotech company into a biopharma company.

Innovent has developed a rich pipeline covering a variety of novel and validated therapeutic targets and drug modalities (including monoclonal antibodies, bispecific antibodies, fusion proteins, CAR-T and small molecules), spanning multiple major therapeutic areas including oncology, metabolic, immunology and ophthalmology diseases, and promising tremendous clinical and commercial potential as monotherapies or combination therapies to address unmet medical needs.

Innovent aims to further develop into a global leading biopharma company. In Oct 2020, the Company appointed Dr. Yong Jun Liu, a renowned world class scientist and successful leader in biopharmaceutical industry as president, responsible for the Company’s global R&D, portfolio strategy, business development as well as international operation.

**Figure 1: Milestones of Innovent**



Source: Company data, CMBIS

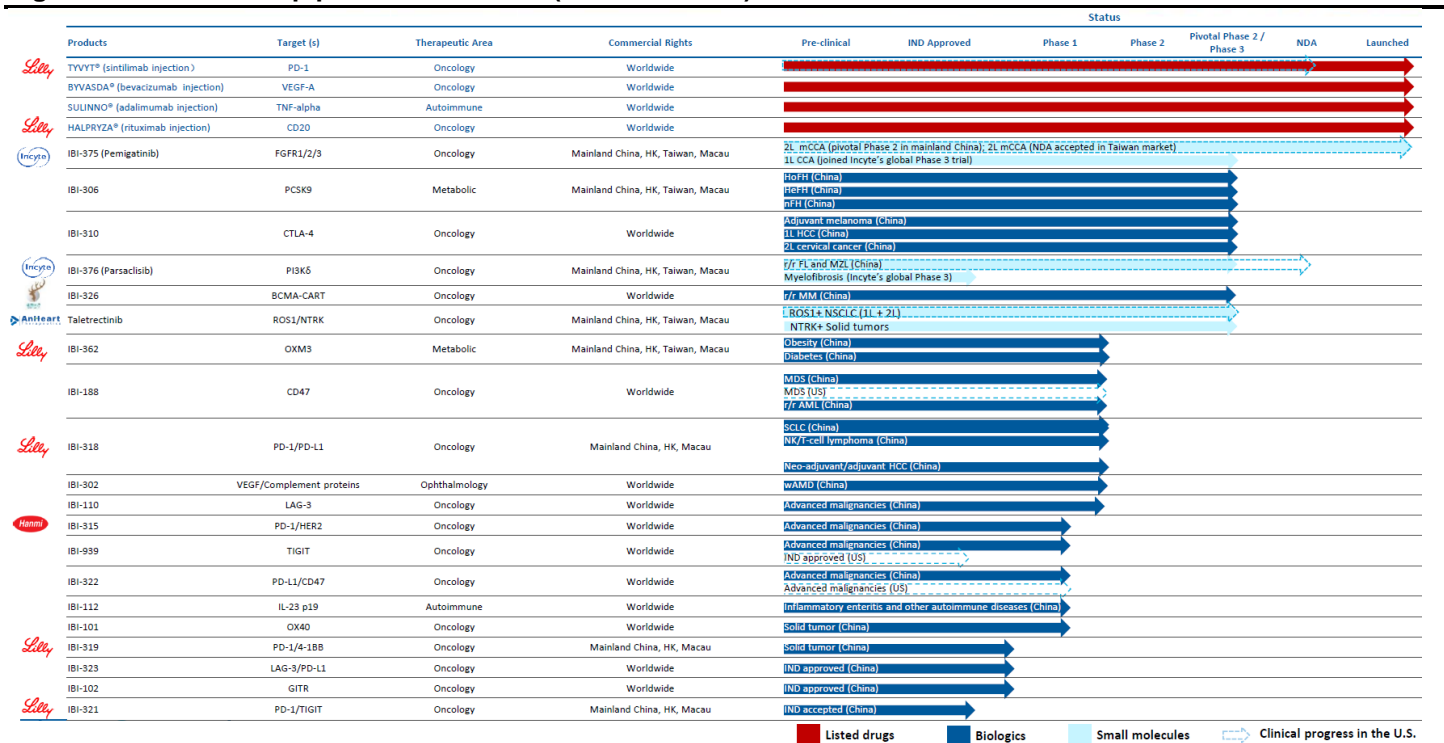
## Rich product portfolio and highly innovative pipelines

Leveraging strong R&D platforms, Innovent has built a robust pipeline of 25 clinical-stage assets in the fields of cancer, metabolic, autoimmune diseases and other major therapeutic areas, with 5 products, including Tyvyt (Sintilimab injection, PD-1 antibody), Byvasda (bevacizumab injection), Sulinno (adalimumab injection) and Halpryza (rituximab injection) approved by the NMPA for marketing in Mainland China and IBI375 (Pemigatinib, FGFR1/2/3 inhibitor) approved by TFDA in Taiwan, 6 assets in pivotal clinical trials, and additional 14 molecules in early clinical stage.

Tyvyt was approved by the NMPA in Dec 2018, and came to the market in 2019. Tyvyt was the first PD-1 inhibitor included in the NRDL in 2019 in China. Subsequently, Tyvyt was approved by the NMPA for 1L ns-NSCLC, 1L s-NSCLC and 1L HCC in 2021. In May 2021, the US FDA accepted for review a BLA for Tyvyt in combination with pemetrexed and platinum chemotherapy for 1L ns-NSCLC.

Innovent also has successfully marketed three biosimilar products. Byvasda (bevacizumab biosimilar) is a recombinant humanized anti-VEGF monoclonal antibody drug, and was firstly approved by the NMPA for treatment of advanced NSCLC and metastatic colorectal cancer in Jun 2020. In Dec 2020, Byvasda was granted new indication approval by the NMPA for adult recurrent glioblastoma. Sulinno (adalimumab biosimilar) is a recombinant human anti-TNF- $\alpha$  monoclonal antibody was firstly approved by the NMPA for the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriasis in Sep 2020. After that, Sulinno was granted new indications approval by the NMPA for the treatment of polyarticular juvenile idiopathic arthritis, pediatric plaque psoriasis and non-infectious uveitis. Halpryza (rituximab biosimilar) is a monoclonal antibody that targets the CD20 antigen expressed on the surface of B-lymphocytes, and was approved by NMPA in Sep 2020 for patients with DLBCL, FL and CLL.

Figure 2: Robust R&D pipeline of Innovent (as of Jun 2021)



Source: Company data, CMBIS

Besides the five approved drugs mentioned above, Innovent has six innovative drugs in phase III or registrational clinical stage, including IBI306 (PCSK9 antibody), IBI310 (CTLA-4 antibody), IBI376 (PI3K $\delta$  inhibitor), IBI326 (BCMA-CART), taletrectinib (ROS1/NTRK inhibitor) and HQP1351 (olverembatinib, third-generation BCR-ABL TKI).

IBI375 (pemigatinib, Pemazyre) is a kinase inhibitor of FGFR isoforms 1, 2 and 3. Pemazyre was approved by the US FDA in Apr 2020 for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or other rearrangement as detected by an FDA-approved test, which made it the first and only FDA-approved treatment for this indication. Pemigatinib obtained approval by TFDA for 2L mCCA in Jun 2021. In Mainland China, in Jul 2021, the NMPA has accepted the NDA for pemigatinib for the treatment of 2L mCCA patients with FGFR2 fusion or rearrangement.

IBI306 is a recombinant fully human anti-proprotein convertase substilisin/kexin type 9 (PCSK9) monoclonal antibody for the treatment of hypercholesterolemia. In 2020, Innovent has completed the patient enrolment for a Phase 3 clinical trial in China for heterozygous familial hypercholesterolemia (HeFH). In Jan 2021, Innovent has completed the patient enrolment for a Phase 3 clinical trial in China

evaluating IBI306 for the treatment of non-familial hypercholesterolemia. IBI306 is also assessed in a pivotal Phase 2 trial for homozygous familial hypercholesterolemia.

IBI310 is one of the leading CTLA-4 molecules under clinical trials in China. Currently, IBI310 in combination with Tyvyt is assessed in a phase III trial as an adjuvant treating melanoma and in a phase II trial for second-line or above cervical cancer. In Jan 2021, Innovent started the patient enrolment for the Phase 3 clinical study in China evaluating IBI310 in combination with Tyvyt for first-line advanced HCC. BMS's combination of Opdivo and Yervoy has proven the concept of synergetic effect by PD-1 and CTLA-4, which has been approved for metastatic melanoma regardless of BRAF status, and poor-risk advanced RCC by the US FDA, and has been trialed in many indications, including NSCLC, GC, EC, HCC and CRC.

IBI376 (parsaclisib, PI3K $\delta$  inhibitor) is a highly selective, potent and differentiated PI3K $\delta$  inhibitor designed to reduce hepatotoxicity, which is being assessed in a pivotal phase II study, evaluating its efficacy and safety in patients with relapsed or refractory follicular lymphoma (r/r FL), and results were published in ASH 2020. IBI376 shows the best-in-class potential in multiple B cell malignancies. We expect Innovent to submit NDA to the NMPA for IBI376 for r/r FL by early 2022E.

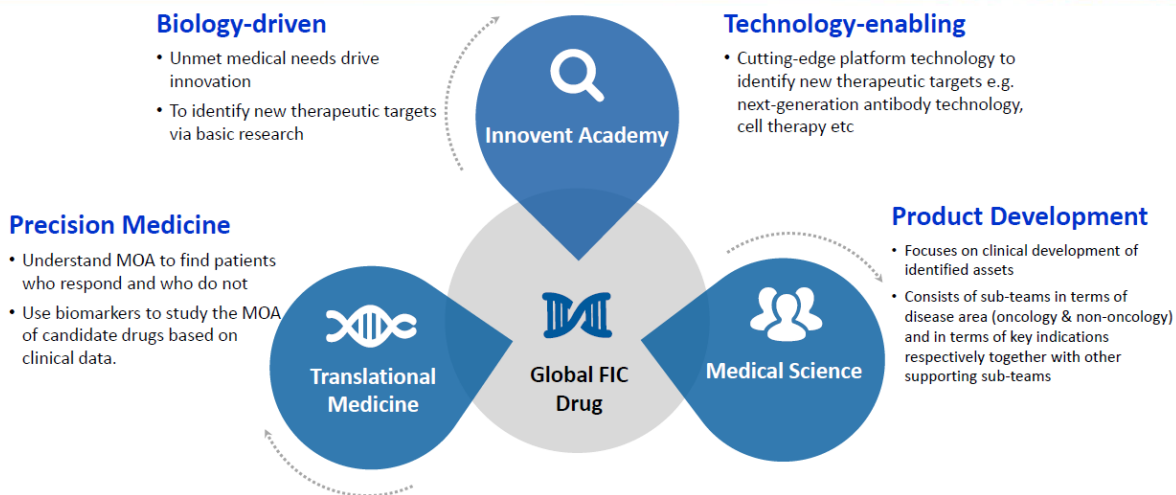
In Jun 2021, Innovent entered into an exclusive license agreement with AnHeart Therapeutics for the co-development and commercialization of taletrectinib, an investigational next-generation TKI designed to effectively target ROS1 and NTRK. Innovent will obtain exclusive rights to co-develop and commercialize taletrectinib in Greater China. Taletrectinib is currently undergoing three phase 2 studies, including 1) the phase 2 study for first line treatment of TKI-naive and second line treatment of TKI-pretreated ROS1-positive NSCLC in China, 2) the phase 2 study for NTRK-positive solid tumors in China, and 3) the phase 2 study for first line and second line treatment of ROS1-positive NSCLC globally. We expect taletrectinib to receive approval from NMPA in 2023E.

Furthermore, in Jul 2021, Innovent announced a strategic collaboration with Ascentage Pharma (6855 HK) regarding 1) the joint commercialization of HQP1351 (olverembatinib) in China; 2) the collaborative clinical development of APG-2575 (lisaftoclax, Bcl-2 inhibitor) with Halpryza (rituximab biosimilar) and letaplimab (IBI188, CD47 mAb); and 3) the equity investment in Ascentage Pharma. HQP1351 is the first China-developed third-generation BCR-ABL TKI targeting drug-resistant chronic myeloid leukemia (CML). At present, an NDA for HQP1351 has been submitted and subsequently granted Priority Review status and a Breakthrough Therapy Designation (BTD) by the NMPA.

## Comprehensive R&D platform

Innovent is committed to building a world class R&D organization with deep understanding in science, cutting edge technology platform, international collaboration, and global professionals. Innovent has successfully established comprehensive and strong capabilities in R&D platform, laying a solid foundation for Innovent's rich innovative drug pipelines. It has developed state-of-the-art technology platforms for the entire bio-innovation value chain, including discovery platform, clinical trial platform and CMC platform. Innovent is also building a laboratory in the US for further expansion and development of innovative candidates in overseas market.



**Figure 3: Innovent's integrated R&D platform in goal for potentially first-in-class drugs**


Source: Company data, CMBIS

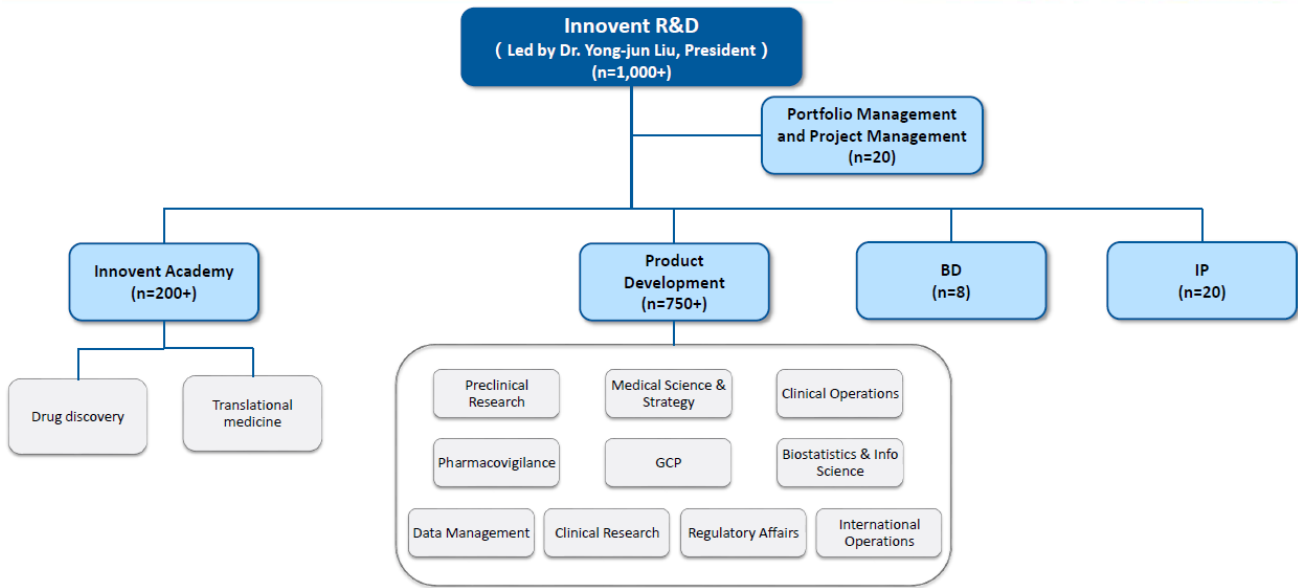
Innovent has established a complete discovery platform for therapeutic monoclonal antibodies, covering the various stages from antibody generation, antibody engineering, in vitro potency, in vivo efficacy to developed capabilities, etc. The Company also established its own platforms of novel antibodies such as bispecific antibodies and nanobodies. By combining internal innovation with external collaborations, the Company has established a robust antibody R&D pipeline covering various therapeutic areas.

Innovent has built a comprehensive clinical trial operating platform for developing innovative drugs, covering the full process for all study stages from Phase I through Phase III, while also being ready to support Phase IV post-marketing clinical trials. The Company has also established all the essential functions including clinical medical functions, clinical pharmacology, clinical trial operations, data management and statistical analysis, PV, and regulatory affairs. The Company has also started upgrading its end-to-end electronic operating systems, which will assure that the clinical development team performs at the global standards of quality and efficiency.

Based on the concept of Quality by Design (QbD), Innovent has established a complete, product-oriented platform that facilitates new drug lead candidates' developability assessment, antibody production, cell line development, cell culture, purification, formulation and fill/finish process development and scale-up, analytical development, technology transfer, commercial manufacturing and quality system.

Led by Dr. Yong Jun Liu, Innovent has approximately 950 R&D staff as of end-2020, covering functions such as drug discovery, translation medicine, product development, BD, IP, etc.

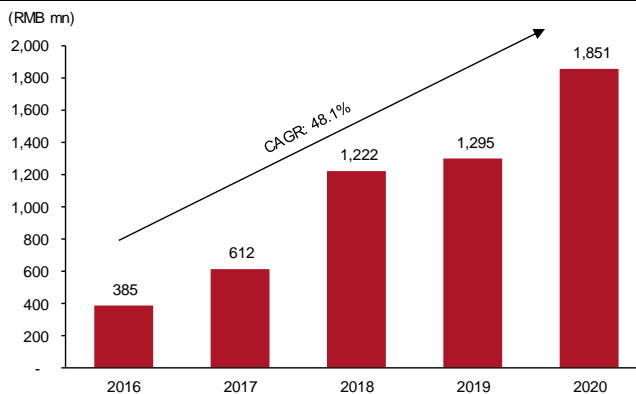
**Figure 4: Innovent’s comprehensive R&D team (as of Nov 2020)**



Source: Company data, CMBIS

Innovent spent RMB1,851mn in R&D during 2020. The steadily growing R&D expenses were mainly spent on progressing clinical trials of late-stage and prioritized assets, and expanding collaboration and licensing programs. Innovent leads the industry peers in China in terms of both R&D investment scale and R&D spending efficiency. Leveraging the strong execution in drug research and clinical development in China, Innovent is gradually upgrading its R&D to a global platform to accelerate innovation.

**Figure 5: Innovent’s R&D spending increases steadily**



Source: Company data, CMBIS

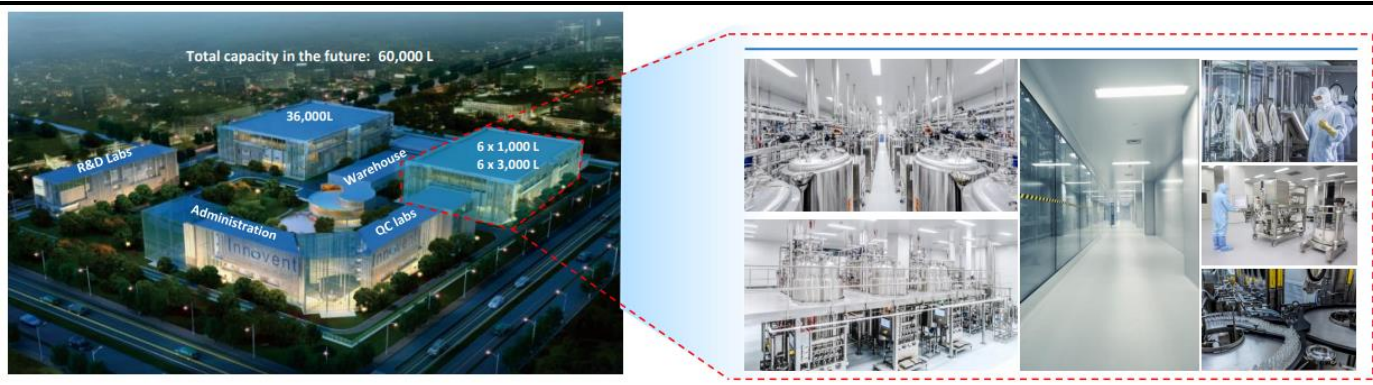
### Sufficient manufacturing capacity

Innovent has built a high-end biopharmaceutical manufacturing facility with a gross floor area of 93,000m<sup>2</sup>. This manufacturing facility is in compliance with the current Good Manufacturing Practices (GMP) standards of the NMPA, FDA and EMA.

In 2020, Innovent has expanded manufacturing capacity from 5,000L to a total of 24,000L to support the production needs for commercial product and clinical stage candidates in the pipeline. The 24,000L production capacity consists of the first manufacturing facilities housing six 1,000L disposable bioreactors (M1a) and the second manufacturing facilities housing six 3,000L stainless steel bioreactors (M1b), both of which have received GMP certification from the NMPA for the manufacturing Tyvyt and other varies of productions. The capacity expansion should ensure the sufficient supply of near-term production needs as well as strengthen the cost advantage of Tyvyt by materially lowering the production cost.

In 2020, the Company started the construction of a new manufacturing facility (the M2 site) in Suzhou that is designed to house additional twelve 3,000L production capacities, which once completed, will expand the Company’s production capacity to a total of 60,000L. Innovent plans to finish the M2 facility construction by the end of 2021.

**Figure 6: Manufacturing base of Innovent**



Source: Company data, CMBIS

**Wide global partnership enhances the R&D and commercialization capability**

Innovent has strong track record in BD deals, including both in-licensing and out-licensing cooperation. Through in-license deals with Adimab, Eli Lilly, Hanmi, Incyte, Roche, Alector and AnHeart, Innovent has significantly expanded its R&D pipelines, which also proves the acknowledge of Innovent’s capacity in R&D and commercialization by both MNC and domestic biotech companies.

**Figure 7: Innovent’s wide global partnership**

- Lilly**
  - Total deal value exceeds **US\$2.5bn<sup>1</sup>**
  - Including upfront payment of **US\$256m<sup>1</sup>**
- Incyte**
  - Licensed in 3 clinical-stage molecules
  - Demonstrated our capability to help global partners bring their innovative therapies into China
- Roche**
  - Access to Roche’s bispecific antibody and Universal CART technologies
  - Out-license ex-China global rights of up to **US\$ 2.1bn** payments and royalties

Source: Company data, CMBIS

### **Innovent's major in-licensing deals:**

In 2013, Innovent and Adimab initiated a partnership to discover antibodies against multiple targets selected by Innovent. The partnership has been expanded multiple times to add additional programs and to access Adimab's bispecifics capabilities. Innovent currently has more than 12 programs in development derived from the Adimab Platform.

Eli Lilly has been Innovent's strategic partner since 2015. The strategic alliance with Eli Lilly is comprised of licensing, co-development and co-branding arrangements in China for Tyvyt and IBI301 (rituximab biosimilar). In addition, Innovent and Eli Lilly has agreed to collaborate in the discovery, development and commercialization of three PD-1-based bi-specific antibodies, including IBI318 and IBI319.

In 2017, Innovent and Hanmi Pharmaceutical (Hanmi) entered into a global strategic partnership to co-develop and co-commercialize IBI315, a first-in-class anti-PD-1/HER2 bispecific antibody. The bispecific antibody constructed using contributions from both Hanmi and Innovent. Under the terms of the agreement, Hanmi and Innovent will coordinate efforts in the global development of the asset with Hanmi playing a lead role in global/ex-China development, registration and commercialization efforts, and Innovent playing a lead role for manufacturing, China development, registration, and commercialization.

In 2018, Innovent and Incyte entered into a strategic collaboration agreement for three clinical-stage product candidates discovered and developed by Incyte - pemigatinib (FGFR1/2/3 inhibitor), itacitinib (JAK1 inhibitor) and pascalisib (PI3K $\delta$  inhibitor). Under the agreement, Innovent will receive rights to develop and commercialize the three product candidates in hematology and oncology in Mainland China, Hong Kong, Macau and Taiwan.

In Mar 2020, Innovent has entered into a licensing agreement Alector (ALEC US), to develop and commercialize an anti-SIRP $\alpha$  antibody, AL008, for the treatment of oncology indications in China. Under the agreement, Innovent will lead the development and commercialization of the molecule in China, including the manufacturing of the product. Alector will lead development of AL008 outside of China. Innovent will pay Alector up to US\$11.5mn in development milestones, US\$112.5mn in sales milestones, and future sales royalties.

In Jun 2020, the Company entered into a strategic collaboration with Roche, which will focus on the discovery, clinical development and commercialization of bispecific antibodies and multiple cell therapies for oncology indications. Innovent will pay upfront, development and commercial milestone payments, and royalties, to non-exclusively access certain Roche technologies that enable the discovery and development of specific 2:1 T-cell bispecific antibodies (TCB) and the universal CAR-T platform. Innovent will create, develop, manufacture, and commercialize the products. Roche retains an option right to license each product for ex-China development and commercialization and will pay option exercise payments totaling US\$140mn plus additional milestone payments up to US\$1.96bn. Additionally, Roche will pay double-digit up to mid teen percentage royalties on each product.

In Jun 2021, Innovent announced to enter into an exclusive license agreement with AnHeart Therapeutics for the co-development and commercialization of taletrectinib, an investigational next-generation TKI designed to effectively target ROS1 and NTRK. Innovent will obtain exclusive rights to co-develop and commercialize taletrectinib in Greater China, including Mainland China, Hong Kong, Macau and Taiwan.

In Jul 2021, Innovent announced a strategic collaboration with Ascentage Pharma to joint commercialize HQP1351 (olverembatinib) in China. HQP1351 is the first China-developed third-generation BCR-ABL TKI targeting drug-resistant chronic myeloid leukemia (CML) with NDA filed to the NMPA. According to the agreement, Innovent and Ascentage Pharma will be jointly responsible

for the subsequent R&D and commercialization of HQP1351 in China and the two companies will equally split the profit generated by the joint commercialization. Innovent will pay US\$30mn upfront payment and up to US\$115mn milestone payments.

In addition to in-licensing efforts, Innovent also completed several successful out-licensing deals which will enhance the Company's globalization progress.

#### **Innovent's major out-licensing deals:**

In Aug 2020, Lilly announced to obtain an exclusive license for Tyvyt for geographies outside of China and to pursue registration of Tyvyt in the US and other markets. In return, Innovent will receive an upfront payment of US\$200mn and will be eligible for up to US\$825mn potential development and commercial milestones, as well as tiered double-digit royalties on net sales. This is the first step of Innovent's globalization. We believe the Company further enhance its global presence supported by its highly innovative pipelines.

In Jan 2020, Innovent entered into an out-license agreement with Coherus BioSciences to commercialize Byvasda in the US and Canada.

#### **Proven commercial capability**

As of end-2020, Innovent had 1,300 commercialization employees which mainly focus on oncology area. With a sizable commercial team, Innovent has successfully promoted Tyvyt in Chinese market and achieved RMB2.29bn sales from Tyvyt in 2020, up 125% YoY.

In 2020, Innovent received approvals for three biosimilars (IBI301, IBI303 and IBI305). With more comprehensive commercial product portfolio, Innovent will further enhance its commercial capability, in our view.

## Tyvyt (sintilimab): first-mover in commercial and clinical

### Fast clinical progress in large indications

Tyvyt was approved by the NMPA for treatment of relapse/refractory classical Hodgkin's Lymphoma (r/r cHL) in Dec 2018, 1L ns-NSCLC in combination with pemetrexed and platinum chemotherapy in Feb 2021, 1L s-NSCLC in combination with gemcitabine and platinum chemotherapy in Jun 2021 and 1L HCC in combination with Byvasda (bevacizumab biosimilar) in Jun 2021. Besides four approved indications (r/r cHL, 1L ns-NSCLC, 1L s-NSCLC and 1L HCC), Tyvyt has submitted sNDA to the NMPA for 2L s-NSCLC (submission in Jan 2021).

Furthermore, Tyvyt is being assessed in multiple registrational Phase 3 studies for many large indications, including 1L ESCC, EGFR+ TKI failure NSCLC and 1L GC. The Phase 3 study (ORIENT-15) for 1L ESCC has met the predefined OS primary endpoint in Jun 2021. We expect the Company to file sNDA for Tyvyt for treatment of the above-mentioned three indications in 2021 or early 2022.

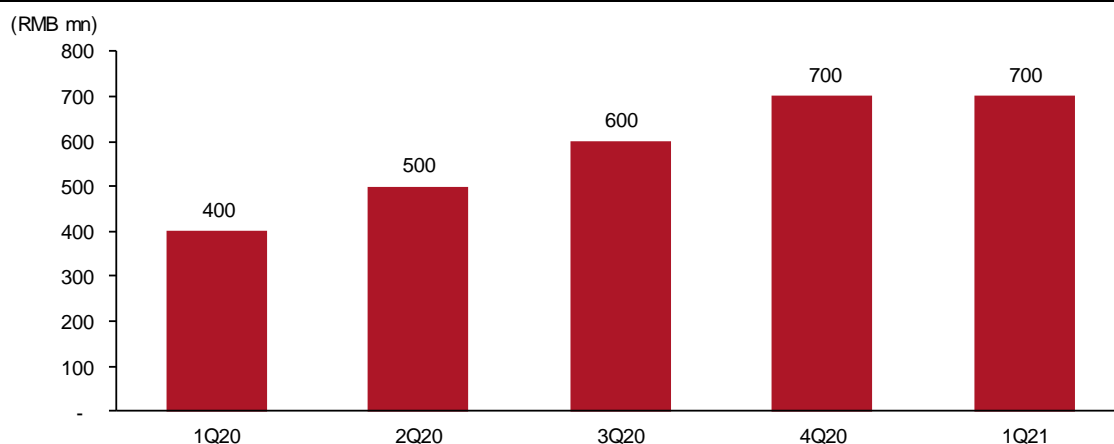
**Figure 8: Tyvyt's clinical trials (as of 30 Jun 2021)**

INDICATION	MONO-/COMBO-THERAPY (OTHER COMPONENTS)	STATUS					
		1A	1B	PHASE 2	PHASE 3	NDA FILED	NDA APPROVED
<b>China</b>							
r/r Classical Hodgkin's Lymphoma	Mono						●
1L Non-squamous NSCLC	Combo (pemetrexed and cisplatin)						●
1L Squamous NSCLC	Combo (gemcitabine and platinum)						●
2L Squamous NSCLC	Mono					●	
1L Hepatocellular Carcinoma	Combo (IBI-305 /biosimilar to bevacizumab)						●
EGFR+ TKI Failure NSCLC (MRCT)	Combo (IBI-305 /biosimilar to bevacizumab)				●		
1L Gastric Cancer	Combo (capecitabine and oxaliplatin)				●		
1L Gastric Cancer (CPS ≥10)	Combo (Ramucizumab)				●		
1L Esophageal Carcinoma (MRCT)	Combo (paclitaxel and cisplatin)/5-FU and cisplatin)				●		
2L Classical Hodgkin's Lymphoma	Combo (ICE)				●		
Melanoma (adjuvant)	Combo (IBI-310/CTLA-4 mAb )				●		
1L Hepatocellular Carcinoma	Combo (IBI-310/CTLA-4 mAb )				●		
2L Hepatocellular Carcinoma	Combo (IBI-310/CTLA-4 mAb )			●			
2L/+ Cervical cancer	Combo (IBI-310/CTLA-4 mAb )			●			
2L ESCC	Mono			●			
r/r NK/T-cell Lymphoma	Mono			●			
3L CRC	Combo (IBI-310/CTLA-4 mAb )			●			
Refractory Gastrointestinal Cancer	Mono		●				
1L Gastric Cancer	Combo (capecitabine and oxaliplatin)		●				
2L NSCLC	Mono		●				
1L/2L Melanoma	Mono		●				
1L Squamous NSCLC	Combo (gemcitabine and cisplatin)		●				
1L/2L Neuroendocrine Tumor	Combo (EP/IP)		●				
Solid Tumors/colorectal cancer	Combo (Fruquintinib)		●				
Solid Tumors/cholangiocarcinoma	Combo (Surufatinib)		●				
3L colorectal cancer	Combo (Chidamide)		●				
2L Hepatocellular Carcinoma	Combo (siRNA)		●				
<b>U.S.</b>							
1L Non-squamous NSCLC	Combo (pemetrexed and cisplatin)					●	
1L Esophageal Carcinoma (MRCT)	Combo (paclitaxel and cisplatin)/5-FU and cisplatin)				●		
Solid Tumors	Mono		●				
Late Stage Endometrial Carcinoma	Mono		●				

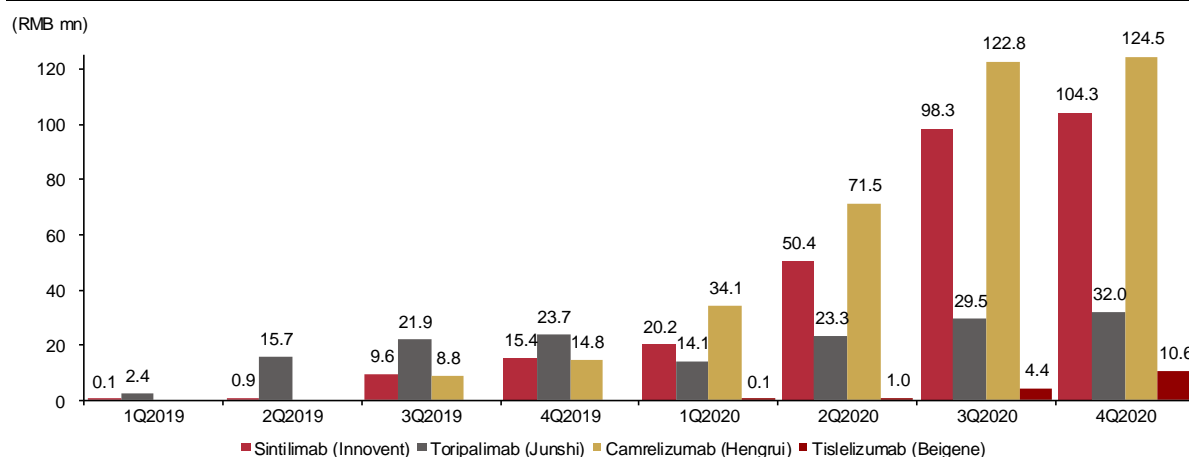
Symbols: ● = completed; ● = completed patient enrollment; ● = in progress; ● = to be initiated within next quarter.

Source: Company data, CMBIS

Innovent has successfully launched its first drug, Tyvyt, which was approved by the NMPA in the end of 2018. Tyvyt generated over RMB1,016mn revenue in the first year of commercialization in 2019. After the inclusion of NRDL in 2020, Tyvyt recorded RMB2.29bn sales in 2020 which surged 125% YoY. As of end-2020, Tyvyt is the second largest domestic PD-1 antibody in terms of sales revenue in China.

**Figure 9: Quarterly sales of Tyvyt (1Q20-1Q21)**

Source: Company data, CMBIS; Note: the sales data were from Innovent's financial statements

**Figure 10: Quarterly sales of four domestic PD-1 antibodies in China (sample hospital sales)**

Source: CMBIS; Note: the data were collected from sample hospitals and could be skewed.

## Competitive PD-1/L1 market in China; clinical speed is key

Tyvyt is the second approved domestic PD-1 antibody in China. To date, there are eight PD-1/L1 antibodies approved in China, including four foreign brands and four domestic brands, covering 12 indications. MSD's pembrolizumab and Hengrui's camrelizumab have obtained most labels so far.

In addition, four domestic PD-1 antibodies have filed NDAs to the NMPA. They are zimberelimab of Gloria Pharma, penpulimab of Akeso/ Sino Biopharm, geptanolimab of Genor Biopharma and serplulimab of Henlius Biotech. Meanwhile, two domestic PD-L1 antibodies have submitted NDAs to the NMPA, including sugemalimab of Cstone Pharma and envafolimab of Alphamab/ Simcere Pharma.

In our view, the competition of PD-1/L1 market will be very fierce, with 8 commercial-stage products and 6 NDA-stage products.

To date, all of the approved domestic PD-1 antibodies have been included into the NRDL. Tyvyt was the first PD-1 antibody included into the NRDL while reimbursement has been limited to 2L cHL patients. As Tyvyt has been approved for 1L ns-NSCLC, 1L s-NSCLC and 1L HCC, the reimbursement coverage could be expanded to these three large indications after this year's negotiation in 4Q21, in our view.

Three domestic PD-1 antibodies were included into the NRDL during last year's negotiation, effective from 1 Mar 2021. Hengrui Pharma's Airuika was eligible for the reimbursement of 2L cHL, 2L HCC, 1L ns-NSCLC and 2L ESCC. Beigene's Baize'an was allowed for the reimbursement of 2L cHL and 2L UC. In addition, Junshi Biosciences' Tuoyi was included for reimbursement of 2L melanoma.

**Figure 11: Approved PD-1/L1 antibodies in China (as of 30 Jun 2021)**

Company	Compound	Target	Indication	Regimen	Approval date	Trial ID	Regimen	NRDL	Cost per month (First year cost, After PAP)
BMS	Opdivo (Nivolumab)	PD-1	2L NSCLC	Mono	2018-06-15	CM078/ NCT02613507/ CTR20150767	3mg/kg; Q2W	N	9,212
			2L HNSCC	Mono	2019-09-30	CM 141/ NCT02105636	3mg/kg; Q2W	N	9,212
			2L GC	Mono	2020-03-13	Attraction-2/ NCT02267343	3mg/kg; Q2W	N	9,212
			1L MPM	+Yervoy	2021-06-08	CM 743/ NCT02899299/ CTR20170913	3mg/kg; Q2W	N	9,212
MSD	Keytruda (Pembrolizumab)	PD-1	2L Melanoma	Mono	2018-07-26	KN 151/ NCT02821000	200mg; Q3W	N	11,945
			1L ns-NSCLC	+Chemo	2019-04-02	KN 042/ NCT02220894	200mg; Q3W	N	11,945
			1L s-NSCLC	+Chemo	2019-11-26	KN 042/ NCT02220894	200mg; Q3W	N	11,945
			1L PD-L1+ NSCLC	Mono	2019-09-30	KN 042/ NCT02220894	200mg; Q3W	N	11,945
			2L ESCC	Mono	2020-06-19	KN 181/ NCT02564263/ CTR20160588	200mg; Q3W	N	11,945
			1L HNSCC (CPS ≥ 20)	Mono	2020-12-08	KY 04/ CTR20201774	200mg; Q3W	N	11,945
			1L CRC (MSH/dMMR)	Mono	2021-06-08	CTR20200103	200mg; Q3W	N	11,945
			2L Melanoma	Mono	2018-12-21	NCT03013101	3mg/kg; Q2W	Y	4,245
Junshi	Tuoyi (toripalimab)	PD-1	2L NPC	Mono	2021-02-10	POLARIS-02/ NCT02915432	3mg/kg; Q2W	N	4,245
			2L UC	Mono	2021-04-07	POLARIS-03/ NCT03113266	3mg/kg; Q2W	N	4,245
			2L cHL	Mono	2018-12-24	CTR20170281	200mg; Q3W	Y	3,317
Innovent	TYVYT (Sintilimab)	PD-1	1L ns-NSCLC	Combo	2021-02-03	CTR20180975	200mg; Q3W	N	3,317
			1L s-NSCLC	Combo	2021-06-03	CTR20181437	200mg; Q3W	N	3,317
			1L HCC	Combo	2021-06-28	CTR20182545	200mg; Q3W	N	3,317
			2L cHL	Mono	2019-06-03	NCT03155425	200mg; Q2W	Y	6,274
Hengrui	Airuika (Camrelizumab)	PD-1	2L HCC	Mono	2020-03-04	NCT02989922	3mg/kg; Q3W	Y	4,183
			1L ns-NSCLC	+Chemo	2020-06-19	SHR-1210-303/ NCT03134872	200mg; Q3W	Y	4,183
			2L ESCC	Mono	2020-06-19	NCT03099382	200mg; Q2W	Y	6,274
			2L NPC	+Chemo	2021-04-29	NCT03558191/ CTR20180865	200mg; Q2W	N	6,274
			1L NPC	+Chemo	2021-06-10	NCT03707509/ CTR20181864	200mg; Q3W	N	4,183
			2L cHL	Mono	2019-12-27	NCT03209973	200mg; Q3W	Y	6,229
			2L UC	Mono	2020-04-10	NCT04004221/ CTR20170071	200mg; Q3W	Y	6,229
Beigene	Baize'an (Tislelizumab)	PD-1	1L s-NSCLC	+Chemo	2021-01-14	NCT03594747/ CTR20181746	200mg; Q3W	N	6,229
			1L ns-NSCLC	+Chemo	2021-06-22	RATIONALE 304/ NCT03663205	200mg; Q3W	N	6,229
			2L HCC	Mono	2021-06-22	RATIONALE 208/ NCT03419897	200mg; Q3W	N	6,229
AZ	Imfinz (Durvalumab)	PD-L1	1L maintenance Stage III NSCLC	Mono	2019-12-06	Pacific/ NCT02125461/ CTR20181576	10mg/kg; Q2W	N	12,077
			1L SCLC	+Chemo	2020-02-13	Impower 133/ NCT02763579	1,200mg; Q3W	N	10,933
Roche	Tecentriq (Atezolizumab)	PD-L1	1L HCC	+Avastin	2021-06-04	Imbrave 150/ NCT03434379/ CTR20180665	1,200mg; Q3W	N	10,933

Source: Insight, Yaozh.com, CMBIS estimates

Off-label use of PD-1/L1 antibodies are currently common in China. However, with approved labels and NRDL inclusion, PD-1/L1 antibodies can get access to hospital channels more easily. Thus, we think Tyvyt is well-positioned in the competitive PD-1/L1 antibody market thanks to its fast clinical speed. Besides four approved indications (r/r cHL, 1L ns-NSCLC, 1L s-NSCLC and 1L HCC), Tyvyt has submitted sNDA to the NMPA for 2L s-NSCLC (submission in Jan 2021). Furthermore, Tyvyt is being assessed in multiple registrational Phase 3 studies for many large indications, including 1L ESCC, EGFR+ TKI failure NSCLC and 1L GC. That said, thanks to the fast progress in the



development of large indications, we expect Tyvyt to continue to lead other domestic PD-1/L1 antibodies in terms of market share in China.

**Figure 12: Clinical landscape of major PD-1/L1 antibodies in China (as of 30 Jun 2021)**

Indication	Line of treatment	Keytruda Pembrolizumab Merck	Opdivo Nivolumab BMS	Tecentriq Atezolizumab Roche	Imfinzi Durvalumab AstraZeneca	Tuoyi Toripalimab Junshi	Tyvyt Sintilimab Innovent	AiRuiKa Camrelizumab Hengrui	BGB-A317 Tislelizumab BeiGene	CS1001 Sugemalimab C-Stone	GLS010 Gloria	HLX20 Henlius	AK105 penpulimab Akesobio
GC	Adj./Neo-adj.	Ph3	Ph3					Ph2					
	1L	Ph3 (Failed OS) Ph3 (Failed OS) Ph3 (Failed OS)	Ph3				Ph3 Ph3 (CPS≥10)	Ph3	Ph3	Ph3			
	2L	Ph3	Approved			Ph2		Ph3		Ph1/2			
NSCLC	stage III	Adj./Neo-adj.	Ph3	Ph3 Ph3	Ph3	Ph3	Ph1	Ph2					
	1L	Ph3			Approved			Ph3	Ph3 (Terminated)	Ph3			
	2L	Ph3											
NSCLC	1L	Approved (ns) Approved (s) Approved (PD-L1+)	Ph3	Ph3 (PD-L1+) Ph3 (ns)	Ph3 Ph3	Ph3	Approved (ns) Approved (s)	Approved (ns) NDA (s)	Approved (ns) Approved (s)	NDA (s+ns)		Ph3 (ns)	Ph3 (ns) Ph3 (s)
	2L	Ph3 Ph3	Approved Ph3	Ph2 (EGFR+) Ph3 Ph3 Ph3		Ph3	NDA (s) Ph3 (EGFR+ TKI failure)		NDA				
ESCC	Adj./Neo-adj.		Ph3					Ph1/2 Ph2	Ph3 (Locally ESCC)				
	1L	Ph3	Ph3			Ph3	Ph3	NDA	Ph3	Ph3		Ph3	
HCC	2L	Approved	Ph3	Ph3			Ph2	Approved	Ph3				
	Adj./Neo-adj.	Ph3	Ph3	Ph3	Ph3 Ph3	Ph2/3	-	Ph2					
HCC	1L	Ph3	Ph3 (Failed OS) Ph3	Approved Ph3	Ph3		Approved	Ph3 Ph3	Ph3 Ph3				Ph2
	2L	Ph3 Ph3			Ph3		Ph1b	Approved	Approved	Ph1b/2		Ph2	
MSI-H/dMMR (CRC)	1L							p2					
HNSCC	2L	Approved	Ph3				Ph2(3L)	Ph2	NDA			NDA	
	Adj./Neo-adj.	Approved		Ph3		Ph3	Ph2						
SCLC	Adj./Neo-adj.				Ph3								
	1L		Ph3 (Failed OS) Ph3 (Failed OS) P3 * Failed OS	Approved	Ph3 Ph3	Ph3		Ph3	Ph3			Ph3	
UC	2L					Ph2		Ph2					
	Adj./Neo-adj.	Ph3	Ph3	Ph3	Ph3				Ph3				
RC	1L	Ph3	Ph3	Ph3	Ph3 (failed PFS)	Approved			Approved				
	2L	Ph3	Ph3	Ph3									
NPC	Adj./Neo-adj.						Ph3	Ph3					
	1L					NDA		Approved	Ph3				Ph2
BC	2L					Approved Ph3		Approved					Ph2
	Adj./Neo-adj.	Ph3		Ph3									
TNBC	1L			Ph3									
	2L			Ph3		Ph3							
NKTCL	1L					Ph1		Ph2					
	2L	P2											
cHL	1L						Ph2	Ph2	Ph2	Ph2			
	2L						Approved Ph3	Approved	Approved Ph3 (3L)	Ph2	NDA		NDA
Melanoma	Adj.						Ph2	Ph3	Ph2				
	1L	Ph3					Ph3	Ph2	Ph2				
CCA	2L	Approved		Ph2		Approved	Ph1	Ph2					
	Adj./Neo-adj.	Ph3			Ph3								
mCRPC	1L	Ph3											
	2L		Ph2	Ph3									
Cervical cancer	1L	Ph3			Ph3						Ph2		
	2L							Ph2					
dometrial carcinc	1L	Ph3											
	2L												
MPM	Adjvant/neoadjuvant												
	1L		Approved										
	2L												

Source: Companies' data, Insight, CMBIS

## Strong efficacy evidence for multiple indications

### Classical Hodgkin's Lymphoma (cHL)

Tyvyt was approved by the NMPA in Dec 2018 based on the data of ORIENT-1 study. The ORIENT-1 study is a multicenter, single-arm, Phase 2 clinical trial, assessing the efficacy and safety of Tyvyt in r/r cHL. Subjects received 200 mg of Tyvyt every three weeks in this study until disease progression. A total of 96 subjects with r/r cHL were enrolled, and the study's primary endpoint was ORR assessed by an independent imaging assessment committee (IRRC). 79.2% of the patients treated with Tyvyt

achieved a best overall objective response (week 24 data), 17.7% of the patients achieved a complete response at week 15 (PET scan data), 33.3% of the patients obtained a complete response at week 24 (CT scan data, source: CSCO 2018), and the disease control rate is 97.9% at week 24. These clinical data are similar to the results of nivolumab and pembrolizumab.

Further, in Jun 2020, Innovent updated the results of ORIENT-1 study at the ASCO 2019 Annual Meeting. As of the data cutoff on 30 Sep 2019, the ORR was 85.4% (82/96) based on IRRC review, of which 41 patients (42.7%) achieved CR.

**Figure 13: Clinical efficacy comparison of approved PD-1 antibodies for r/r cHL**

Company	BMS	MSD	Innovent	Beigene	Hengrui
Compound	Nivolumab	Pembrolizumab	Tyvyt	Tislelizumab	Camrelizumab
Trial ID	CheckMate-205	Keynote-087	ORIENT-1	NCT03209973	NCT03155425
Patients (N)	243	210	96	70	75
PFS	15.0m	13.7m	NR (ASCO 2019)	NR (EHA 2019)	NA
ORR	<b>71.0%</b>	<b>71.9%</b>	<b>85.4% (ASCO 2019)</b>	<b>87.1% (EHA 2019)</b>	<b>84.8%</b>
CR	<b>21.0%</b>	<b>27.6%</b>	<b>29.2% (ASCO 2019)</b>	<b>62.9% (EHA 2019)</b>	<b>30.3%</b>
PR	50.0%	44.3%	56.2% (ASCO 2019)	24.2% (EHA 2019)	54.4%

Source: Company data, CMBIS

### Non-small cell lung cancer (NSCLC)

Lung cancer is a malignancy with the highest morbidity and mortality in China. NSCLC accounts for about 80-85% of lung cancer. Approximately 70% of people with NSCLC have locally advanced or metastatic NSCLC at initial diagnosis, rendering the patients with no chance of radical resection. Meanwhile, even after radical surgery patients still have a high chance of recurrence and eventually die from disease progression.

In China, about 60% of NSCLC cases are non-squamous NSCLC, of which nearly 50% patients are gene-driven negative, while about 30% of people with NSCLC in China are of squamous subtype, and targeted therapy is not appropriate for advanced s-NSCLC patients without EGFR-sensitive mutations or ALK gene rearrangements. There are large unmet medical needs for such patients with advanced lung cancer. Using immune checkpoint inhibitors (such as PD-1/L1 antibodies) have provided new clinical approaches in the first-line treatment of recurrent or metastatic advanced NSCLC.

Tyvyt is leading its major other domestic PD-1 antibodies in the clinical progress of lung cancer indications.

**1L ns-NSCLC:** In Feb 2021, the NMPA approved Tyvyt in combination with pemetrexed and platinum chemotherapy as first-line therapy for people with ns-NSCLC. The approval was based on a randomized, double-blind, Phase 3 clinical trial (ORIENT-11), which evaluated Tyvyt or placebo in combination with pemetrexed and platinum chemotherapy as first-line therapy for people with advanced or recurrent ns-NSCLC without sensitizing EGFR mutations or ALK rearrangements. A total of 397 participants were enrolled. The median PFS of Tyvyt combination arm and placebo combination arm assessed by IRRC was 8.9 months and 5.0 months respectively, with HR (95%CI) = 0.482 (0.362,0.643), P < 0.00001.

**1L s-NSCLC:** In Jun 2021, the NMPA approved the sNDA for Tyvyt as first-line therapy for s-NSCLC in combination with gemcitabine and platinum chemotherapy. The approval was based on the results of the ORIENT-12 study (NCT03629925). The study is a randomized, double-blind, Phase 3 clinical trial evaluating Tyvyt or placebo in combination with gemcitabine and platinum chemotherapy as first-line treatment for advanced or metastatic s-NSCLC. A total of 357 subjects were enrolled. An updated analysis showed that the median PFS assessed by IRRC was 5.5 months in the Tyvyt combination arm versus 4.9 months in the placebo combination arm (HR=0.536, 95% CI: 0.422-0.681, P<0.00001),

while the median PFS assessed by the investigators was 6.7 months in the Tyvyt combination arm versus 4.9 months in the placebo combination arm (HR=0.532, 95% CI: 0.419-0.674, P< 0.00001).

**2L s-NSCLC:** In Jan 2021, the NMPA has accepted the sNDA for Tyvyt monotherapy as second-line therapy for s-NSCLC. This sNDA was based on a randomized, open-label, Phase 3 clinical trial (ORIENT-3), evaluating Tyvyt as a second-line therapy for patients with advanced or recurrent s-NSCLC whose cancer had progressed on first-line platinum-based chemotherapy (NCT03150875). In Apr 2021, the results of ORIENT-3 study were released in an oral presentation at the American Association for Cancer Research (AACR) Annual Meeting. A total of 290 patients were enrolled in ORIENT-3 and randomized in a 1:1 ratio to receive either Tyvyt 200mg or docetaxel every three weeks. Based on the primary analysis population (280 patients, excluding patients on the docetaxel arm who received immunotherapy prior to disease progression), Tyvyt demonstrated a statistically significant improvement in OS compared to docetaxel, meeting the pre-specified primary endpoint. The median OS was 11.79 months for patients on the Tyvyt arm and 8.25 months for those on the docetaxel arm (HR=0.74, 95% CI: 0.56-0.96, P=0.02489). The median PFS as assessed by investigators was 4.30 months vs 2.79 months (HR=0.52, 95% CI: 0.39-0.68, P<0.00001), and the confirmed ORR was 25.5% vs 2.2% (P<0.00001), respectively. Safety was consistent with previous studies of Tyvyt, and no new safety signals were identified.

### Hepatocellular carcinoma (HCC)

**1L HCC:** In Jun 2021, the NMPA has approved the sNDA for Tyvyt in combination with bevacizumab as first-line therapy for HCC, which was based on the pre-specified interim analysis of ORIENT-32 study. ORIENT-32 is a Phase 3 randomized, open-label, multi-center study in China to evaluate the efficacy and safety of Tyvyt in combination with bevacizumab compared to sorafenib in the 1L HCC (NCT03794440). A total of 571 subjects were enrolled. In Nov 2020, the results were released in a late-breaking proffered oral presentation at the European Society of Medical Oncology Asia (ESMO Asia) Virtual Congress. Compared to sorafenib, Tyvyt plus bevacizumab demonstrated a 43.1% decreased risk of all-cause mortality (HR 0.569, 95%CI: 0.431-0.751, P<0.0001); the median OS was not reached in the Tyvyt plus bevacizumab arm versus 10.4 months in the sorafenib arm. Tyvyt plus bevacizumab also demonstrated 43.5% decreased risk of progression as assessed by IRRC (HR 0.565 95%CI: 0.455-0.701, P<0.0001); median PFS was 4.6 months in the Tyvyt plus bevacizumab arm versus 2.8 months in the sorafenib arm.

Note that Roche's "Tecentriq + Avastin" combo-therapy was approved in China in Oct 2020. The approval was based on the Chinese patient's subgroup data of trial IMbrave150, which was a phase III trial comparing "Tecentriq + Avastin" and sorafenib as first-line treatment for locally advanced HCC.

**Figure 14: Efficacy data of Tecentriq in combination with Avastin in unresectable advanced HCC**

	Tecentriq + Avastin
Patients (N)	104
ORR	36%
CR	12%
PR	24%
SD	36%
PD	24%
DCR	71%
PFS	7.3m
OS	17.1m

Source: Companies' data, CMBIS; Note: Data showed above were based on RECIST 1.1 criteria.

Innovent is also evaluating the safety and efficacy of the combination of Tyvyt and IBI310 (CTLA-4 mAb) in treating 2L HCC patients in a Ph Ib study.

## Esophageal cancer (EC)

In Jun 2020, Innovent announced the results of ORIENT-2 study, a pivotal clinical study of Tyvyt as a second-line treatment for locally advanced or metastatic esophageal squamous cell carcinoma (ESCC) at the 56th ASCO Annual Meeting. We think the trial design was similar to Pembrolizumab's KEYNOTE-180 study.

The ORIENT-2 study was a randomized, open-label, multicenter, Phase 2 clinical study comparing the efficacy and safety of Tyvyt with chemotherapy (paclitaxel or irinotecan) in second-line advanced or metastatic ESCC patients. A total of 190 subjects were enrolled in the study and randomly assigned in a 1:1 ratio to receive either Tyvyt or chemotherapy (paclitaxel or irinotecan). The study's primary endpoint was overall survival (OS). As of 2 Aug 2019, compared with paclitaxel/irinotecan, Tyvyt demonstrated a statistically significant improvement in OS in the intent-to-treat (ITT) population (HR = 0.70,  $P = 0.032$ ). The median OS in the Tyvyt-treated group and the chemotherapy-treated group were 7.2 months vs 6.2 months and the 12-month OS rates were 37.4% vs 21.4%, respectively.

In Jun 2021, Innovent announced the phase 3 study (ORIENT-15, NCT03748134) met the predefined OS primary endpoint, which is a global randomized, double-blind, multi-center clinical study evaluating Tyvyt in combination with chemotherapy (cisplatin plus paclitaxel or cisplatin plus 5-FU) for the first-line treatment of ESCC. In the interim analysis, Tyvyt in combination with chemotherapy demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of OS compared to placebo in combination with chemotherapy, regardless of PD-L1 expression status.

## Gastric cancer (GC)

Innovent is conducting a Phase III study in China evaluating the safety and efficacy of Tyvyt at 200 mg Q3W dose level in combination with capecitabine and oxaliplatin in patients with first-line GC (Orient-16). The patient enrollment has been completed. We think the design of this trial is similar to Bavencio (avelumab)'s JAVELIN Gastric 100 study (NCT02625610).

The Company also initiated a phase III study in China evaluating the safety and efficacy of Tyvyt in combination with ramucirumab as a first-line treatment for patients with advance gastrointestinal cancers with combined positive score (CPS)  $\geq 10$  (ORIENT-106 study).

To date, BMS's Opdivo (nivolumab) is the first and only immunotherapy approved for GC in China, which was approved for treatment of gastric/gastroesophageal junction cancer (GC/GEJ) patients previously treated with  $\geq 2$  chemotherapy regimens. The approval was based on a phase 3 Attraction-2 study in Asian patients. According to the 3-year follow-up results of ATTRACTION-2 study, OS of the nivolumab group was significantly longer compared to the placebo group (median 5.3 months vs 4.1 months). In addition, nivolumab group has higher 3-year survival rate than placebo group (5.6% vs 1.9%). For responders ( $n = 32$ ) in the nivolumab group, the median OS of was 26.7 months and the 3-year survival rate was 35.5%.

Despite the fact that no PD-1/L1 antibody has been approved for 1L GC in China yet, nivolumab has been approved by the US FDA for 1L GC. The approval was based on a phase 3 trial evaluating nivolumab in combination with chemotherapy or ipilimumab to treat subjects with previously untreated advanced or metastatic GC/GEJ (Checkmate-649; NCT02872116). According to the data presented at ESMO 2020, among the PD-L1 CPS  $\geq 5$  patient population, the median OS was 14.4 months in nivolumab plus chemotherapy group vs 11.1 months in chemotherapy group (HR = 0.71;  $P < 0.0001$ ) while median PFS was 7.7 months versus 6.1 months (HR = 0.68;  $P < 0.0001$ ).

Many domestic PD-1/L1 inhibitors have started clinical studies in GC, including Tyvyt (phase 3, Orient-16, Orient-106), Hengrui's camrelizumab (phase 3, NCT03813784), Beigene's tislelizumab (phase 3,

NCT03777657) and CStone's sugemalimab (phase 3, Gemstone 303). However, we haven't seen any phase 3 data released so far. However, early clinical studies have shown preliminary efficacy. In a phase 1b trial (NCT02937116), Tyvyt in combination with chemotherapy achieved 85% ORR, 100% DCR, 7.5 months mPFS among the 20 enrolled 1L GC patients.

Considering the completion of patient enrollment for Orient-16 study, we think Tyvyt has the potential to become the first PD-1/L1 therapy approved for 1L GC/GEJ in China.

## Opening up global market potential through collaboration with Eli Lilly

Tyvyt was co-developed and co-promoted by Innovent and Eli Lilly in China. In Aug 2020, Innovent and Eli Lilly announced expansion of their collaboration on Tyvyt. According to the agreement, Eli Lilly will obtain exclusive rights of Tyvyt for regions outside of China. In return, Innovent will receive an upfront payment of US\$200mn and will be eligible for up to US\$825mn in potential development and commercial milestones, as well as tiered double-digit royalties on net sales. In addition, both companies will retain the rights to study Tyvyt in combination with other medicines as part of their own clinical programs.

In May 2021, the US FDA accepted the BLA of Tyvyt in combination with pemetrexed and platinum chemotherapy for the first-line treatment of ns-NSCLC. This submission was primarily based on the results of the Phase 3 ORIENT-11 trial which was conducted in China, assessing the efficacy and safety of Tyvyt in combination with pemetrexed and platinum chemotherapy compared to placebo plus chemotherapy as a first-line treatment for patients with advanced or metastatic ns-NSCLC, with no sensitizing EGFR mutations or ALK rearrangements.

Besides Tyvyt, four other domestic PD-1/L1 antibodies also completed out-licensing deals with global partners. As for the licensing fees, Tyvyt recorded the second-highest upfront payment of US\$200mn, following the US\$650mn upfront payment for Beigene's tislelizumab out-licensing deal with Novartis.

**Figure 15: Domestic PD-1/L1 compounds license-out deals**

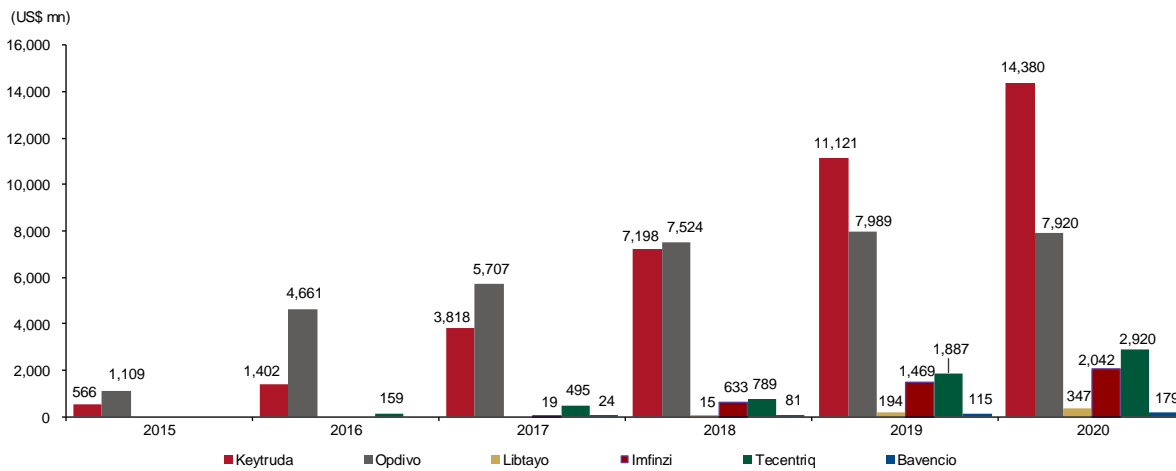
Compound	Company	Partner	License Regions	Upfront fee	Milestone fee	Other fees	Date	Royalty
Toripalimab	Junshi	Coherus BioSciences	US, Canada	US\$150mn	US\$380mn	US\$510mn	2021-02-01	20%
Tislelizumab	Beigene	Novartis	US, Canada, Mexico, EU, UK, Norway, Switzerland, Iceland, Liechtenstein, Russia, and Japan.	US\$650mn	US\$1,550mn		2021-01-11	double-digit
Sugemalimab (PD-L1) and CS1003 (PD-1)	CStone	EQRx	ex-China	US\$150mn	US\$1,150mn		2020-10-27	N/A
Sintilimab	Innovent	Eli Lilly	ex-China	US\$200mn	US\$825mn		2020-08-18	double-digit
Camrelizumab	Hengrui	Crystal Genomics	South Korea	US\$1.5mn	US\$85.75mn		2020-04-20	10-12%

Source: Companies' data, CMBIS

The global PD-1/L1 market is much more sizable than Chinese market. In 2020, Keytruda recorded US\$14.38bn global sales while Opdivo registered US\$7.92bn global sales. According to Evaluate Pharma, the combined global sales of major PD-1/L1 antibodies will grow from US\$28.26bn in 2020 to US\$66.56bn in 2026E.

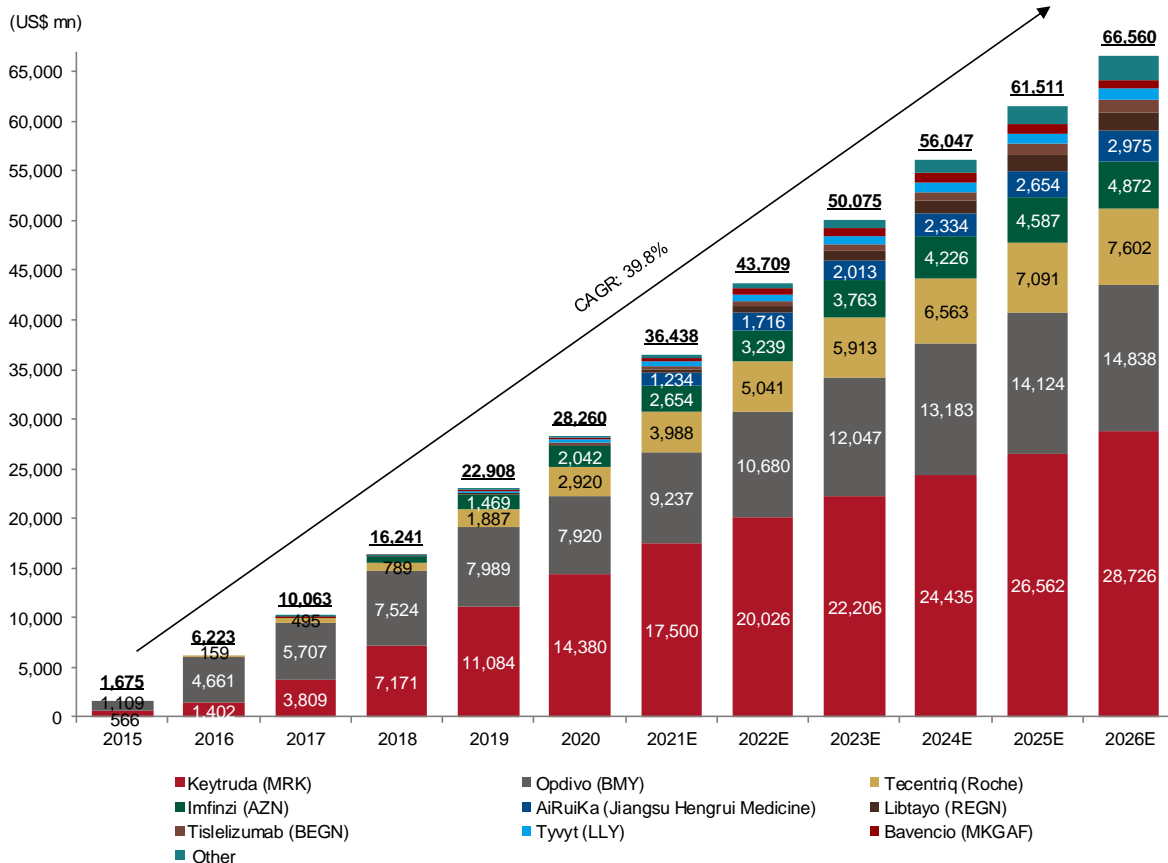
With Innovent's significant cost advantages and Eli Lilly's strong commercial capabilities, we expect Tyvyt to gain a significant market share in the global PD-1/L1 market.

**Figure 16: Global sales of FDA-approved PD-1/L1 antibodies (2014-2020)**



Source: Evaluate Pharma, CMBIS

**Figure 17: Global market size of major PD-1/L1 antibodies (2015-2026E)**



Source: Evaluate Pharma, CMBIS

## Three commercial-stage biosimilars to provide strong cashflows

### IBI305: a bevacizumab (VEGF) biosimilar

Bevacizumab is a fully-humanized recombinant monoclonal antibody that decreases growth of blood vessels (this growth is referred to as angiogenesis) by inhibiting vascular endothelial growth factor A (VEGF-A). VEGF is a family of signaling protein secreted by cancer cells, and they play a key role in tumor angiogenesis, i.e. formation of new blood vessels around tumor tissues.

Avastin (bevacizumab), launched by Roche, has been approved globally for the treatment of multiple malignant tumors, including non-small cell lung cancer, metastatic colorectal cancer, glioblastoma, renal cell carcinoma, cervical cancer, and epithelial ovarian, fallopian tube, or primary peritoneal cancer. In China, Avastin has been approved for the treatment of patients with advanced non-small cell lung cancer and metastatic colorectal cancer.

Innovent's IBI305 (Byvasda) has completed a randomized, double blind, multi-center, Phase 3 study in China evaluating the efficacy, safety and immunogenicity of IBI305 in combination with chemotherapy compared to bevacizumab in combination with chemotherapy in patients with advanced or recurrent ns-NSCLC.

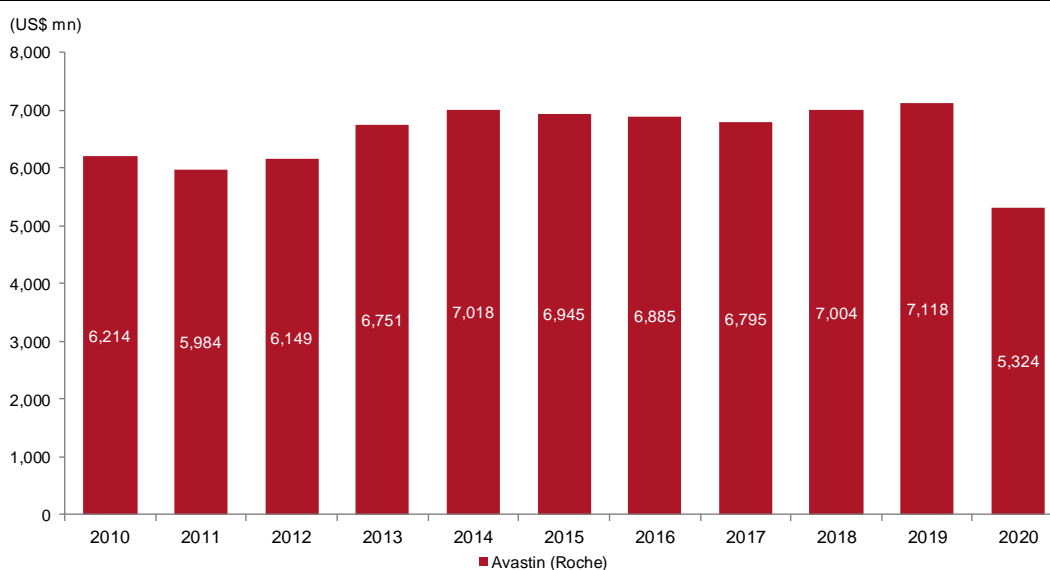
Byvasda was firstly approved by the NMPA in Jun 2020 for treatment of advanced NSCLC and metastatic colorectal cancer. In Dec 2020, Byvasda has been approved by the NMPA of China for the treatment of adult recurrent glioblastoma (GBM, the most common malignant primary brain tumor), which is the third approved indication of Byvasda in China.

Besides China market, Byvasda is targeting the global market through out-licensing arrangement. In Jan 2020, Innovent entered into an out-license agreement with Coherus BioSciences to commercialize Byvasda in the US and Canada. In Jan 2021, Innovent announced to license out Byvasda's development and commercialization rights in Indonesia to PT Etana Biotechnologies Indonesia.

### Market size and landscape of Bevacizumab biosimilars

Avastin's worldwide sales peaked at US\$7,118mn in 2019, according to Evaluate Pharma.

**Figure 18: Aggregate worldwide sales of Avastin (2010-2020)**



Source: Evaluate Pharma, CMBIS

Competition of bevacizumab market is fierce in China. To date, the NMPA has approved three bevacizumab biosimilars, which are developed by Qilu Pharma, Innovent and Luye Pharma. In addition, five bevacizumab biosimilars have filed NDA to the NMPA and ten are under phase III trials. As the second-to-market bevacizumab biosimilar in China, we think Byvasda enjoys early mover advantages in this fiercely competitive market.

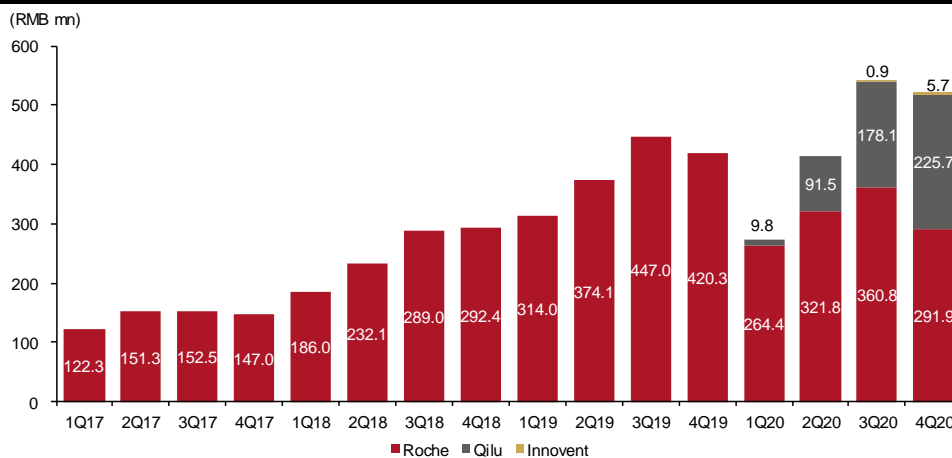
**Figure 19: Clinical landscape of bevacizumab biosimilars in China (only late-stage included)**

Compound	Company	Progress	Last update date	Related Clinical trials
IBI305	Innovent	Approved	2020-06-17	CTR20160874, CTR20160848, CTR20182545, CTR20182550, CTR20190972
LY01008	Luye Pharma	Approved	2021-04-30	CTR20170191, CTR20171412, CTR20201573
QL1101	Qilu Pharmaceutical	Approved	2019-12-06	CTR20160098, CTR20161024
HLX04	Henlius	NDA	2020-09-09	CTR20160931, CTR20171503, CTR20191263
TAB008	TOT	NDA	2020-09-05	CTR20160522, CTR20170244
BAT1706	Bio-Thera	NDA	2020-06-24	CTR20160411, CTR20170799, CTR20181752
MIL60	BETA Pharmaceuticals	NDA	2020-06-17	CTR20160789, CTR20170658
BP102	Hengrui	NDA	2020-04-15	CTR20170174, CTR20180147
JS501	HuaOTai Biopharm	Phase III	2020-12-09	CTR20181610, CTR20202435
TRS003	Teruisi Pharm	Phase III	2020-09-09	CTR20191049
AWWB	Amgen	Phase III	2020-04-14	CTR20200442
SIBP 04	SIBP CNBG	Phase III	2020-01-22	CTR20191923, CTR20192708
bvzr	Pfizer	Phase III	2019-11-05	CTR20192191, CTR20192551
AK-3008	Aosaikang Pharmaceutical	Phase III	2019-04-29	CTR20181254, CTR20190071
WBP264	Hualan Genetic	Phase III	2018-08-02	CTR20170373, CTR20181297
TQB2302	Chia Tai-Tianqing	Phase III	2018-07-02	CTR20171308, CTR20180857, CTR20201154
GB222	Genor	Phase III	2017-12-15	CTR20170128, CTR20171085, CTR20180047
SCT 510	SCT	Phase II/III	2020-10-23	CTR20202027

Source: Insight, Companies' data, CMBIS

Reviewing the sales of bevacizumab from sample hospitals, the market share of Avastin was gradually taken by biosimilars, while the total sales of bevacizumab in China was still growing. We expect Innovent's Byvasda to further gain market share thanks to its cost advantages.

**Figure 20: Sales of bevacizumab and its biosimilars in China (sample hospitals)**



Source: PDB, CMBIS



## IBI301: a rituximab (CD20) biosimilar

Rituximab, a chimeric monoclonal antibody targeted against B-cell marker CD20, was firstly approved by US FDA in 1997. Globally, rituximab has been approved for the treatment of non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), rheumatoid arthritis (RA), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and moderate to severe pemphigus vulgaris (PV).

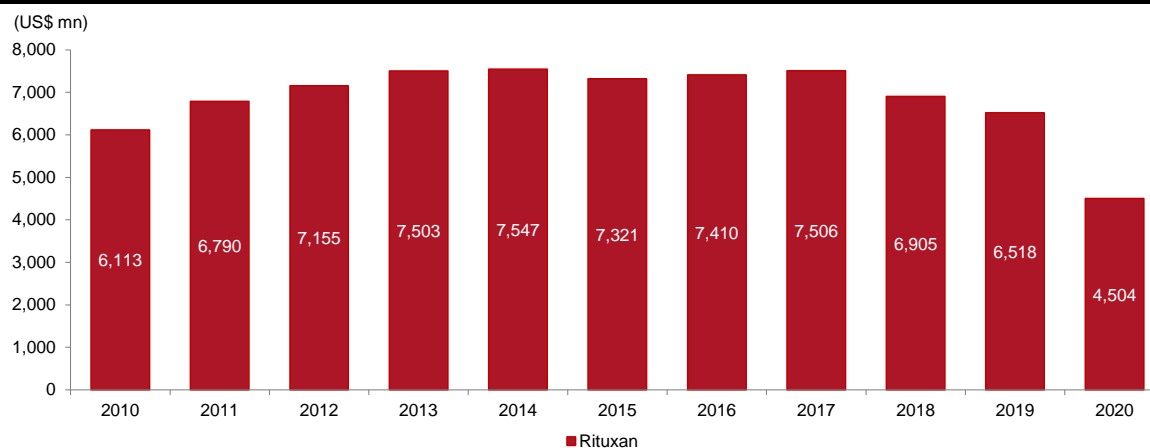
Malignant lymphoma is one of the most common hematological malignancies in China. It is one of the top ten malignant tumors with high morbidity and mortality. In recent years, the incidence of malignant lymphoma has been rising. According to histopathology, lymphoma can be divided into Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL), of which NHL accounts for the majority. NHL is a general term for a series of related but different lymphoid malignant tumors. Most (80-85%) originates from B cells. The rest originate from T cells or NK cells. More than 95% of B-cell non-Hodgkin's lymphoma cells express CD20. The most common type of NHL in China is diffuse large B-cell lymphoma (DLBCL), accounting for 40-50% (about 30-40% in Western countries). DLBCL is a moderately malignant to highly malignant invasive lymphoma that progresses rapidly and leads to the death of patients within a few months without treatment.

Innovent's IBI301 (Halpryza) is a rituximab biosimilar co-developed with Eli Lilly. In Sep 2020, Halpryza was approved by the NMPA in Oct 2020 for treatment of diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), and chronic lymphocytic leukemia (CLL).

### Market size and competition landscape of rituximab biosimilars

Rituxan's worldwide sales peaked at US\$7,547mn in 2014, according to Evaluate Pharma.

**Figure 21: Aggregate worldwide sales of Rituxan (2010-2020)**



Source: Evaluate Pharma, CMBIS

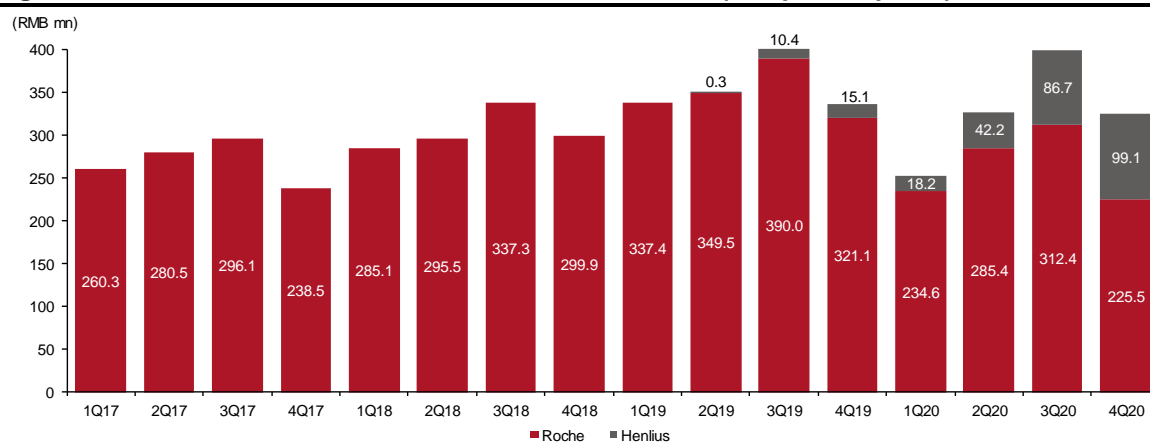
To date, the NMPA has approved two rituximab biosimilars with Innovent's Halpryza being the second-to-market rituximab biosimilar in China. In addition, six rituximab biosimilars under phase III trials in China. We think the competition in rituximab market in China is moderate compared with other biosimilars and Innovent enjoys early mover advantages.

**Figure 22: Development landscape of rituximab biosimilars in China (only late-stage included)**

Compound	Company	Progress	Last update date	Related Clinical trials
IBI301	Innovent	Approved	2020-09-30	CTR20160770, CTR20160493, CTR20140762
HLX01	Henlius	Approved	2019-02-22	CTR20150727, CTR20150583, CTR20140764, CTR20140400, CTR20171434
H02	New Time Pharmaceutical	Phase III	2020-08-17	CTR20170502, CTR20200889
SHSW	SIBP CNBG	Phase III	2019-07-01	CTR20181068, CTR20191124
WBP263	Hualan Genetic	Phase III	2019-04-17	CTR20171351, CTR20190424
TQ	Chia Tai-Tianqing	Phase III	2018-12-11	CTR20171394, CTR20182377
GB241	Genor	Phase III	2018-11-28	CTR20160948, CTR20181465
JHL1101	Chime Biologics	Phase III	2018-09-30	CTR20181725, CTR20181696

Source: Insight, Companies' data, CMBIS

According to PDB, the quarterly sales of Rituxan peaked in 3Q19, while the sales of Henlius Biotech's HLX01 maintained rapid growth. As the second rituximab biosimilar approved in China, we expect Halpryza to gain significant market share in China.

**Figure 23: Sales of rituximab and its biosimilars in China (sample hospitals)**

Source: PDB, CMBIS

## IBI303: an adalimumab (TNF- $\alpha$ ) biosimilar

Adalimumab is a fully human monoclonal antibody that can be used for treatment of various inflammatory and immune diseases. Adalimumab has been approved worldwide for the treatment of 17 diseases, including rheumatoid arthritis, ankylosing spondylitis, psoriasis, psoriasis arthritis, juvenile idiopathic arthritis, Crohn's disease (including pediatric Crohn's disease), ulcerative colitis, hidradenitis suppurativa, uveitis, etc. Humira was approved in China in 2020 for treatment of rheumatoid arthritis, ankylosing spondylitis and psoriasis.

IBI303 (Sulinno) is adalimumab biosimilar developed by Innovent, and its clinical results were published in the Inaugural Issue of *The Lancet Rheumatology* in 2019. Innovent has completed a Phase 3 clinical trial in China to evaluate the safety, efficacy and immunogenicity of IBI303 compared to Humira at a dose level of 40 mg subcutaneous (SC) Q2W in adult patients with active ankylosing spondylitis.

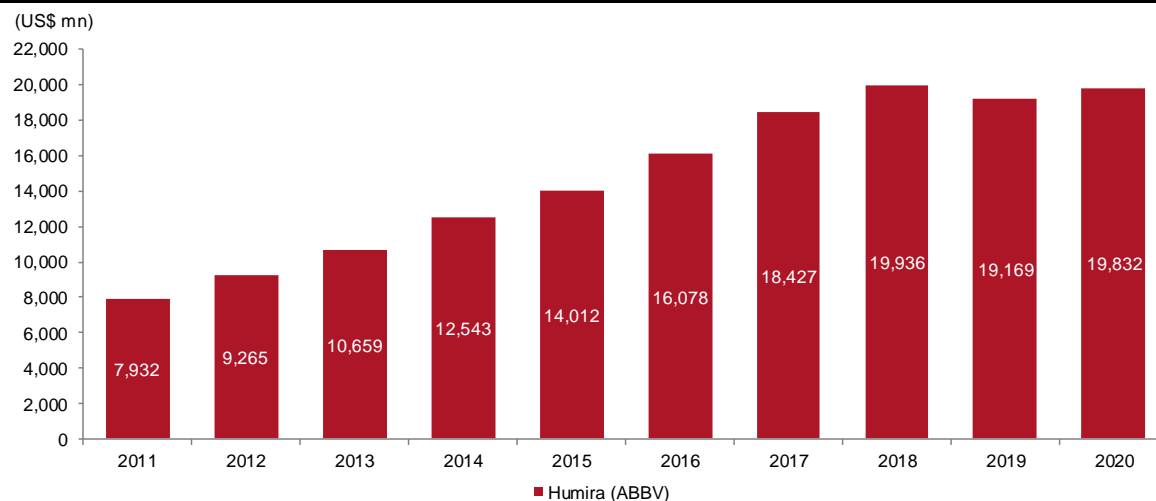
Sulinno was firstly approved by NMPA for the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriasis in Sep 2020. In Nov 2020, Sulino was further approved by NMPA for the treatment of polyarticular juvenile idiopathic arthritis (pJIA). In Dec 2020, Sulino obtained approvals for two new

indications, including 1) pediatric plaque psoriasis and 2) non-infectious intermediate uveitis, posterior uveitis and panuveitis in adults.

### Market size and competition landscape of adalimumab biosimilars

Humira is the best-selling drug among all anti-TNF $\alpha$  mAbs with its worldwide sales peaked at US\$19,936mn in 2018, according to the Evaluate Pharma.

**Figure 24: Aggregate worldwide sales of Humira (2011-2020)**



Source: Evaluate Pharma, CMBIS

To date, the NMPA has approved four adalimumab biosimilars which were developed by Bio-Thera, Hisun Pharma, Innovent and Henlius. Innovent's Sulinno was the third approved adalimumab biosimilar in China. In addition, two adalimumab biosimilars developed by Chia Tai Tianqing and Shanghai Junshi have filed NDA and additional five biosimilars are under phase III trials. Competition in China's adalimumab market is very fierce.

**Figure 25: Clinical landscape of adalimumab biosimilars in China (only late-stage included)**

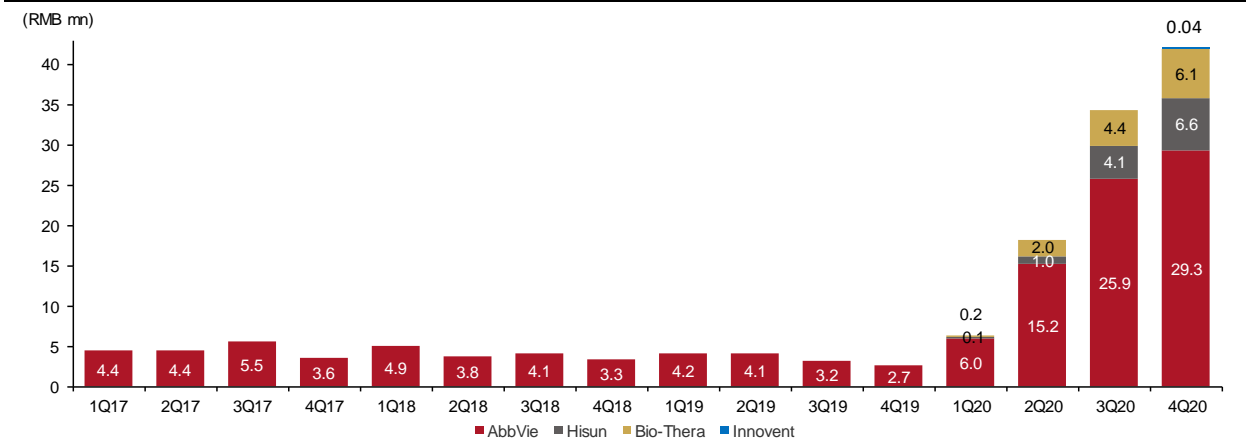
Compound	Company	Progress	Last update date	Related Clinical trials
IBI303	Innovent	Approved	2020-09-02	CTR20160687, CTR20160628, CTR20160219
HLX03	Henlius	Approved	2020-12-02	CTR20160930, CTR20171123
HS016	Hisun Pharmaceutical	Approved	2019-12-06	CTR20160450, CTR20160398
BAT1406	Bio-Thera	Approved	2019-11-04	CTR20160825, CTR20160565, CTR20160267, CTR20170188
TQZ2301	Chia Tai Tianqing	NDA	2020-06-16	CTR20182070, CTR20181863
UBP 1211	Shanghai Junshi	NDA	2019-11-13	CTR20160711, CTR20170415
WHSW	WIBP CNBG	Phase III	2020-11-03	CTR20191036, CTR20202167
BC002	Danhong Pharmaceutical	Phase III	2020-08-10	CTR20190678, CTR20201600
HL01	Hualan Genetic	Phase III	2020-02-07	CTR20180539, CTR20200016
SCT630	SCT	Phase III	2019-06-06	CTR20182380, CTR20190933
DB101	Tonghua Dongbao Pharmaceutical	Phase III	2019-02-26	CTR20170863, CTR20190112

Source: Insight, Companies' data, CMBIS

Data from PDB showed that China's adalimumab market experienced significant growth in 2020 which was mainly due to the NRDL inclusion of the drug from the beginning of 2020. With the launch of more

adalimumab biosimilars, the overall market will continue to grow thanks to improving affordability, in our view.

**Figure 26: Sales of adalimumab and its biosimilar in China (sample hospitals)**



Source: PDB, CMBIS

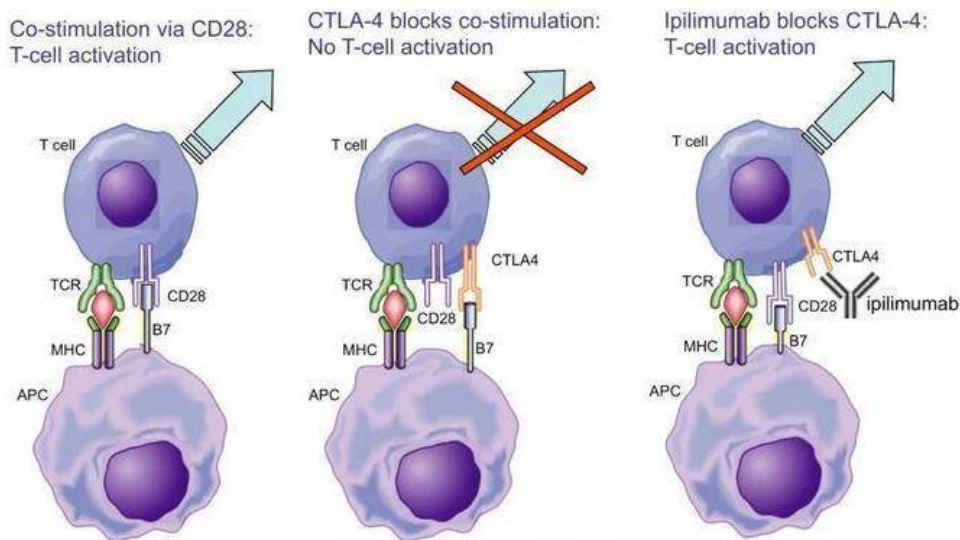
## Blockbuster oncology candidates entering into commercial stage

### IBI310: a CTLA-4 antibody

#### Mechanism of action

IBI310 is a fully human mAb that binds to an immune checkpoint inhibitor called Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) which Innovent owns global rights. Similar to PD-1, CTLA-4 receptors are located on the surface of T cells and are negative regulators of T-cell immune function. CTLA-4 binding to B7 prevents T cells from killing other cells, including cancer cells. Unlike PD-1, CTLA-4 regulates T-cell proliferation early in an immune response, whereas PD-1 suppresses T cells later in an immune response. Inhibition of CTLA-4 results in increased activation of the immune system (releasing the 'brakes' on the immune system), hence enabling T cells to kill cancer cells.

**Figure 27: MOA of CTLA-4 blocking in tumor therapy**



Source: Lebbé et al. ESMO 2008, CMBIS

CTLA-4 provides a new approach for immunotherapy in many diseases, including tumors. IBI310 can interfere with the binding of CTLA-4 and CD80/CD86 on antigen presenting cells, thereby blocking the inhibitory effect on T cell activation. IBI310 can promote the activation and amplification of T cells, and enhance the anti-tumor ability of the immune system.

#### IBI310 has rich combination opportunities with Tyvyt

Ipilumab (Yervoy) developed by BMS has been the only approved CTLA-4 antibody drug worldwide. To date, the US FDA has approved Yervoy in combination with Opdivo for treatment of various types of cancer, including melanoma, RCC, CRC, HCC, NSCLC and malignant pleural mesothelioma.

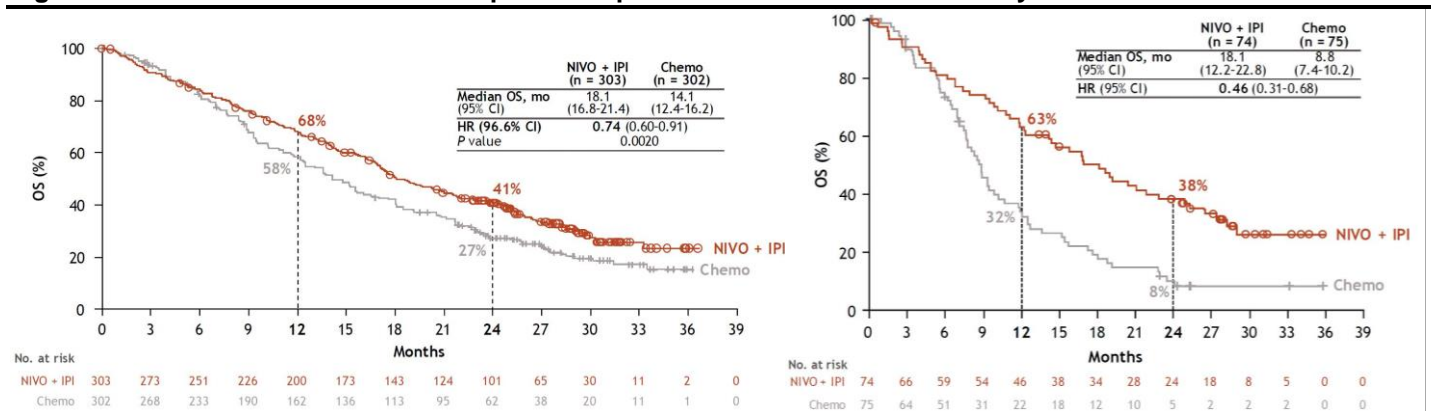
In Jun 2021, the NMPA approved Yervoy in combination with Opdivo (nivolumab, PD-1 antibody) as a first line treatment of unresectable non-epithelioid malignant pleural mesothelioma (非上皮样恶性胸膜间皮瘤). This is the first immune-combination therapy approved in China.

The phase III CheckMate-743 trial is the first study that has shown improved OS with first-line Opdivo+Yervoy vs platinum-based chemotherapy in patients with unresectable malignant pleural

mesothelioma. In this open-label trial, 605 patients from sites in 21 countries were randomly assigned to receive Opdivo+Yervoy (n=303) or chemotherapy (n=302). Opdivo was given at 3 mg/kg every 2 weeks and Yervoy at 1 mg/kg every 6 weeks for up to 2 years. Chemotherapy consisted of cisplatin or carboplatin plus pemetrexed. Median overall survival was 18.1 months (95% confidence interval [CI]=16.8–21.4 months) in the Opdivo+Yervoy group vs 14.1 months (95% CI=12.4–16.2 months) in the chemotherapy group (HR=0.74, 96.6% CI = 0.60–0.91, P=0.0020). Moreover, at 2 years, 41% of patients treated with the Opdivo+Yervoy combination were alive compared to just 27% of patients who underwent chemotherapy treatment.

In addition, the Opdivo+Yervoy dual immunotherapy also showed improvements in survival rates in non-epithelioid malignant pleural mesothelioma subgroup (n=74). Median OS was doubled in the dual immunotherapy combination group (n=74) at 18.1 months compared to chemo group (N=75) at 8.8 months (HR, 0.46; 95% CI, 0.31-0.68). This combination therapy received NMPA approval for this indication in Jun 2021.

**Figure 28: OS in all-comers and non-epithelioid patients in Checkmate-743 study**



Source: The Lancet. 2021; 397: 375-386; CMBIS

IBI310 is developed by Innovent as an innovative drug candidate in accordance with NMPA regulations even though IBI310 has the same amino acid sequence as ipilimumab. In Jun 2020, Innovent announced the preliminary results of the Phase 1 clinical trial about anti-CTLA-4 monoclonal antibody (NCT03545971) at the 56th ASCO Meeting (Abstract No. 302489).

The NCT03545971 study is an open-label study and was consisted of two parts, namely phase 1a study and phase1b study, which were designed to evaluate the tolerability, safety and anti-tumor activity of IBI310 and its combination with Tyvyt in the treatment of subjects with advanced malignant tumors, respectively. In the phase 1a study, subjects with advanced solid tumors who have progressed from standard treatment were dosed with IBI310; while in the phase 1b study, subjects with advanced melanoma were treated with IBI310 in combination with Tyvyt.

As of 12 Nov 2019, a total of 10 subjects were enrolled in phase 1a study and 17 subjects were enrolled in phase 1b study. There were no DLTs in both phases, and the dose expansion in phase 1b is currently ongoing. The most common treatment related AE was pruritus in both phase 1a and phase 1b studies, and no Grade 3 or higher AEs occurred in phase 1a and only one subject in phase 1b experienced a grade 3 or higher TRAE (AST increased). There were no TEAE caused death.

**Figure 29: Phase 1a/1b safety data of IBI310 (N=27)**

Melanoma subtypes	Phase 1a: IBI310 (N=10)	Phase 1b: IBI310+Tyvyt (N=17)
Mucosal	4 (60%)	5 (31.3%)
Acral	3 (30%)	2 (12.5%)
Non-chronic sun damaged	1 (10%)	9 (56.3%)
Chronic sun damaged	0	1 (5.9%)

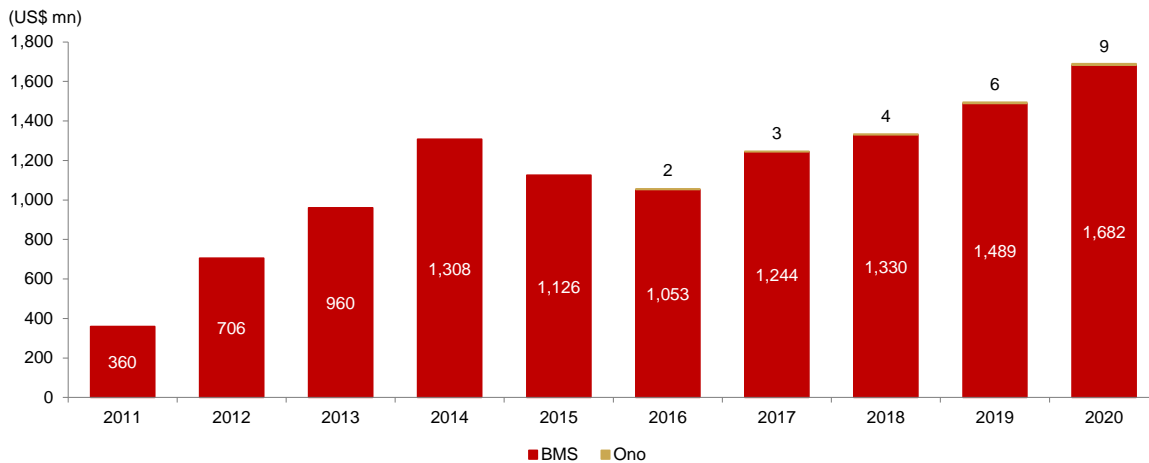
Melanoma subtypes	Phase 1a: IBI310 (N=10)	Phase 1b: IBI310+Tyvyt (N=17)
DLT	No DLT	No DLT
AE ≥ grade 3	No AE ≥ grade 3	One AEs ≥ grade 3: AST increased

Source: ASCO 2020, CMBIS

Currently, Innovent is assessing IBI310 in combination with Tyvyt in several clinical studies in China, including a phase 3 trial for adjuvant treatment of melanoma (FPI in Apr 2020), a pivotal Phase 2 trial for the second line or after of cervical cancer (FPI in Dec 2020), and a phase 3 trial for the first line of HCC (FPI in Feb 2021).

### Commercial prospects and competitive landscape of CTLA-4 antibody

Yervoy is the only approved CTLA-4 antibody drug worldwide. Yervoy is promoted by BMS and Ono Pharma together, and recorded worldwide sales of US\$1,691mn in 2020.

**Figure 30: Aggregate worldwide sales of Yervoy**

Source: Evaluate Pharma, CMBIS

Yervoy was approved in China in Jun 2021, becoming the first-to-market CTLA-4 antibody in China. In addition, IBI310 and AstraZeneca's tremelimumab are the two CTLA-4 monoclonal antibodies (mAbs) under phase 3 trials in China. We think IBI310 has potential to become the third-to-market CTLA-4 mAb in China, following Yervoy and tremelimumab.

There are two CTLA-4 based bispecific antibodies developed by domestic biotech companies, including KN046 (PD-L1/CTLA-4 bispecific antibody) developed by Alphamab and AK104 (PD-1/CTLA-4 bispecific antibody) developed by Akeso. Both of these two bispecific antibodies are now in pivotal trials in China.

We believe Innovent's inhouse combination of IBI310 (CTLA-4 antibody) and Tyvyt (PD-1 antibody) will enjoy significant competitive advantages in terms of combination clinical trials, combination commercial promotion and cost efficiencies.

**Figure 31: CTLA-4 antibodies competition landscape in China (only late-stage candidates included)**

Candidates	Targets	Companies	Indications	Progress
Ipilimumab	CTLA-4	BMS	malignant pleural mesothelioma, NSCLC, SCLC, melanoma, NPC, HCC, RCC, CRC, GC, UC	Approved in Jun 2021
Tremelimumab	CTLA-4	AstraZeneca	NSCLC, SCLC, HCC, UC	Phase 3
<b>IBI310</b>	<b>CTLA-4</b>	<b>Innovent</b>	<b>Melanoma, CRC, HCC</b>	<b>Phase 3</b>
KN046	PD-L1/CTLA-4	Alphamab	NSCLC, HCC, Thymic cancer, TNBC, GC	Phase 3
AK104	PD-1/CTLA-4	Akeso	NPC, PTCL, NSCLC, GC, Melanoma, TNBC, Cervical cancer, UC, HCC	Pivotal Phase 2
HL06 (Ipilimumab biosimilar)	CTLA-4	Hualan Bio	Solid tumor	Phase 2
Quavonlimab (MK-1308)	CTLA-4	MSD	Solid tumor	Phase 2
YH001	CTLA-4	Eucure Biopharma	Melanoma, solid tumor	Phase 2

Source: Insight, CMBIS

## IBI375 (pemigatinib), an innovative FGFR1/2/3 inhibitor

### Strategic partnership with Incyte

In Dec 2018, Innovent and Incyte entered into a strategic collaboration for three clinical-stage product candidates discovered and developed by Incyte, including pemigatinib (FGFR1/2/3 inhibitor), itacitinib (JAK1 inhibitor) and piasclisib (PI3K $\delta$  inhibitor). Innovent has received the rights to develop and commercialize the three assets in hematology and oncology in Mainland China, Hong Kong, Macau and Taiwan.

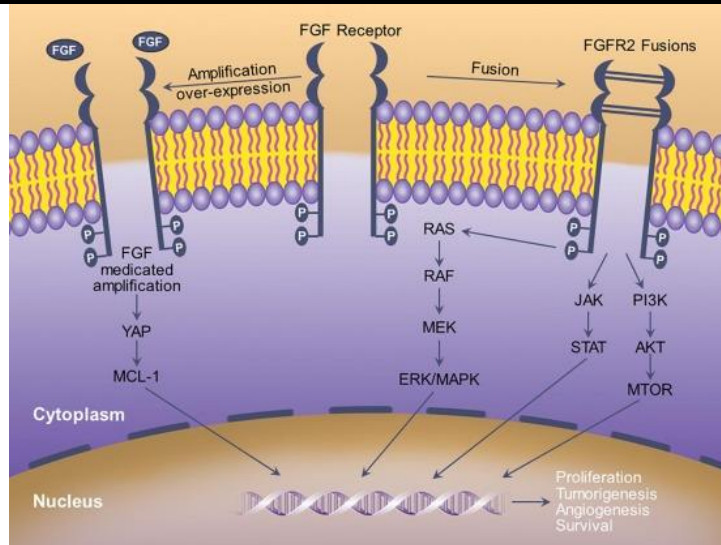
Innovent paid US\$40mn upfront payment to Incyte and agreed to pay up to US\$129mn potential development and regulatory milestones. After commercialization, Innovent will pay up to US\$202.5mn potential sales milestones and tiered royalties from the highteens to the low-twenties on future sales revenue.

### MoA of FGFR1/2/3 inhibitor

Fibroblast growth factor receptors (FGFRs) play an important role in tumor cell proliferation and survival, migration and angiogenesis (the formation of new blood vessels). Activating fusions, rearrangements, translocations and gene amplifications in FGFRs are closely correlated with the development of various cancers.

Pemazyre (pemigatinib) is a potent, selective, oral inhibitor of FGFR isoforms 1, 2 and 3. In preclinical studies, Pemazyre has demonstrated selective pharmacologic activity against cancer cells with FGFR alterations.



**Figure 32: FGFRs play an important role in tumor cell proliferation and survival**


Source: Cancer Treatment Reviews, Volume 78, Aug 2019, Pages 1-7, CMBIS

Pemazyre has already been marketed by Incyte in the US, Europe and Japan. The US FDA had granted Pemazyre Breakthrough Therapy designation for the treatment of previously treated, advanced/metastatic or unresectable FGFR2 translocated cholangiocarcinoma. In Apr 2020, the US FDA approved Pemazyre for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or rearrangement as detected by an FDA-approved test.

Cholangiocarcinoma is a rare cancer that forms in the bile duct. It is classified based on its anatomical origin: intrahepatic cholangiocarcinoma (iCCA) occurs in the bile duct inside the liver and extrahepatic cholangiocarcinoma occurs in the bile duct outside the liver. In Asia, cholangiocarcinoma is the second most common primary liver cancer with a high incidence due to relatively widespread infection of HBV and parasites. FGFR2 fusions or rearrangements occur almost exclusively in iCCA, where they are observed in 10-16% of patients.

Patients with cholangiocarcinoma are often diagnosed at a late or advanced stage when the prognosis is poor. The treatment options for patient who relapse after surgery or have advanced / metastatic disease are limited and the recommended therapy method is systemic chemotherapy with gemcitabine plus cisplatin, which has a medium overall survival of less than a year.

Data from previous clinical trials of Pemazyre in participants with advanced cholangiocarcinoma with FGFR2 fusion as second line or later treatment has demonstrated satisfactory safety and compelling efficacy signals.

### Development status of Pemazyre (pemigatinib)

**In the US**, in Apr 2020, the US FDA has approved Pemazyre for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a FGFR2 fusion or other rearrangement. Pemazyre is the first and only FDA-approved treatment for this indication, which was approved under accelerated approval based on the results from a phase 2 study (FIGHT-202, NCT02924376). The study included three cohorts: Cohort A (FGFR2 fusions or rearrangements), Cohort B (other FGF/FGFR genetic alterations) and Cohort C (no FGF/FGFR genetic alterations).

In cohort A (FGFR2 fusions or rearrangements), Pemazyre monotherapy resulted in a confirmed ORR of 36% (38/107) based on an independent central radiographic review, including 3 patients (3%) with

CR and 35 patients (33%) with PR. In these patients. The DCR was 82%, median DoR was 7.5 months, and median PFS was 6.9 months. Preliminary OS data were 21.1 months.

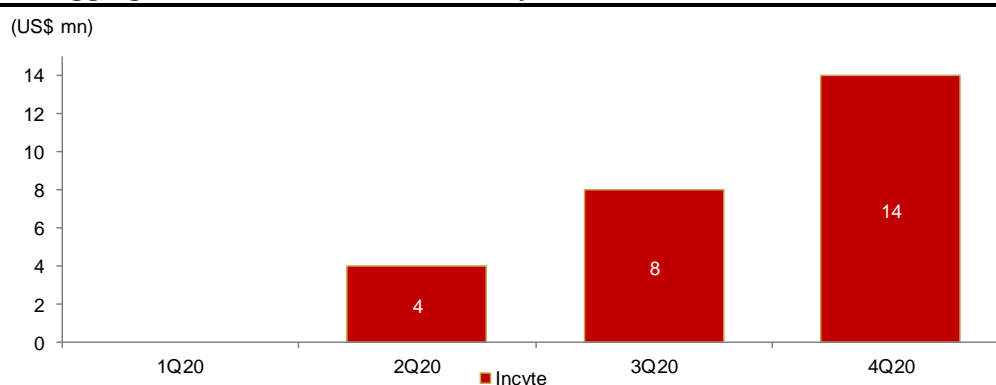
**Figure 33: Efficacy data of Pemazyre in 2L+ cholangiocarcinoma in FIGHT-202 trial**

Cohorts	Cohort A FGFR2 fusions or rearrangements	Cohort B Other FGF/FGFR genetic alterations	Cohort C No FGF/FGFR genetic alterations
Patients (N)	107	20	18
ORR	36%	0%	0%
CR	3%	0%	0%
PR	33%	0%	0%
SD	47%	40%	22%
DCR	82%	40%	22%
mDoR	7.5m	NA	NA
mPFS	6.9m	2.1m	1.7m
mOS	21.1m	6.7m	4.0m

Source: ESMO 2019, CMBIS

According to Evaluate Pharma, the global sales of Pemazyre reached US\$14mn in 4Q20 and has been consistently growing in the past few quarters.

**Figure 34: Aggregate worldwide sales of Pemazyre**



Source: Evaluate Pharma, CMBIS

**In China,** in Mar 2020, Innovent has initiated a pivotal phase 2 registrational trial of pemigatinib to evaluate the efficacy and safety of pemigatinib in patients with advanced cholangiocarcinoma with FGFR2 fusions or rearrangements who have progressed from at least one prior systemic therapy in China. Innovent also joined the global phase 3 trial sponsored by Incyte evaluating pemigatinib for 1L cholangiocarcinoma (FIGHT-302 study) with the first patient in China dosed in May 2021.

In Jul 2021, the NMPA accepted the NDA for pemigatinib for the treatment of 2L mCAA with FGFR2 fusion or rearrangement. The NDA submission to NMPA was based on the CIBI375A201 Study (NCT04256980), a bridging study of the FIGHT-202 (NCT02924376), which is a Phase 2, multi-center, open-label, single-arm study evaluating the safety and efficacy of in adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with FGFR2 fusion or rearrangement. Among the 108 patients with FGFR 2 fusion/rearrangement enrolled in FIGHT-202 study, receiving pemigatinib at a dosage of 13.5mg, the ORR was 37% (95% CI: 27.94%, 46.86%), including 4 complete responses (3.7%) and 36 partial responses (33.3%). The median duration of response (DOR) was 8.08 months (95% CI: 5.65, 13.14) and the median PFS based on IRRC assessment was 7.03 months (95% CI: 6.08, 10.48). Pemigatinib could provide long lasting response with a median overall survival (OS) of 17.48 months (95% CI: 14.42, 22.93).

In Jun 2021, the results of the Phase 1 study of pemigatinib in Chinese patients with advanced solid tumors were released at the ASCO Annual Meeting. 12 patients with 5 different cancer types (colorectal cancer, gastric cancer, cholangiocarcinoma, esophageal carcinoma and breast cancer) and with FGF/FGFR1-3 alterations were enrolled. As of 31 Jan 2021, all patients received at least once treatment, the safety was controllable with the most common treatment related AEs of hyperphosphatemia, decreased appetite and diarrhea. Two patients reported  $\geq$  grade 3 TRAEs, which were hyponatremia and proteinuria. There were no TEAEs leading to death or treatment discontinuation. Among 11 efficacy evaluable patients, 2 of them had PR as evaluated by investigators with 1 cholangiocarcinoma harboring FGFR2 point mutation and the other esophageal carcinoma carrying FGFR1 mutation. 3 patients had a best overall response of SD. The ORR was 16.7% (95%CI: 2–48%) and DCR was 41.7% (95%CI: 15–72%).

Competition of FGFR inhibitors in China is relatively fierce. Infigratinib of LianBio initiated a phase 3 trial in cholangiocarcinoma in Feb 2021. Pemigatinib has already started its pivotal phase 2 trial in cholangiocarcinoma in Mar 2020. We believe pemigatinib is a potential first-in-class FGFR inhibitor for treatment of cholangiocarcinoma in China.

In addition, pemigatinib was approved in the Taiwan market (trade name: Pemazyre) in Jun 2021.

**Figure 35: Clinical landscape of FGFR inhibitors in China**

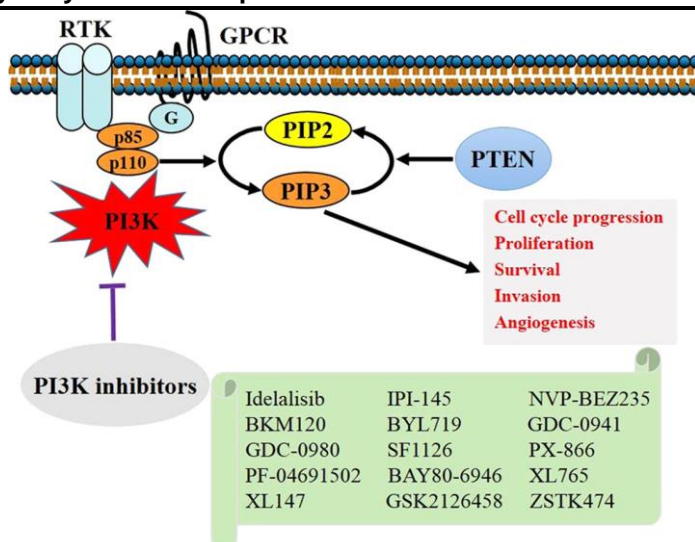
Candidates	Targets	Format	Company	Progress	Indication
Infigratinib	FGFR 1/2/3/4	Small molecule	LianBio / Novartis	Phase 3	Cholangiocarcinoma
Rogaratinib	FGFR 1/2/3/4	Small molecule	Bayer	Phase 3	UC
Pemigatinib	FGFR 1/2/3	Small molecule	Innovent/ Incyte	Pivotal Phase 2	Cholangiocarcinoma
Bemarituzumab	FGFR 2	mAb	Zailab/ Five Prime	Phase 2	GC
Derazantinib	FGFR 1/2/3/4	Small molecule	Sinovant/ Basilea Pharma	Phase 2	Cholangiocarcinoma
Fisogatinib	FGFR4	Small molecule	Cstone/ Blueprint	Phase 2	HCC
ICP-192	FGFR 1/2/3/4	Small molecule	Innocare	Phase 2	Cholangiocarcinoma, UC
ICP-105	FGFR4	Small molecule	Innocare	Phase 1	Solid tumor
AZD 4547	FGFR 1/2/3/4	Small molecule	Abbisko/ AstraZeneca	Phase 1	UC and solid tumor
BPI-17509	FGFR 1/2/3	Small molecule	Betta Pharma	Phase 1	Solid tumor
TT-00434	FGFR 1/2/3	Small molecule	TransThera Biosciences	IND approval	Solid tumor

Source: Insight, Companies' data, CMBIS

## IBI376 (parsaclisib): a differentiated PI3K $\delta$ inhibitor

In Dec 2018, Innovent entered into a research collaboration and licensing agreement with Incyte and received exclusive development and commercialization rights of parsaclisib (PI3K $\delta$  inhibitor) and other two assets in Mainland China, Hong Kong, Macau and Taiwan.

PI3K $\delta$  is an important anticancer target implicated in malignant B-cell growth, survival and proliferation which has demonstrated potency and selectivity in preclinical studies and has potential therapeutic utility in the treatment of patients with hematologic malignancies such as lymphoma.

**Figure 36: PI3K plays key roles in cell proliferation and survival**


Source: APSB, 2017: 7, 27-37; CMBIS; Note: Selected PI3K inhibitors approved or in clinical trials showed here.

Parsaclisib (IBI376) is an investigational novel oral inhibitor of phosphatidylinositol 3-kinase delta (PI3K $\delta$ ) isoforms. Parsaclisib has demonstrated potency and selectivity in preclinical studies and has potential therapeutic utility in the treatment of lymphoma.

In Mar 2021, the NMPA granted Breakthrough Therapy Designation (BTD) for parsaclisib for the treatment of patients with relapsed/refractory follicular lymphoma (r/r FL). The BTD designation for parsaclisib is based on the results observed in an ongoing pivotal phase 2 study assessing parsaclisib as a monotherapy for the treatment of relapsed or refractory FL / Marginal Zone Lymphoma (MZL) patients in China (CTR2019239). The study had first patient dosed in Apr 2020.

FL is a B-cell cancer that originates from the uncontrolled division of specific types of B-cells known as centrocytes and centroblasts. Although it is classified as indolent lymphoma, and the current immunochemotherapy has achieved good efficacy, it still often relapses following by aggressive diseases, which may lead to death within 1 to 2 years. There is an unmet medical need for treatment options for recurrent or refractory follicular lymphoma.

### Development status of Parsaclisib (IBI376)

Incyte is currently evaluating parsaclisib as a monotherapy in several ongoing phase 2 trials as treatment for non-Hodgkin lymphomas (follicular, marginal zone and mantle cell), and autoimmune hemolytic anemia. Pivotal trials of parsaclisib in combination with ruxolitinib (a JAK inhibitor) for the treatment of patients with myelofibrosis are also underway. In addition, Incyte plans to initiate a trial to evaluate parsaclisib in combination with tafasitamab for non-Hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL). Notably, the US FDA has granted orphan drug designation and Fast Track Designation (FTD) to parsaclisib as a treatment for patients with FL, MZL and mantle cell lymphoma (MCL).

**In CITADEL101 study**, a phase 1/2 clinical trial (NCT02018861), carried out by Incyte, parsaclisib has demonstrated potent efficacy and favorable safety in patients with relapsed or refractory B-cell malignancies, alone or in combination with a Janus kinase 1 inhibitor (itacitinib) or chemotherapy. 72 patients received parsaclisib monotherapy (5-45 mg once daily). Expansion doses were 20 and 30 mg once daily; intermittent dosing at 20 mg (once daily for 9 weeks, then once weekly) was explored. In

non-Hodgkin lymphoma (NHL), objective response rates to monotherapy were 71% in FL, 78% in MZL, 67% in MCL, and 30% in DLBCL. 93% of responses occurred at first assessment.

**Figure 37: Efficacy data of pascalisib in different cancers (CITADEL101 study)**

Cancer types	Patients (N)	ORR	CR/CMR	PR/PMR	SD	PD/PMD	NE/NA
DLBCL	23	30%	17%	13%	17%	48%	4%
GCB	19	32%	21%	11%	16%	47%	5%
ABC	2	50%	0%	50%	0%	50%	0%
<b>FL</b>	<b>14</b>	<b>71%</b>	<b>21%</b>	<b>50%</b>	<b>7%</b>	<b>14%</b>	<b>7%</b>
<b>MZL</b>	<b>9</b>	<b>78%</b>	<b>33%</b>	<b>44%</b>	<b>11%</b>	<b>11%</b>	<b>0%</b>
<b>MCL</b>	<b>9</b>	<b>67%</b>	<b>44%</b>	<b>22%</b>	<b>22%</b>	<b>0%</b>	<b>11%</b>
HL	10	20%	0%	20%	30%	40%	10%
CLL	6	33%	0%	33%	33%	17%	17%
WM	1	100%	0%	100%	0%	0%	0%

Source: Blood (2019) 133 (16): 1742–1752, CMBIS

Pascalisib also showed good tolerability. In the safety analysis, no dose-limiting toxicities were identified, and maximum tolerated dose was not reached. Most common nonhematologic treatment-emergent adverse events (TEAEs) were diarrhea/colitis (36%), nausea (36%), fatigue (31%), and rash (31%). Grade 3/4 neutropenia occurred in 19% of patients. Serious TEAEs (>2 patients) were diarrhea/colitis (n = 9), pyrexia (n = 4), hypotension (n = 3), and sepsis (n = 3).

**Figure 38: Major TEAEs in patients receiving pascalisib monotherapy (CITADEL101 study)**

All doses (N = 72), n (%)	Any grade	Grade 3	Grade 4
Any TEAE	68 (94)	29 (40)	12 (17)
Diarrhea/colitis	26 (36)	6 (8)	1 (1)
Nausea	26 (36)	0	0
Fatigue	22 (31)	0	0
Rash	22 (31)	4 (6)	0
Cough	17 (24)	0	0
Vomiting	17 (24)	0	0
Dizziness	13 (18)	0	0
Pyrexia	13 (18)	1 (1)	0
Hypokalemia	12 (17)	1 (1)	0
Abdominal pain	11 (15)	1 (1)	0
Constipation	11 (15)	0	0
Decreased appetite	11 (15)	0	0
Night sweats	11 (15)	0	0
Pruritus	10 (14)	0	0
Back pain	9 (13)	0	0
Chills	9 (13)	0	0
Leukopenia	36 (50)	6 (8)	0
Neutropenia	32 (44)	10 (14)	4 (6)
Lymphopenia	25 (35)	13 (18)	2 (3)
Thrombocytopenia	25 (35)	2 (3)	5 (7)
Anemia	22 (31)	6 (8)	NA

Source: Blood (2019) 133 (16): 1742–1752, CMBIS

**As for CITADEL203, CITADEL204 and CITADEL205 studies**, which were designed to enable the registration of pascalisib, preliminary results have been presented in ASH 2020 Meeting, including results in r/r FL (CITADEL203), BTK-naïve MZL (CITADEL204) and r/r MCL (CITADEL205).

In these studies, patients received pascalisib 20mg once daily for eight weeks followed by either 20mg once weekly (weekly-dosing group, WG) or 2.5mg once daily (daily-dosing group, DG). Subsequently, daily dosing was selected as the preferred regimen and patients initially enrolled in the WG were allowed to switch to DG. Objective durable responses were reported in 75% of patients with refractory FL, 57% of patients with MZL and 71% of MCL.

Figure 39: Efficacy data of pascalisib in FL, MZL and MCL (CITADEL203, 204, 205)

	ORR (95% CI), %	mDOR (95% CI), months	mPFS (95% CI), months	mOS (95% CI), months
<b>CITADEL-203: R/R FL</b>				
DG (N=95)	75 (65-83)	14.7 (12.0-17.5)	15.8 (13.8-19.1)	-
All (N=118)	73 (64-81)	15.9 (12.0-NE)	15.8 (13.2-19.3)	-
<b>CITADEL-204: R/R MZL</b>				
DG (N=72)	56.9 (44.7-68.6)	NR (8.1-NE)	NR (11.0-NE)	-
All (N=100)	57.0 (46.7-66.9)	12.0 (9.3-NE)	19.4 (13.7-NE)	-
<b>CITADEL-205: R/R MCL (BTK Inhibitor Treatment Naive)</b>				
DG (N=77)	71 (60-81)	9.0 (6.7-14.7)	11.1 (8.3-NE)	NR (NE-NE)
All (N=108)	70 (61-79)	14.7 (7.7-NE)	11.1 (8.3-19.2)	NR (NE-NE)
<b>CITADEL-205: R/R MCL (Previously Treated with Ibrutinib)</b>				
DG (N=41)	29 (16-46)	3.7 (1.9-NE)	3.7 (1.8-4.1)	11.2 (7.9-NE)
All (N=53)	25 (14-38)	3.7 (1.9-NE)	3.7 (1.8-3.9)	11.2 (7.9-17.1)

Source: ASH 2020, CMBIS

In terms of cross trial comparison, pascalisib demonstrated significantly higher ORR in FL and MZL than other major PI3K inhibitors, indicating that pascalisib has best-in-class potential thanks to superior efficacy and better safety profile (lower hepatotoxicity).

Figure 40: Pascalisib showed better efficacy than other major PI3K Inhibitors

Compound	Targets	Company	Efficacy			
			DLBCL (n)	FL (n)	MCL (n)	MZL (n)
<b>Pascalisib (US data)</b>	<b>PI3Kδ</b>	<b>Incyte</b>	<b>30% (23)</b>	<b>73% (118)</b>	<b>67% (9)</b>	<b>57% (100)</b>
ZYDELIG (idelalisib)	PI3Kδ	Gilead	NA	54% (72)	0.4	57%
COPIKTRA (duvelisib)	PI3Kδ, PI3Kγ	Takeda/ Infinity/ Verastem	NA	41% (83)	NA	33% (18)
UKONIQ (umbralisib)	PI3Kδ	TG Therapeutics	27% (11)	45% (22)	79% (11)	NA
ALIQOPA (copanlisib)	pan-PI3K	Bayer	25% (40)	59% (104)	64% (11)	70%

Source: Company presentation, CMBIS

**Opportunities in myelofibrosis as a combination therapy:** Based on positive Phase II data, Incyte has started two pivotal trials of ruxolitinib in combination with pascalisib in 1L myelofibrosis (LIMBER313) and in myelofibrosis patients with a suboptimal response to ruxolitinib monotherapy (LIMBER304), respectively.

**Development status in China:** Innovent is conducting a pivotal phase 2 registrational trial in China evaluating the efficacy and safety of pascalisib in patients with r/r FL or MZL with first patient dosed in Apr 2020. We expect Innovent to file NDA for pascalisib in China for r/r FL in early 2022E. Innovent also plans to start the China part of the Incyte-sponsored global Phase 3 trial for pascalisib in combination with ruxolitinib for the second line treatment of myelofibrosis in 2021.

### Clinical landscape of PI3K inhibitors

**Globally,** many PI3K inhibitors are being tested in various clinical trials. To date, five PI3K inhibitors (Idelalisib, copanlisib, duvelisib, alpelisib and umbralisib) have been approved by the US FDA.

1) Zydelig (idelalisib), an oral PI3K $\delta$  inhibitor, was the first FDA-approved PI3K inhibitor for the treatment of patients with r/r CLL/SLL or FL who progressed on prior therapies. It's worth noting that Zydelig carries a blackbox warning due to safety concerns such as hepatotoxicity, diarrhea, pneumonitis, etc.

2) Aliqopa (copanlisib) is an intravenous highly potent and reversible pan-class I PI3K inhibitor with significant activity against  $\alpha$  and  $\delta$  isoforms. Copanlisib was approved by the US FDA for treatment of patients with relapsed FL with at least two prior systemic therapies.

3) Copiktra (duvelisib), an oral highly selective PI3K  $\delta/\gamma$  inhibitor, was approved by US FDA in 2018 for the treatment of adult patients with r/r CLL/SLL after at least two prior therapies and r/r FL after at least two prior systemic therapies. Copiktra also carries a black box warning.

4) Piqray (alpelisib) is a potent oral selective PI3K $\alpha$  inhibitor targeting PIK3CA mutated cancers. In 2019, the US FDA approved Piqray in combination with fulvestrant for the treatment of HR+/HR $^-$ , PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

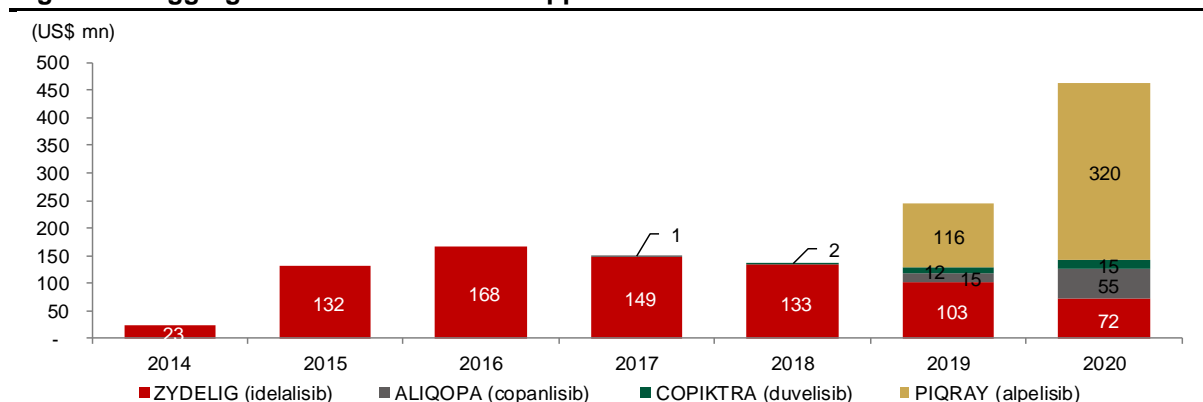
5) Ukoniq (umbralisib) is a next-generation highly specific, oral inhibitor targeting the  $\delta$  isoform of PI3K. Ukoniq was approved by US FDA in Feb 2021 for r/r MZL with at least one prior anti-CD20-based regimen and r/r FL with at least three prior lines of systemic therapy.

**Figure 41: Global approved PI3K inhibitors**

Compound	Targets	Company	Time of FDA approval	Approved indications	Administration
ZYDELIG (idelalisib)	PI3K $\delta$	Gilead	2014	r/r CLL in combination with rituximab r/r FL with at least two prior systemic therapies r/r SLL with at least two prior systemic therapies	Oral
ALIQOPA (copanlisib)	pan-PI3K	Bayer	2017	r/r FL with at least two prior systemic therapies	I.V.
COPIKTRA (duvelisib)	PI3K $\delta$ , PI3K $\gamma$	Takeda/ Verastem/ Secura Bio	2018	r/r CLL/SLL with at least two prior systemic therapies r/r FL with at least two prior systemic therapies	Oral
PIQRAY (alpelisib)	PI3K $\alpha$ (PIK3CA)	Novartis	2019	Postmenopausal women with adv/m BC (HR+/HER2-/PIK3CAm)	Oral
UKONIQ (umbralisib)	PI3K $\delta$	TG Therapeutics	2021	r/r MZL with at least one prior anti-CD20-based regimen r/r FL with at least three prior lines of systemic therapy	Oral

Source: Int. J. Mol. Sci. 2021, 22, 3464, CMBIS

**Figure 42: Aggregate worldwide sales of approved PI3K inhibitors**



Source: Evaluate Pharma, CMBIS

**In China**, there are more than twenty PI3K inhibitor candidates under clinical research. More than five PI3K candidates have entered into pivotal clinical studies. However, most of these candidates are pan-PI3K inhibitors, which may have unwanted safety AEs, including nausea, vomiting, fatigue, diarrhea, increase in AST/ALT and hyperglycemia, etc. Innovent's pascalisib is a next-generation highly selective potent PI3K $\delta$  inhibitor with superior safety profile and potent efficacy.

**Figure 43: Clinical landscape of PI3K inhibitors in China (only late-stage candidates included)**

Compound	Targets	Company	Progress	Indications
Copanlisib	PI3K $\delta$ /PI3K $\alpha$	Bayer	NDA	FL
Duvelisib	PI3K $\gamma$ /PI3K $\delta$	CSPC	NDA	FL
YY-20394	PI3K $\delta$	YL-Pharma	NDA	FL
Alpelisib	PI3K $\alpha$	Novartis	Phase 3	BC, TNBC
Buparlisib	Pan-PI3K	Adlai Nortye	Phase 3	HNSCC
GDC-0077	PI3K $\alpha$	Roche	Phase 3	BC
<b>Pascalisib</b>	<b>PI3K<math>\delta</math></b>	<b>Innovent</b>	<b>Pivotal Phase 2</b>	<b>FL, MZL</b>
BEBT-908	PI3K	BeBetter Med	Phase 2	CLL/SLL, FL, MZL, DLBCL, PTCL
HMPL-689	PI3K $\delta$	Chi-Med	Phase 2	FL, MZL
TQ-B3525	PI3K $\gamma$ /PI3K $\delta$	Chia-Tai Tianqing	Phase 2	FL, MCL
SHC014748M	PI3K $\delta$	SanHome Pharmaceutical	Phase 2	PTCL, FL, MZL

Source: Insight, companies' data, CMBIS

## Taletrectinib: a next-generation ROS1/NTRK inhibitor

In Jun 2021, Innovent and AnHeart Therapeutics (Anheart) announced an exclusive license agreement for the co-development and commercialization of taletrectinib in Greater China, including Mainland China, Hong Kong, Macau and Taiwan. According to the agreement, AnHeart will receive an upfront payment, R&D fees, and potential milestone payments totaling US\$189mn in addition to tiered royalties based on annual net sales of taletrectinib in Greater China.

Taletrectinib is an investigational next-generation TKI designed to effectively target ROS1 and NTRK fusion mutations with potential to treat TKI-naïve or pre-treated patients. ROS1 rearrangement is estimated to be an oncogenic driver in approximately 2-3% of NSCLC patients, and NTRK rearrangement is estimated to be an oncogenic driver in approximately 0.5% of patients with other advanced solid tumors.

In Jun 2021, the preliminary results from a phase II clinical study to investigate taletrectinib in treating patients with ROS1 fusion positive NSCLC (NCT04395677) were presented at the ASCO 2021 Annual Meeting. In the crizotinib treatment-naïve patients (n=15), the overall response rate (ORR) was 93% (14/15) and the disease control rate (DCR) was 93% (14/15). In the crizotinib pre-treated patients (n=5), the ORR was 60% (3/5); and the DCR was 100% (5/5). ROS1 G2032R resistant mutations were identified in three of the five patients and all three patients experienced tumor regressions. In addition, taletrectinib has shown a manageable safety profile characterized primarily by gastrointestinal adverse events, with reversible increases of aspartate aminotransferase (AST) and alanine aminotransferase (ALT).



**Figure 44: Competitive analysis of approved and investigational ROS1 NSCLC agents**

Compound	Sponsor	Status	BBB <sup>5</sup>	Median PFS	ORR	Efficacy against crizotinib resistance
Crizotinib	Pfizer	Approved for ROS1 NSCLC in all major markets	✗	15.9 mon <sup>1</sup>	72% (n=127) <sup>1</sup>	✗
Entrectinib	Roche	Approved for ROS1 NSCLC in Japan and US	✓	15.7 mon <sup>2</sup>	67.1% (n=161) <sup>2</sup>	✗
Repotrectinib	Turning Point Therapeutics	Phase II	✓	Naïve: 24.6 mon (N=11) 1 prior TKI: 3.6 mon (N=18) <sup>3</sup>	Naïve: 12/14 (86%) <sup>6</sup> 1 prior TKI: 7/18 (39.0%) <sup>3</sup>	✓
Taletrectinib	AnHeart Therapeutics	Phase II	✓✓	Naïve: <b>29.1</b> mon (N=11) 1 prior ROS1 TKI: <b>14.2</b> mon (N=8) <sup>4</sup>	Naïve: 6/9 (66.7%) 1 prior ROS1 TKI: 2/6 (33.3%) <sup>4</sup>	✓

Source: AnHeart Therapeutics, CMBIS

- Note: 1. Crizotinib PFS is based on an East Asian study, which is comparable to taletrectinib Phase I patient population; this study does not include brain metastatic patients, but taletrectinib and entrectinib studies included brain metastatic patients
2. Krebs, M.G. et al Efficacy and safety of entrectinib in locally advanced/metastatic ROS1 fusion positive NSCLC: An updated integrated analysis. *Annals of Oncology* (2020) 31 (suppl\_4): S754-S840. 10.1016/annonc/annonc283
3. Based on page 22 of TP's November 20, 2019 company overview, describing phase 1 results of repotrectinib with data cutoff in July 2019.
4. Based on US and Japan Phase 1 studies with data cutoff on 19 Aug 2020.
5. BBB refers to ability to cross the blood brain barrier.
6. Based on phase 1 (n=7 cutoff date 22 Jul 2019) + phase 2 (n=7 cutoff date 10 Jul 2020) combined data of patients at or above phase 2 recommended dose. See Turning Point October 2020 corporate presentation.

Taletrectinib is currently undergoing three phase 2 studies, including 1) the phase 2 study for first line treatment of TKI-naïve and second line treatment of TKI-pretreated ROS1-positive NSCLC in China, 2) the phase 2 basket study for NTRK-positive solid tumors in China (FPI on 18 Jun 2021), and 3) the phase 2 study for first line and second line treatment of ROS1-positive NSCLC globally. We expect taletrectinib to receive approval from NMPA in 2023E.

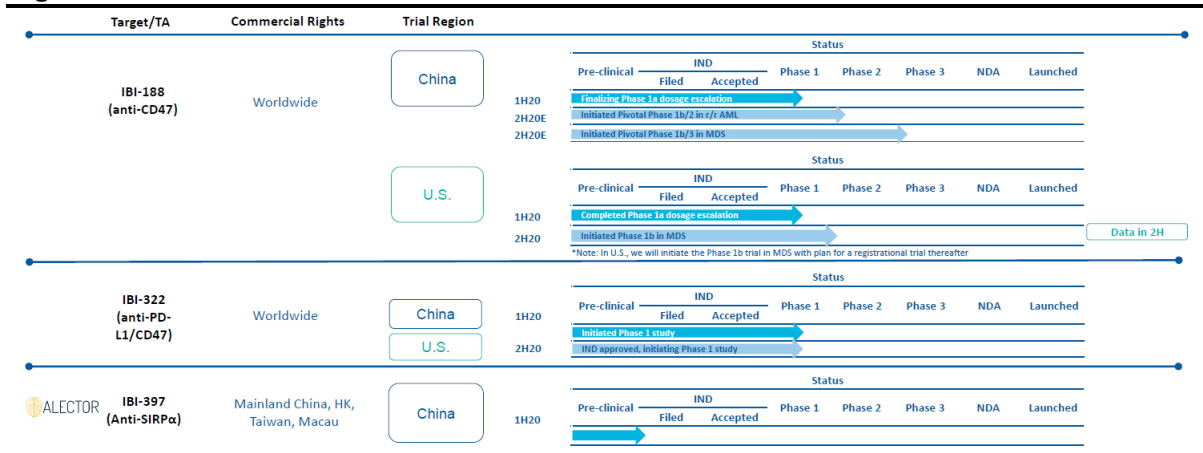
## Lead positioning in next-generation I/O targets

### Strong franchise in CD47-SIRPα pathway

Leveraging its strong R&D capacity, Innovent has built up a comprehensive innovative portfolio covering next-generation immuno-oncology (I/O) targets, including CD47/ SIRPα, TIGIT, LAG3, 4-1BB, etc.

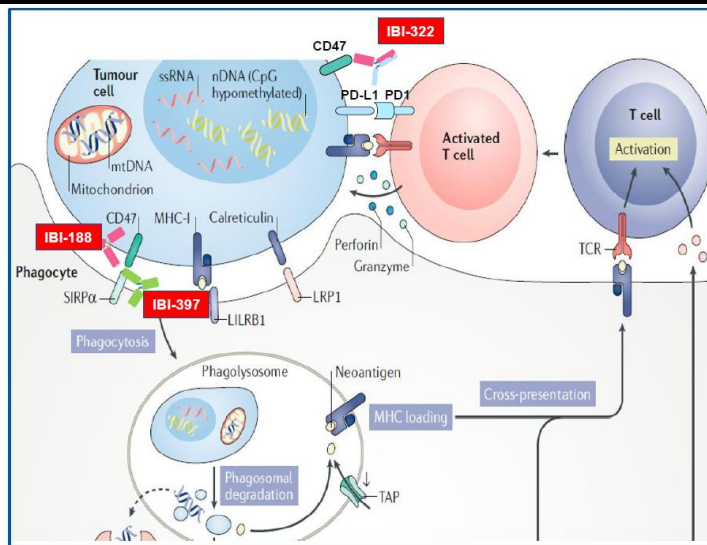
It's worth noting that Innovent is an early mover in CD47-SIRPα pathway with three assets under development, including clinical-stage IBI188 (a CD47 antibody) and IBI322 (a PD-L1/CD47 bispecific antibody), and preclinical stage IBI397 (AL008, a SIRPα antibody).

**Figure 45: Innovent's CD47/SIRPα franchise**



Source: Company presentation, CMBIS

CD47/ SIRPα is the next potential blockbuster I/O target following PD-1/PD-L1. Unlike other immuno-oncology targets being explored, the CD47-SIRPα pathway is involved in tumor progression by delivering a “don't eat me” signal to tumor-engulfing macrophages, thereby protecting tumors from natural attacks by macrophages. Blockade of this pathway represents one of the most effective tumor killing mechanisms and may synergize with T cell checkpoint inhibitors in various tumor types.

**Figure 46: MOA of CD47/ SIRP $\alpha$  blocking in tumor therapy**


Source: Company presentation, CMBIS

Anemia during CD47 treatment has been a major concern of CD47 drugs. Due to the inherent epitope sharing between tumor cells and normal red blood cells (RBCs), the first-wave of clinical stage CD47 antibodies were found in clinical trials to bind to RBCs and cause significant hematologic adverse effects, such as severe anemia, which has hampered the development of these CD47 antibodies as a potential cancer therapy.

Although there is no approved anti-CD47 therapies yet, many drug candidates are under development around the world. The most leading asset is Hu5F9-G4 (Magrolimab) developed by Forty Seven, a subsidiary of Gilead. Magrolimab is currently in Phase 2/3 clinical studies for a number of hematological cancers, including myelodysplastic syndrome, acute myeloid leukemia, nonHodgkin lymphoma and solid tumors. Magrolimab has been granted Breakthrough Therapy designation by FDA and PRIME scheme eligibility by the European Commission for the MDS indication.

Other anti-CD47 biological candidates are all in early phase of development. In China, six anti-CD47 biological candidates are in early clinical phase while another three candidates may start clinical studies soon. So far, the development of some CD47 targeting drug candidates were terminated due to hematologic adverse effects, such as SRF231 by Surface Oncology, CC-90002 by Celgene.

**Figure 47: Competition landscape in CD47/ SIRPα biological therapies**

Product	Molecule	Company	US status	China status
Magrolimab (Hu5F9-G4, GS-4721)	CD47 mAb	Gilead / Forty Seven	BTD for ewly diagnosed MDS (+ Azacitidine)	
			Phase 3 in 1L higher-risk MDS (+ Azacitidine)	
			Phase 2 in DLBCL (+ Rituximab)	
			Phase 2 in AML (+ Azacitidine)	
			Phase 1 in AML (+ Atezolizumab)	
			Phase 1/2 in DLBCL (+ Rituximab + Gem/OX)	N/A
			Phase 1 in DLBCL (+ Rituximab + Atezolizumab)	
			Phase 1 in DLBCL (+ Rituximab + Acalabrutinib)	
			Phase 1 in Bladder (+ Rituximab + Atezolizumab)	
			Phase 1/2 in CRC (+ Cetuximab)	
Phase 1 in Ovarian cancer (+ Avelumab)				
TTI-621	CD47 WT SIRPα fusion protein	Trillium Therapeutics	Phase 1 in hematologic malignancies and selected solid tumors (Mono/ +Rituximab/ +Opdivo)	N/A
TTI-622	CD47 WT SIRPα fusion protein	Trillium Therapeutics	Phase 1 in r/r Lymphoma or Myeloma (Mono/ +Rituximab/ +Opdivo/ +PI)	N/A
ALX148	CD47 affinity SIRPα fusion protein	ALX Oncology	Phase 2 in HNSCC (+ Keytruda)	
			Phase 1 in HNSCC (+ Keytruda + 5 FU + Platinum)	
			Phase 1 in GC (+ Herceptin)	
			Phase 1 in GC (+ Herceptin + Cyramza + Paclitaxel)	N/A
			Phase 1 in BC (+ Zanidatamab)	
			Phase 1/2 in higher risk MDS (+ Azacitidine)	
AO-176	CD47 mAb	Arch Oncology	Phase 1/2 in solid tumors (Mono/ +Paclitaxel)	
			Phase 1/2 in r/r MM (Mono/ +Dexamethasone/ +Dexamethasone+bortezomib)	N/A
Lemzoparlimab (TJC4, TJ011133)	CD47 mAb	I-Mab	Phase 1 in r/r advanced solid tumors and lymphoma (+ Keytruda/ + Rituximab)	Phase 1 in r/r advanced solid tumors and lymphoma (+ Keytruda/ + Rituximab)
				Phase 1/2a in r/r AML or MDS (Mono/ +Azacitidine)
TG-1801 (NI-1701)	CD47/CD19 BsAb	TG Therapeutics/ Novimmune	Phase 1 in B-cell lymphoma (Mono/ +Ublituximab)	
			Phase 1b in B-cell lymphoma or CLL (Mono/ +Ublituximab)	N/A
Letaplimab (IBI-188)	CD47 mAb	Innovent	Phase 1b in MDS (+ Azacitidine)	Phase 1b/3 in MDS (+ Azacitidine)
				Phase 1b/2 in r/r AML (+ Azacitidine)
AK117	CD47 mAb	Akeso Biopharma	Phase 1 in advanced solid tumors or lymphomas (Australia)	Phase 1 in advanced solid tumors or lymphomas
				Phase 1 in high-risk MDS (+ Azacitidine)
SI-172154	CD47/CD40 fusion protein	SHATTUCK	Phase 1 in Ovarian cancer	
			Phase 1 in HNSCC	N/A
SHR1603	CD47 mAb	Hengrui Medicine	N/A	Phase 1 in r/r NPC (Mono/ +Gemcitabine+Cisplatin/ +Albumin Paclitaxel)
				Phase 1 in advanced solid Tumors
IMM01	CD47 mAb-Trap fusion protein	Immune Onco	N/A	Phase 2 in r/r lymphoma
				Phase 1 in combination with RTK-mAb
				Phase 1 in combination with ICPI
				Phase 1 in combination with TKI
HX009	PD-1/CD47 BsAb	HanXBiopharma	Phase 1 in advanced solid Tumors (Australia)	Phase 2 in advanced solid Tumors
IMM0306	CD47/CD20 BsAb	Immune Onco	N/A	Phase 1 in r/r CD20+NHL
IBI-322	CD47/PD-L1 BsAb	Innovent	Phase 1a in advanced malignant tumors	Phase 1 in hematologic malignancy
				Phase 1 in advanced malignant tumors
				Phase 1 in advanced malignant tumors (Mono/ Combo)
ZL-1201	CD47 mAb	ZaiLab	Phase 1 in advanced cancer	Phase 1 in advanced solid tumors or lymphomas

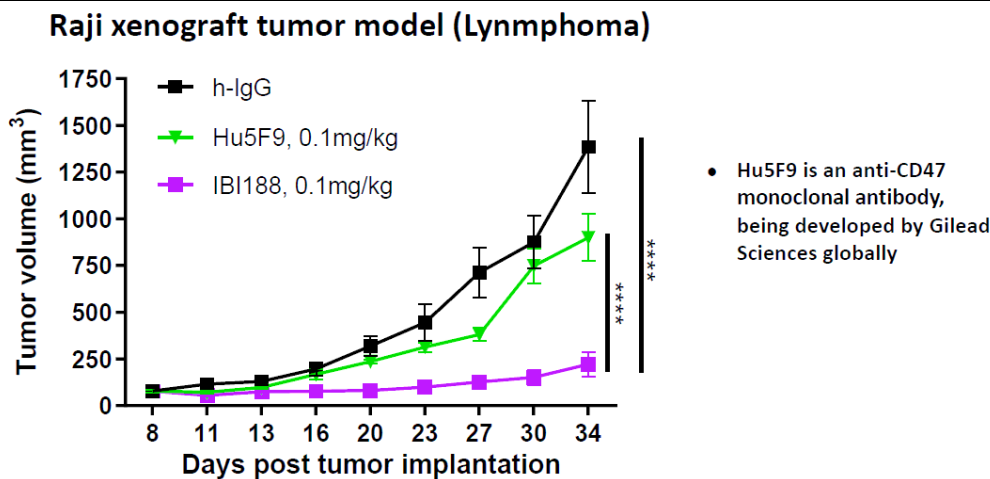
Source: Insight, Clinicaltrials.gov, CMBIS

**IBI188 (letaplimab): an innovative CD47 antibody**

IBI188 (letaplimab) is a fully human anti-CD47 IgG4 monoclonal antibody discovered by Innovent with global intellectual property rights. IBI188 binds to CD47, a surface protein that provides a “don’t eat me” signal to macrophages. Both *in vitro* and *in vivo* experiments showed that letaplimab can bind to the CD47 antigen on the surface of tumor cells, block the CD47-SIRPα signaling pathway, and promote the phagocytosis of tumor cells by macrophages, thereby exerting an anti-tumor effect.

Preclinical data showed that letaplimab had clear target, clear mechanism of action and significant efficacy. In Raji lymphoma model, IBI188 showed better anti-tumor activity than Hu5F9 at 0.1mg/kg dose, a CD47 mAb developed by Gilead.

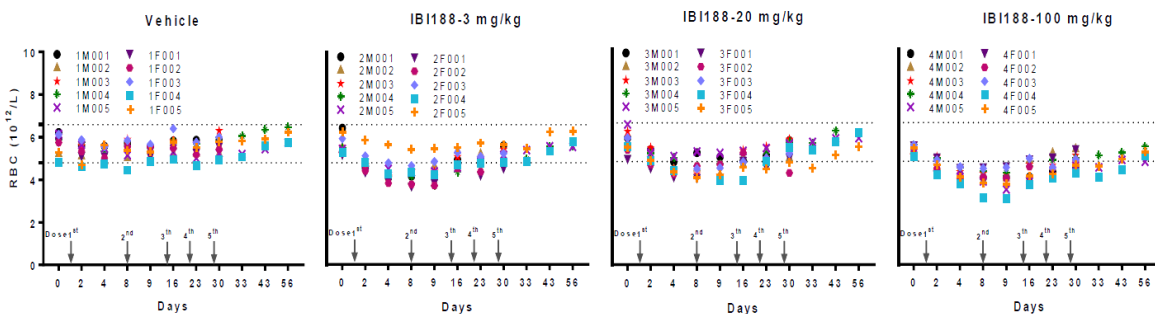
**Figure 48: IBI188 showed robust anti-tumor efficacy in Raji lymphoma model**



Source: Company presentation, CMBIS

Preclinical studies showed that IBI188 was well tolerated at doses up to 100 mg/kg in GLP multi-dose toxicity and safety studies. There was transient and reversible RBC reduction, attributed to high CD47 expression on mature erythrocytes. Thus, IBI188 adopts priming dose strategy in its clinical trials.

**Figure 49: Toxicity of IBI188 in Cynomolgus Monkeys**



Source: Company presentation, CMBIS

In Nov 2020, the results of the US Phase 1a study (NCT03763149) of IBI188 in monotherapy for advanced malignancies, were presented in the form of ePOSTER at the 35th annual meeting of Society for Immunotherapy of Cancer (SITC 2020). The study preset 7 dose groups ranging from 0.1mg/kg to 30mg/kg once a week. A total of 20 subjects were enrolled in this study. As of 18 Jun 2020, IBI188 completed all the preset doses (maximum dose was 30mg/kg QW) without dose-limiting toxicity and was well tolerated in general. Most of the treatment-related adverse events were grade 1-2, with no drug-related adverse reactions leading to permanent discontinuation and treatment-related

deaths. In addition, the overall incidence of anemia was 15% (3/20), with only one subject (5%) had experienced grade 3 transient anemia on the first day of the study drug administration but recovered on the next day. Meanwhile, anti-tumor activity was observed in the monotherapy of IBI188 in this study, with multiple patients obtained stable disease for long period.

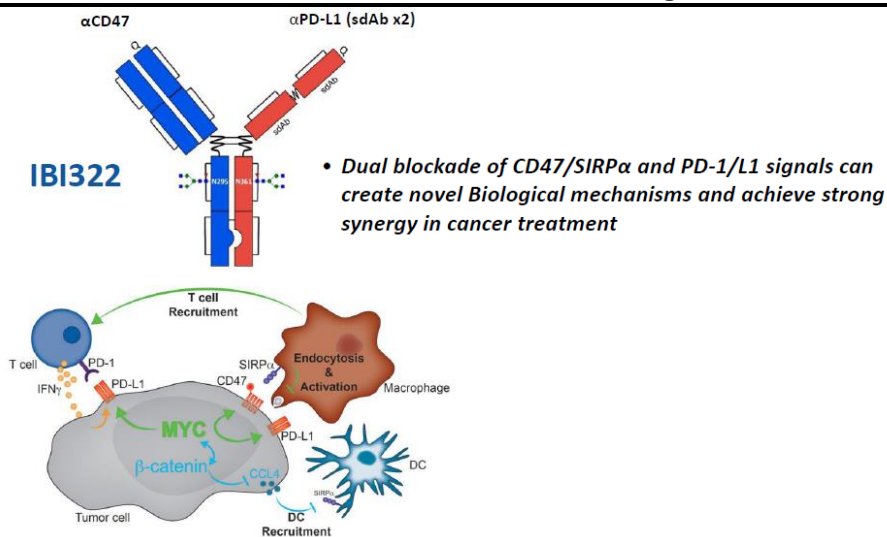
In 2020, Innovent completed Phase 1a dosage escalation for IBI188 in the US and China, and have started Phase 1b for IBI188. Innovent also initiated clinical trials for IBI188 including 1) the Phase 1b/2 trial in China for IBI188 in combination with azacitidine in relapsed/refractory acute myeloid leukemia (r/r AML), 2) the Phase 1b/3 trial in China for IBI188 in combination with azacitidine in MDS, and 3) a Phase 1b trial in the US for IBI188 in combination with azacitidine for MDS. Innovent aims to start phase 3 or pivotal trial for IBI188 in China for the first line treatment of myelodysplastic syndrome (MDS) in 2021.

In addition, as an innate immune checkpoint inhibitor, IBI188 has a synergistic anti-tumor effect with T-cell immune checkpoint inhibitor. Innovent will conduct clinical studies of IBI188 combined with Tyvyt in the treatment of multiple solid tumors.

**IBI322: a potential first-in-class CD47/PD-L1 bispecific antibody**

IBI322 is a recombinant anti-CD47/PD-L1 bispecific antibody developed by Innovent. Pre-clinical studies showed that IBI322 can effectively block CD47–SIRPα interactions and induce macrophages to phagocytize CD47 expressed tumor cells, which is equivalent to anti-CD47 monoclonal antibody. IBI322, on the other way, effectively blocks the binding of PD-1 to PD-L1 and activates CD4+T lymphocyte, which is comparable to anti-PD-L1 monoclonal antibody. Because of PD-L1 expression on tumor cells, IBI322 can selectively bind to tumor cells more potent than anti-CD47 monoclonal antibody, thus reducing the possibility of bind to CD47 on red blood cells, which could ultimately reduce the toxicity associated with anti-CD47 antibodies. Therefore, IBI322 has better antitumor activity and higher safety profile.

**Figure 50: IBI322 has dual blockade of CD47/SIRPα and PD-1/L1 signals**

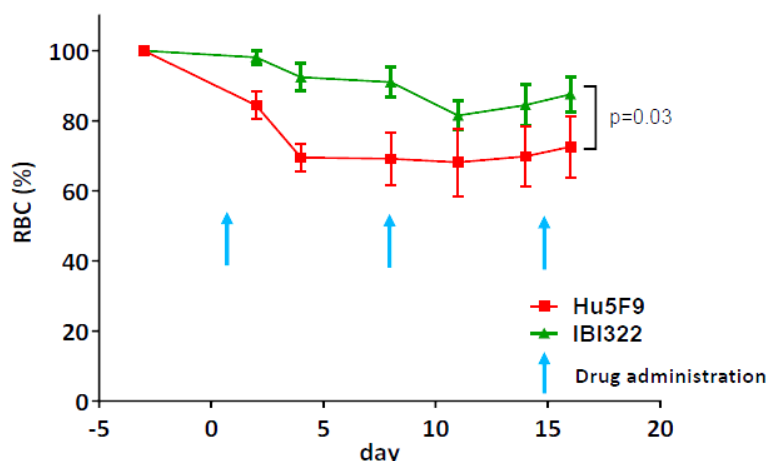


Source: Company presentation, CMBIS

In *Vitro* and In *Vivo* studies showed that IBI322 selectively accumulated on PD-L1/CD47 double positive tumor cells and its binding with red blood cells was weak. In addition, preclinical studies also

demonstrated that IBI322 was better tolerated than hu5F9, with lower RBC toxicities after weekly 10mg/kg dosing in cyno monkeys.

**Figure 51: RBC changes in cyno monkeys for IBI322 vs Hu5F9**



Source: Company presentation, CMBIS

In Aug 2020, the first patient has been dosed in a Phase 1a/1b clinical study to evaluate IBI322 in the treatment of patients with advanced malignancies in China. In early 2021, Innovent has started the patient enrolment for the Phase 1 study for IBI322 in advanced malignancies in the US. Innovent aims to enter Phase 1b for IBI322 and get preliminary Proof-of-Concept (PoC) data in 2021.

### IBI397 (AL008): an innovative SIRP $\alpha$ antibody

In Mar 2020, Innovent has entered into a licensing agreement Alector (ALEC US), to develop and commercialize AL008, an anti-SIRP $\alpha$  antibody, for the treatment of oncology indications in China. Under the agreement, Innovent will lead the development and commercialization of the molecule in China, including the manufacturing of the product. Alector will lead the development of AL008 outside of China. Innovent may pay Alector up to US\$11.5mn in development milestones, US\$112.5mn in sales milestones, and future sales royalties. AL008 is currently at preclinical stage.

IBI397 (AL008) is a potential first-in-class SIRP $\alpha$  inhibitor with a unique dual mechanism of action that non-competitively antagonizes the CD47-SIRP $\alpha$  pathway by inducing the internalization and degradation of the inhibitory receptor on macrophages to relieve immune suppression (a “don’t eat me signal”) while also engaging Fc gamma to promote immuno-stimulatory pathways that drive anti-tumor immunity.

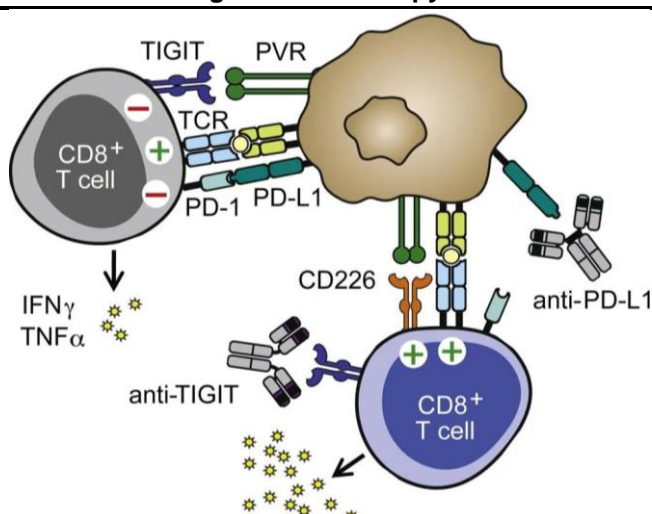
IBI397 monotherapy reduces tumor growth and enhances M1 macrophage activation in a humanized pre-clinical model. In comparison with other SIRP $\alpha$  targeting antibodies, IBI397 binds to all common alleles of SIRP $\alpha$  and has best-in-class potency in tumor cell phagocytosis. IBI397 promotes T cell function and in preclinical studies is not associated with depletion of red blood cells or platelets. These data highlight the potential potency of this differentiated mechanism of simultaneously providing immune-activating signals while removing immune-checkpoint signals and demonstrate the potential activity for IBI397.

## TIGIT franchise: IBI939 (a TIGIT mAb) and IBI321 (a PD-1/TIGIT bispecific antibody)

IBI939 is an innovative anti-T-cell immunoreceptor with Ig and ITIM domains (TIGIT) recombinant fully human monoclonal antibody developed by the Company. TIGIT is a receptor expressed on the surface of T cells and NK cells that can inhibit of immune function after binding to CD155 expressed on cancer cells or dendritic cells.

IBI939 directly binds to TIGIT, relieve the inhibition and depletion of T cells and NK cells, thus activate and enhance the anti-tumor immune response of T cells and NK cells. IBI939 may synergize with anti-PD-1/L1 antibody to improve the anti-tumor efficacy, delay the drug resistance, which may provide more effective treatments for cancer patients.

**Figure 52: MOA of TIGIT blocking in tumor therapy**



Source: Cancer Cell. 2014;26(6):923-937, CMBIS

TIGIT is one of the most promising and prospective targets in tumor immunotherapy. Although no TIGIT antibody has been approved yet, there are more than 10 TIGIT antibodies under research worldwide.

Recent clinical results have shown synergistic enhancement effect of anti-TIGIT antibody in combination with anti-PD-1/L1 antibody for cancer treatment. Roche's tiragolumab is currently the globally most late-stage TIGIT mAb. In Jan 2021, tiragolumab was been granted Breakthrough Therapy Designation (BTD) by the US FDA, in combination with Tecentriq (atezolizumab, PD-L1 mAb) for the first-line treatment of people with metastatic NSCLC with high PD-L1 expression and without EGFR or ALK genomic tumour aberrations. The BTD designation is based on randomised data from the phase II CITYSCAPE trial (NCT03563716). CITYSCAPE provides the first evidence that targeting both TIGIT and PD-L1 may enhance anti-tumour activity by potentially amplifying the immune response.

Full results from CITYSCAPE trial assessing tiragolumab in combination with tecentriq in PD-L1-positive metastatic NSCLC, presented at the ASCO 2020 Virtual Scientific Program, showed that at an average of 10.9 months follow-up, the combination showed an improvement in ORR (37% vs. 21% with Tecentriq alone) and a 42% reduction in the risk of disease worsening or death (PFS) compared with Tecentriq alone. An exploratory analysis in people with high levels of PD-L1 (tumour proportion score; TPS  $\geq$  50%) showed a clinically meaningful ORR vs. Tecentriq alone (66% vs. 24%) and median



PFS was not reached (vs. 4.11 months with Tecentriq alone; HR=0.30, 95% CI: 0.15–0.61). The data suggest that tiragolumab plus Tecentriq was generally well-tolerated, showing similar rates of all Grade 3 or more all-cause adverse events when combining the two immunotherapies compared with Tecentriq alone (48% vs. 44%).

In Jun 2021, GSK and iTeos Therapeutics announced an agreement to co-develop and co-commercialise EOS-448, an anti-TIGIT mAb currently in phase I development. Within the collaboration, GSK and iTeos will share responsibility and costs for the global development of EOS-448 and will jointly commercialise and equally split profits in the US. Outside of the US, GSK will receive an exclusive license for commercialisation and iTeos will receive tiered royalty payments. Under the terms of the collaboration agreement, iTeos will receive an upfront payment of US\$625mn and will be eligible to receive up to an additional US\$1.45bn in milestone payments. This transaction implies large potential in TIGIT therapies as a next generation immuno-oncology agent, in our view.

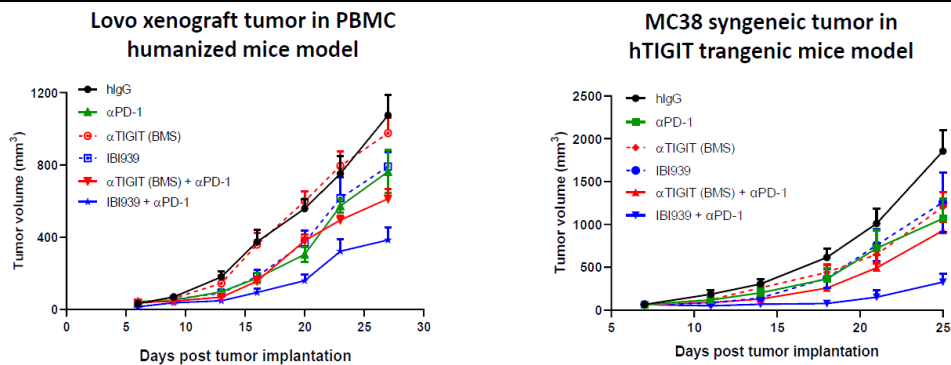
**Figure 53: Competitive landscape of TIGIT candidates under research**

Candidates	Target	Company	US Status	China Status
Tiragolumab	TIGIT	Roche	Phase 3 in NSCLC/SCLC/ESCC Phase 2 in CC/HNSCC/NHL	Phase 3 in NSCLC/SCLC/ESCC
MK-7684A (Vibostolimab)	TIGIT	MSD	Phase 3 in NSCLC Phase 2 in NSCLC/melanoma/mCRPC	IND approved in NSCLC/advanced solid tumor
BGB-A1217 (Ociperlimab)	TIGIT	Beigene	Phase 3 in NSCLC Phase 2 in CC	Phase 2 advanced ESCC
AB154	TIGIT	Arcus Bioscience	Phase 3 in NSCLC Phase 2 in NSCLC	NA
BMS-986207	TIGIT	BMS	Phase 1/2 in MM/solid tumor	NA
Etigilimab	TIGIT	Oncomed Pharma	Phase 1/2 in solid tumor	NA
SEA-TGT	TIGIT	Seattle Genetics	Phase 1/2 in solid tumor	NA
ASP8374 (PTZ-201)	TIGIT	Astellas	Phase 1 in solid tumor/GBM	NA
OMP-313M32	TIGIT	Mereo Biopharma	Phase 1 in solid tumor	NA
EOS-448	TIGIT	iTeos Therapeutics/GSK	Phase 1 in solid tumor	NA
COM902	TIGIT	Compugene	Phase 1 in advanced malignancies	NA
IBI321	TIGIT/PD-1	Innovent	NA	Phase 2 in advanced solid tumor
IBI939	TIGIT	Innovent	NA	Phase 1 in NSCLC/advance solid tumor
JS006	TIGIT	Junshi	NA	Phase 1 in advanced solid tumor
BAT6005	TIGIT	Bio-Thera	NA	IND filing
BAT6021	TIGIT	Bio-Thera	NA	IND filing
HB0030	TIGIT	Huaota Biopharm	NA	IND filing

Source: Insight, Clinicaltrials.gov, CMBIS

### IBI939: a novel TIGIT antibody

IBI939 has high TIGIT binding affinity and strong ligand blocking activity. In preclinical studies, IBI939 exhibited strong anti-tumor activities as monotherapy or in combination with anti-PD-1 antibody in different tumor models.

**Figure 54: In-vivo efficacy of IBI939**

Source: Company presentation, CMBIS

In May 2020, the first patient has been successfully dosed in a Phase 1a clinical study (CIBI939A101) conducted in China to evaluate IBI939 in the treatment of patients with advanced malignancies. The primary objectives of the study are to evaluate the safety, tolerability, and initial anti-tumor efficacy of IBI939, either as monotherapy or in combination with Tyvyt. Innovent started enrolling patients for Phase 1b of IBI939 in combination with TYVYT for advanced lung cancer in early 2021 and aims to complete Phase 1b study in 2021.

In addition, Innovent submitted IND application for a Phase 1 study of IBI939 in the US in Dec 2020, with IND approval received in Jan 2021.

### IBI321: a PD-1/TIGIT bispecific antibody

IBI321 is a novel PD-1/TIGIT bi-specific antibody co-developed with Eli Lilly. IBI321 combines PD-1 and TIGIT inhibition to release PD-1/PD-L1 as well as TIGIT/PVR inhibition of intratumoral T/NK cells, to enhance T/NK cell mediated anti tumor efficacy. In addition, IBI321 bridges PD-1 and TIGIT on the same cell (T cells, NK cells) to maximal activation of CD 226 /PVR and relieve tumor immunosuppression. Innovent received NMPA's IND approval for IBI321 in May 2021.

## LAG-3 franchise: IBI110 (a LAG-3 mAb) and IBI323 (a PD-L1/LAG-3 bispecific antibody)

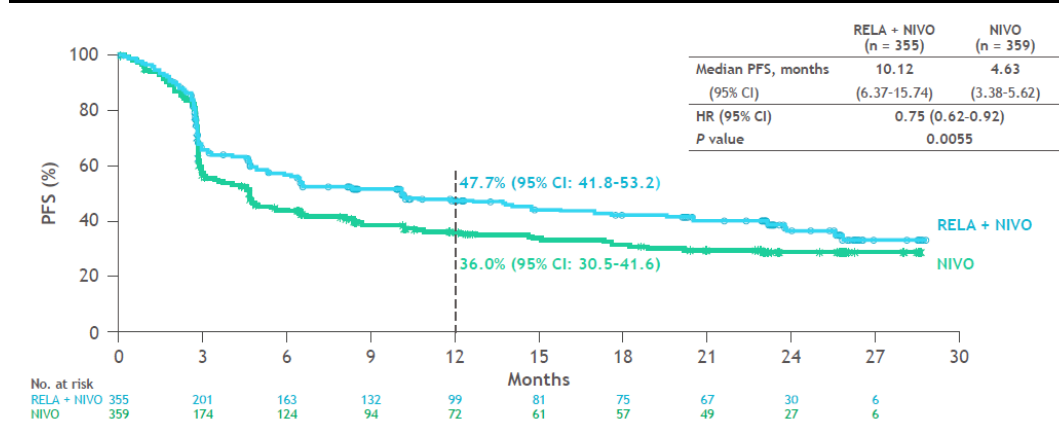
Lymphocyte-activation gene 3 (LAG-3) is an immune checkpoint receptor protein that functions to control T cell response, activation and growth. LAG-3 binds to a major histocompatibility complex class II (MHC class II) antigen and negatively regulates the proliferation, activation and homeostasis of T-cells. LAG-3 is believed to drive cytotoxic T-cell tolerance and immune exhaustion. Blocking LAG-3 binding to the MHC class II antigen should restore activities of tumor infiltrating T cells, reverse T-cell exhaustion and drive T-cell activation.

LAG-3 and PD-1 are two distinct inhibitory immune checkpoints that are often co-expressed on tumor infiltrating lymphocytes (TILs) and contribute to tumor-mediated T-cell exhaustion. Combination therapy of LAG-3 antibody and PD-1 inhibitor enables T-cell activation, leading to the initiation of an improved immune response and promoting tumor cell death.

Globally, there's no approved LAG-3 targeted therapy yet. The latest clinical-stage LAG-3 candidate is relatlimab developed by BMS and Ono Pharma. Other global LAG-3 candidates include Merck's MK-4280, Prima BioMed/Immutep's IMP321 (Eftilagimod Alpha), Immutep/ Novartis' IMP701 (LAG525), Tesaro/Anaptyso's TSR033, Regeneron's REGN3767, etc.

In Mar 2021, BMS announced primary results from the Phase II/III RELATIVITY-047 (CA224-047) trial evaluating the fixed-dose combination of relatlimab and nivolumab versus nivolumab alone in patients with previously untreated metastatic or unresectable melanoma. The trial met its primary endpoint of progression-free survival. This is the first regimen to demonstrate a statistical benefit over anti-PD-1 monotherapy in metastatic melanoma. Among patients treated with the combination, the median PFS (mPFS) was significantly longer at 10.12 months (95% CI: 6.37-15.74) vs. 4.63 in those who received nivolumab (95% CI: 3.38-5.62); (HR=0.75; 95% CI: 0.62-0.92, p=0.0055). The PFS benefit of the fixed-dose combination was observed early, at the time of the first scan, and was consistent over time. In addition, the fixed dose combination was well-tolerated and there were no new safety signals reported in either the relatlimab and nivolumab combination arm or the nivolumab arm.

**Figure 55: Relatlimab+Nivolumab showed significantly longer PFS in melanoma**



Source: BMS, CMBIS

In China, several LAG-3 targeted therapies are under early-stage clinical research while Innovent has leading positioning with two clinical-stage assets, including IBI110 (a LAG-3 mAb) and IBI323 (a PD-L1/LAG-3 bispecific antibody).

Figure 56: Competitive landscape of LAG-3 antibodies under research in China

Candidates	Companies	Target	Format	US status	China status
MGD013	ZaiLab	PD-1/LAG-3	BsAb	Phase 2/3 in GC/HNSCC Phase 2 in HNSCC Phase 1/2 in HCC	Phase 2 in HCC, CCA
Relatlimab	BMS	LAG-3	mAb	Phase 2/3 in melanoma Phase 2 in NSCLC/SCLC/HNSCC/ CRC/ GC/melanoma/soft tissue sarcomar/NHL/MM	IND submitted
MK 4280	MSD	LAG-3	mAb	Phase 2 in NSCLC Phase 1/2 in NHL/RCC	Phase 1 in solid tumor
RO-7247669	Roche	PD-1/LAG-3	BsAb	Phase 2 in ESCC Phase 1/2 in advanced liver cancer	NA
REGN3767	Regeneron	LAG-3	mAb	Phase 2 in Breast cancer Phase 1/2 in solid tumor	NA
IMP321	Immutep/ Wuxi Apptec	LAG-3	Fusion protein	Phase 2 in NSCLC/HNSCC/BC Phase 1/2 in melanoma	NA
LAG525	CoStim Pharmaceuticals	LAG-3	mAb	Phase 2 in SCLC/TNBC/melanoma Phase 1/2 in solid tumor	NA
BI754111	Boehringer Ingelheim	LAG-3	mAb	Phase 2 in solid tumor	NA
GSK2831781	GSK/ Immutep	LAG-3	mAb	Phase 2 in Ulcerative Colitis	NA
EMB-02	EpiMab	PD-1/LAG-3	BsAb	Phase 1/2 in advanced solid tumor	IND approved in solid tumor
FS118	F-Star/ Merk KGaA	PD-L1/LAG-3	BsAb	Phase 1/2 in solid tumor	NA
INCAGN2385	Incyte/ Agenus	LAG-3	mAb	Phase 1/2 in melanoma	NA
TSR-033	AnaptysBio/ TESARO	LAG-3	mAb	Phase 1 in solid tumor	NA
Sym022	Symphogen	LAG-3	mAb	Phase 1 in solid tumor/lymphoma	NA
XmAb-22841	Xencor	CTLA-4/LAG-3	BsAb	Phase 1 in solid tumor	NA
DNV3	CentryMed	LAG-3	mAb	NA	Phase 2 in Solid tumor, lymphoma
IBI110	Innovent	LAG-3	mAb	NA	Phase 1 in solid tumor
IBI323	Innovent	PD-L1/LAG-3	BsAb	NA	Phase 1 in solid tumor
EOC202	Wuxi AppTec	MBP/LAG-3	Fusion protein	NA	Phase 1 in BC
LBL-007	Leads Biolabs	LAG-3	mAb	NA	Phase 1 in Melanoma, solid tumor, lymphoma
SHR-1802	Hengrui	LAG-3	mAb	NA	Phase 1 in Solid tumor
KL-A289	Kelun	LAG-3	mAb	NA	Phase 1 in Solid tumor
HLX 26	Henlius	LAG-3	mAb	NA	IND approved in solid tumor, lymphoma

Source: Insight, Clinicaltrials.gov, CMBIS

### IBI110: a fully human LAG-3 mAb

IBI110 is a fully human monoclonal antibody drug candidate developed by Innovent. Pre-clinical animal study data show that IBI110 has good in vivo anti-tumor efficacy when combined with an anti-PD-1 antibody.

A phase Ia/Ib dose-escalation study of IBI110 as a single agent and in combination with Tyvyt in patients with advanced solid tumors is ongoing. Innovent has released the results at ASCO 2021 Annual Meeting. At data cutoff (9 Feb 2021), 40 patients were enrolled and received treatment. 22 subjects were assigned in dose groups of 7 (0.01mg/kg~20mg/kg) in Phase Ia, the prespecified dose escalation had been completed and no DLT was observed. No AEs led to discontinuation of IBI110 or Tyvyt and no treatment-related death was reported. In terms of efficacy, a subject with advanced ovarian cancer who progressed on multiple prior systemic therapies achieved partial response after IBI110 monotherapy treatment and was still in the study for more than 6 months. 18 subjects were assigned in dose groups of 5 (0.3mg/kg~5mg/kg) in Phase Ib of IBI110 in combination with Tyvyt, the prespecified dose escalation had been completed and no DLT, AEs leading to discontinuation or death was observed. At data cutoff (26 Apr 2021), three subjects had achieved PR with an ORR of 16.7% (3/18) in phase 1b, demonstrating a synergistic anti-tumor activity of IBI110 and Tyvyt. This trial has proved that IBI110 alone or plus Tyvyt has acceptable toxicity and shows preliminary antitumor activity.

## IBI323: a LAG-3/PD-L1 bispecific antibody

IBI323 is a bispecific antibody targeting both PD-L1 and LAG-3 which Innovent owns global rights. Preclinical studies showed that IBI323 effectively blocks both the PD-1/PD-L1 and LAG-3 pathways and can generate more effective and durable activation of T lymphocyte activation than the combination of anti-PD-L1 monoclonal antibody and anti-LAG monoclonal antibody. Besides, through the bridging effect of bispecific antibody, tumor cells expressing PD-L1 can be drawn closer to T lymphocyte expressing LAG-3, thus forming stable TCR: MHC immune synapses and enhancing T lymphocyte activation. Therefore, IBI323 shows advantages compared with two drugs combination according to the mechanism.

IBI323 received IND approval from the NMPA in Oct 2020. In Jul 2021, the first patient has been dosed in a Phase 1 study of IBI323 in China. The objective of this open-label, multi-center Phase 1 dose escalation and expansion study is to evaluate the safety, tolerability, potential optimal dosage and preliminary efficacy of IBI323 in patients with advanced malignant tumors whose cancer progressed on standard-of-care treatment (NCT04916119). Innovent also plans to prepare an IND application with the US FDA.

Besides IBI323, two bispecific candidates are also assessed in clinical trials in China, including Zailab/Macrogenics' MGD013 (PD-1/LAG-3 bispecific antibody) at phase 2 trials, EpiMab's EMB-02 (PD-1/LAG-3 bispecific antibody) at phase 1 trial.

## Rich bispecific I/O pipelines

Innovent has constructed rich pipelines of bispecific I/O therapies with six candidates under development, including IBI322 (PD-L1/CD47), IBI321 (PD-1/TIGIT), IBI323 (LAG-3/PD-L1), IBI319 (PD-1/4-1BB), IBI318 (PD1/PD-L1) and IBI315 (PD1/HER2).

Furthermore, in Jun 2020, Innovent entered into a strategic collaboration with Roche that focuses on the discovery and development of bispecific antibodies and multiple cell therapies, which enables the Company to access certain Roche technologies in the discovery and development of specific 2:1 T-cell bispecific antibodies (TCB) as well as the universal CAR-T platform.

**Figure 57: Innovent's key bispecific pipelines**

Compound	Targets	Clinical progress	Indications	Technique platform
IBI318	PD-1/PD-L1	Phase 3	SCLC/NKTCL	Zymework's Asymmetric
IBI315	PD-1/HER2	Phase 1	Solid tumor	Hanmi's Pentabody
IBI322	PD-L1/CD47	Phase 1	Hematological malignance/ Solid tumor	NanoBody Fusion protein
IBI323	PD-L1/CD47	Phase 1	Solid tumor	NanoBody Fusion protein
IBI319	PD-1/4-1BB	Phase 1	Solid tumor	Non-common light chain antibody

Source: Insight, CMBIS

Many PD-1/L1 based bispecific antibodies are under development in China. The hot targets include PD-(L)1/CD47, PD(L)1/CTLA-4, PD-(L)1/ TGF- $\beta$ , etc.

**Figure 58: Other bi-specific antibodies targeting PD-1 or PD-L1 under research in China**

Candidates	Companies	Target	Technique p	Progress in China
KN046	AlphaMab	PD-L1/CTLA-4	NanoBody Fusion protein	Phase 3
SHR-1701	Hengrui	PD-L1/TGF-β	TGFβRII Fusion protein	Phase 3
MGD013	ZaiLab	PD-1/LAG-3	DART	Phase 2
AK112	AkesoBio	PD-1/VEGF	Tetrabody: scFv Fusion protein	Phase 2
AK104	AkesoBio	PD-1/CTLA-4	Tetrabody: Fusion protein	Phase 2
PM8002	BioTheus	PD-L1/TGF-β	NanoBody Fusion protein	Phase 2
PM8001	BioTheus	PD-L1/TGF-β	NanoBody Fusion protein	Phase 2
ES101	Elpiscience	PD-L1/4-1BB	Inhibrx (NanoBody)	Phase 2
HB0025	Huahai Pharma	PD-L1/VEGF	VEGFR1 D2 Fusion protein	Phase 1
Q-1802	QureBio	PD-L1/Claudin 18.2	NanoBody Fusion protein	Phase 1
GNC-039	Baili Pharm	PD-L1/4-1BB/CD3/EGFRvIII	GNC	Phase 1
GNC-038	Baili Pharm	PD-L1/4-1BB/CD3/CD19	scFv Fusion protein	Phase 1
SI-B003	Baili Pharm	PD-1/CTLA-4	scFv Fusion protein	Phase 1
HX009	HanXBio	PD-1/CD47	SIRPα Fusion protein	Phase 1
QL1706	Qilu Pharmaceutical	PD-1/CTLA-4	MabPair	Phase 1
IMM2510	ImmuneOnco	PD-L1/VEGF	VEGFR1 D2 Fusion protein	IND approved
IMM2505	Shenghe Biological	PD-L1/CD47	SIRPα Fusion protein	IND approved

Source: Insight, Companies' data, CMBIS

**IBI318: a potential first-in-class PD-1/PD-L1 bispecific antibody**

IBI318 is a first-in-class anti-PD-1/PD-L1 bispecific antibody co-developed with Eli Lilly. IBI318 is a recombinant fully human immunoglobulin bi-specific antibody which aims to restore T cell activation and generate anti-tumor activities. IBI318 targets and blocks both PD-1 binding to PD-1 protein ligand 2, a protein on the surface of a cell that attaches to certain proteins on the surface of a T cell (PD-L2) and PD-L1 binding to CD80, a cell surface protein which serves as a receptor for T cell activation. Pre-clinical studies demonstrated that due to its bi-specific properties, IBI318 can bridge T cells expressing PD-1 and tumor cells expressing PD-L1 thus enhancing the formation of immune synapses, thereby potentially enhancing anti-tumor activities and increasing anti-tumor efficacy, which are expected to improve anti-tumor activities and curability.

Innovent has completed dosage escalation of the Phase 1a study of IBI318 in advanced malignancies in China and has presented the preliminary results of the Phase 1a study at the 56th annual meeting of ASCO in Jun 2020. Innovnet has initiated Phase1b/2 trials for IBI318 across multiple malignancies in 2020 and aims to complete the Phase 1b part in 2021.

**IBI315: a potential first-in-class PD-1/HER2 bispecific antibody**

IBI315 is a first-in-class PD-1/HER2 bispecific antibody co-developed with Hanmi Pharmaceutical. The first patient was dosed in Nov 2019 for the Phase 1a trial of IBI315 in patients with advanced malignancies in China. Innovent aims to publish the preliminary result of this Phase 1a study at academic conference around the end of 2021.

**IBI319: a novel PD-1/4-1BB bispecific antibody**

We think 4-1BB is a promising target in immune-oncology area. 4-1BB (CD137) is a key co-stimulatory immune checkpoint molecule that plays a role in maintaining immune homeostasis and enhancing anti-tumor immune memory.

Most 4-1BB targeted therapies are at early clinical phase in China and globally. In China, the most late-stage 4-1BB candidates are Adagene's ADG106 (4-1BB mAb) in phase 2 trials and Elpiscience's ES101 (PD-L1/4-1BB bispecific antibody) in phase 2 trials.

IBI319 was discovered through a collaboration between Innovent and Eli Lilly and has been developed in China by Innovent. In Jul 2021, the first patient has been dosed in a Phase 1a/1b study of IBI319 in China (NCT04708210). The objective of this open-label, multi-center Phase 1a/1b dose escalation and expansion study is to evaluate the safety, tolerability, potential optimal dosage and preliminary efficacy of IBI319 in patients with advanced malignant tumors whose cancer progressed on standard-of-care treatment.

## Early mover in CAR-T technologies

Through strategic collaboration with Roche, Innovent get access to Roche technologies in the universal CAR-T platform. In addition, Innovent is cooperating with IASO Bio to co-develop IBI326, a BCMA CAR-T therapy.

### IBI326: a BCMA CAR-T therapy

IBI326, also known as CT103A, is an innovative BCMA CAR-T therapy co-developed by Innovent and IASO Bio indicated for treatment of multiple myeloma.

For multiple myeloma patients, common first-line drug treatments include proteasome inhibitors, immunomodulatory drugs, and alkylating agents. While treatment may result in remission, most patients will inevitably enter the relapsed or refractory stage as there's currently no cure. Previous studies indicate subjects with r/r MM who received high-dose BCMA-targeting CAR-T cells may achieve better remission but have worse adverse events. Moreover, once the disease progresses again, the re-infusion of CAR-T cells will not be effective. IBI326 has been developed to solve the dilemma.

IBI326 is currently under the pivotal phase II clinical trial in China. Innovent and IASO Bio plans to file rolling submission of NDA to the NMPA for IBI326 for the treatment of r/r MM between in early 2022.

In Feb 2021, IBI326 received breakthrough therapy designation from the NMPA for the indication of r/r MM, based on the results observed in ongoing Phase 1/2 study for the treatment of adults with r/r MM being conducted in China.

In Jun 2021, Innovent and IASO Bio announced to have an oral presentation on updated data from the Phase 1 study of IBI326 in patients with r/r MM at the European Hematology Association (EHA) Congress. The clinical data was on 35 patients with R/R MM, who received 1.0, 3.0, or 6.0 × 10<sup>6</sup>/kg IBI326 treatment respectively in the dose-escalation phase and dose-expansion cohort. The 1.0 × 10<sup>6</sup>/kg dose was determined as Recommended Phase II Dose (RP2D). The median age of the 35 patients was 54. The median number of prior treatment regimens was four. Ten patients previously received autologous hematopoietic stem cell transplantation (AHSCT), and 10 patients received murine BCMA CAR-T treatment. As of 1 May 2021, the median follow-up of the 35 patients was 291 days. IBI326 has a rapid onset of action and long-lasting efficacy. The ORR was 97.1% in the 35 patients, among whom 29 patients (82.9%) achieved ≥ VGPR and 20 patients (57.1%) achieved complete response/stringent complete response (CR/sCR). And 34 patients evaluable for MRD achieved minimal residual disease (MRD) negativity, with the median time to MRD negativity 1.3 months.

IBI326 has a good safety profile. Five of the 35 patients had cytokine release syndromes (CRS) of Grade 3 or above. The median time to onset of CRS was 4 days, and all CRS could be efficiently controlled by tocilizumab and/or steroids. ICANS was observed in only one patient whose symptom was drowsiness; the patient later spontaneously relieved without any treatment. As of the cut-off date, three patients had IBI326 persistence for over two years, and the first patient of them achieved persistent sCR.

In China, besides Innovent's IBI326 (CT103A), Carsgen's and Legend's BCMA-CAR-T are also in phase 2 clinical stage. Two other BCMA-CAR-T therapies from Harin Biotechnology and Simcere are in phase 1 trials, while two from Cell Biomed and Unicar Therapy have submitted IND.



**Figure 59: Competition landscape of BCMA-CART therapies**

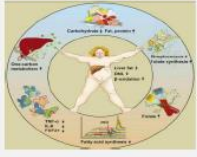



Candidates	Companies	US status	China status
LCAR-B38M/ JNJ-4528/ Cilta-Cel	Legend Biotech/ JNJ	Phase 3 in MM	Phase 2 in MM
BB2121	Celgene/ Blue Bird Bio	Phase 3 in MM	NA
BCMA targeted CAR-T-CT053	Carsgen Therapeutics	Phase 1 in MM	Phase 2 in MM
IBI326/CT103A	Innovent/ IASO Bio	NA	Phase 2 in MM
BCMA CAR-T-HRAIN	Harin Biotechnology	NA	Phase 1 in MM
BCMA CAR-T-PRG	Simcere/ Pregene	NA	Phase 1 in MM
C-4-29	Chongqing Precision Biotech	NA	Phase 1 in MM
BCMA CAR-T-SBM	Cell Biomed	NA	IND pending
PD-1 gene knocked out BCMA CAR-T-Unicar	Unicar Therapy	NA	IND pending

Source: Insight, CMBIS

## Targeting broad chronic disease market

In addition to comprehensive oncology pipelines, Innovent has established rich non-oncology pipelines with innovative therapies targeting the large chronic disease market. Its key non-oncology candidates include IBI306 (PCSK9), IBI362 (OXM3), IBI302 (VEGF/Complement), IBI112 (IL-23 p19), etc.

Figure 60: Innovent non-oncology pipeline overview

DIA/Obesity/NASH		CV	Auto-immune	Ophthalmology
				
<b>IBI-362 (GLP-1/GCGR)</b> Diabetes 1. 1st line 2. Oral failure 3. Add-on insulin		<b>IBI-306 (PCSK9)</b> Hypercholesterolemia 1. HoFH 2. HeFH 3. Non-FH	<b>IBI-303 (TNF-α)</b> 1. AS 2. RA 3. Pso 4. Uveitis	<b>IBI-302 (VEGF/Complement)</b> 1. W-AMD 2. DME 3. GA
<b>IBI-362 (GLP-1/GCGR)</b> 1. Obesity 2. Overweight with complications			<b>IBI-112 (IL-23 p19)</b> 1. Pso 2. Psoriatic Arthritis 3. UC 4. CD	
<b>IBI-362 (GLP-1/GCGR)</b> NASH				

Source: Company presentation, CMBIS

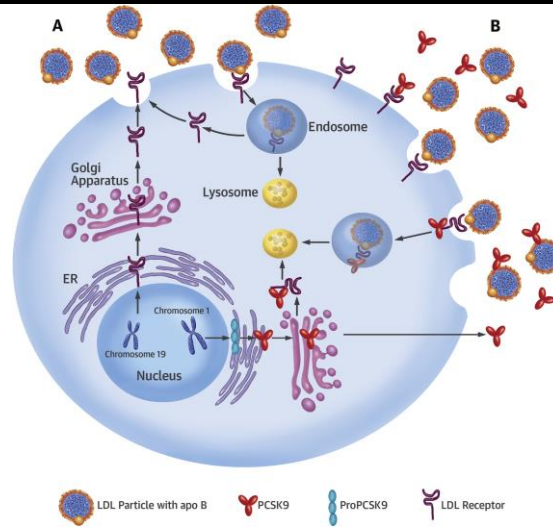
## IBI306 (tafolecimab): an innovative PCSK9 antibody

### Mechanism of action

IBI306 (tafolecimab) is a recombinant fully human monoclonal antibody against proprotein convertase subtilisin/kexin type 9 (PCSK9) for the treatment of hypercholesterolemia. PCSK9 is a key player in plasma cholesterol metabolism and a potential target for treating hypercholesterolemia (defined as too high levels of cholesterol in the blood). Cholesterol is carried in the blood attached to a protein called lipoprotein. There are two main forms of lipoproteins: low-density lipoprotein (LDL) and high-density lipoprotein (HDL). LDL cholesterol is often referred to as the 'bad cholesterol'. In the absence of PCSK9, low-density lipoprotein cholesterol receptor (LDL-R) is recycled back to the cell surface after endocytosis, allowing more circulating LDL to be removed from the plasma. However, in the presence of PCSK9, LDL-R is degraded and is not recycled back to the cell surface, resulting in high levels of LDL cholesterol in the plasma and increased susceptibility to coronary heart disease. Inhibition of PCSK9 using PCSK9 inhibitors leads to lower levels of LDL cholesterol, hence making it a candidate target for treating hypercholesterolemia.

IBI306 targets PCSK9 and inhibits its binding to LDL-R on the liver cell surface, maintaining the expression of LDL-R on the hepatocyte surface, thereby reducing low-density lipoprotein cholesterol (LDL-C) levels.

**Figure 61: The PCSK9 lifecycle and effect on LDL catabolism**



Source: JACC, Volume 72, Issue 3, 17 Jul 2018, Pages 314-329, CMBIS

**IBI306 is under pivotal trials in China**

Innovent holds the global rights of IBI306. Currently, Innovent is conducting three pivotal studies of IBI306 in China, including 1) a phase 3 trial evaluating IBI306 for the treatment of heterozygous familial hypercholesterolemia (HeFH, 杂合子家族性高胆固醇血症, FPI in Dec 2019), 2) a phase 3 trial non-familial hypercholesterolemia (nFH, 非家族性高胆固醇血症, enrollment completed in Jan 2021), 3) a pivotal phase 2 clinical trial for homozygous familial hypercholesterolemia (HoFH, 纯合子家族性高胆固醇血症, FPI in Sep 2019). Innovent aims to have data read out for the phase 3 study of IBI306 in HeFH in 2021.

In Aug 2020, the phase 1 (NCT03366688) and phase 2 (NCT03815812) clinical study results of IBI306 were presented in the 2020 European Society of Cardiology (ESC) annual conference. The incidence rates of treatment-emergent adverse events were comparable between IBI306 treated group and placebo treated group. Among all IBI306 treated subjects, LDL-C reductions were observed, which were (-52.2%, -72.1%) and (-54.30%, -72.26%) respectively in healthy subjects and hypercholesterolemia patients. In addition, compared with the marketed PCSK9 inhibitors, IBI306 preliminarily demonstrated longer dosing interval, which is 6 ~ 8 weeks compared with 2~4 weeks for competing products.

**Figure 62: Comparison of major PCSK9 inhibitor candidates**

	IBI306	Imported PCSK9i (Amgen, Sanofi)	Other domestic PCSK9i
<b>Status</b>	Phase 3	On market	Phase 1/ Phase 2/ Phase 3
<b>Indications</b>	HoFH HeFH Non-HF	HoFH HeFH Non-HF	HoFH Mixed Dyslipidemia
<b>Duration</b>	Q4W or Q6W	Q2W or Q4W	Q2W or Q4W
<b>Efficacy</b>	50-70% LDL-C decreased	50-70% LDL-C decreased	Not disclosed
<b>Safety</b>	Comparable with each other		Not disclosed

Source: Company presentation, CMBIS

## Large market potential in PCSK9 inhibitors

The prevalence of hypercholesterolemia has become increasingly popular in China and across the world which is mainly due to unhealthy diet and life style. According to F&S, the number of hypercholesterolemia patients in China will increase from 79.3mn in 2017 to 110.5mn in 2030.

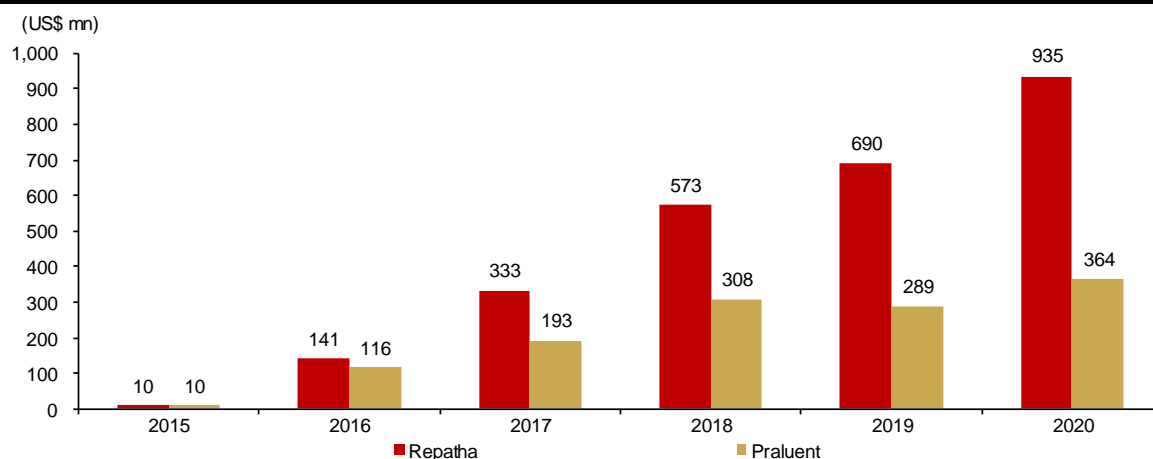
Although statins are currently the first choice for lipid-lowering, many patients cannot achieve satisfactory efficacy standards because of drug efficacy and safety problems.

To date, the US FDA has approved two PCSK9 antibodies, including Amgen's Repatha (evolocumab) and Sanofi's Praluent (alirocumab). Repatha and Praluent are both indicated to 1) reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease, 2) reduce LDL-C as adjunct to diet, alone or in combination with other LDL-C-lowering therapies, in adults with primary hyperlipidemia, including HeFH, 3) reduce LDL-C as an adjunct to other LDL-C-lowering therapies in adult patients with HoFH.

Meanwhile, several small molecule PCSK9 inhibitors are also under research worldwide, In Dec 2020, the European Commission (EC) granted Novartis marketing authorization for Leqvio (inclisiran) for the treatment of adults with hypercholesterolemia or mixed dyslipidemia. Inclisiran (KJX839) is the first small interfering RNA (siRNA) therapy to reduce LDL-C levels via an RNA interference (RNAi) mechanism of action. This approval was based on the results of the ORION trial, where Leqvio administered subcutaneously twice a year provided LDL-C reduction of up to 52% in patients with elevated LDL-C, despite maximally tolerated statin therapy.

The aggregate worldwide sales of these two marketed PCSK9 antibodies reached US\$1,299mn in 2020, according to Evaluate Pharma. The global PCSK9 market has maintained fast growth since 2015, indicating large unmet clinical demand in hypercholesterolemia disease.

**Figure 63: Aggregate worldwide sales of Repatha and Praluent**



Source: Evaluate Pharma, CMBIS

In China, Amgen's Repatha and Sanofi's Praluent have been approved by the NMPA in 2018 and 2019, respectively. Junshi's PCSK9 inhibitors is in phase III clinical trials in China. We think IBI306 has potential to become the third-to-market PCSK9 antibody in China given the fast progress of its three pivotal trials.

**Figure 64: PCSK9 inhibitors under research in China**

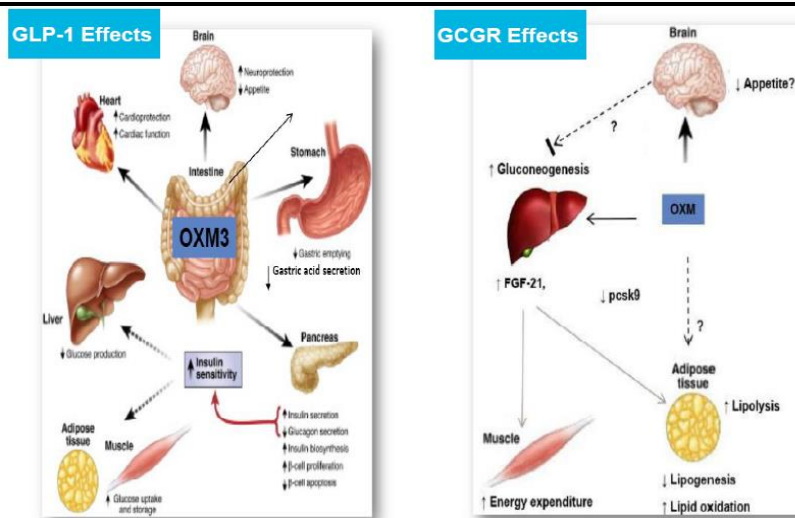
Candidates	Companies	Format	Indications	Progress in China
Evolocumab	Amgen	Antibody	Reduce cardiovascular risk, Lower LDL-C in primary hyperlipidemia and HoFH	Approved in Jul 2018
Alirocumab	Sanofi/Regeneron	Antibody	Reduce cardiovascular risk, Lower LDL-C in primary hyperlipidemia	Approved in Dec 2019
<b>IBI306</b>	<b>Innovent</b>	<b>Antibody</b>	<b>Non-familial hypercholesterolemia, HeFH, HoFH</b>	<b>Phase III</b>
Ongericimab (JS002)	Junshi	Antibody	Primary hypercholesterolemia, HoFH	Phase III
Inclisiran	Novartis	Small molecule	Primary hyperlipidemia	Phase III
SHR-1209	Hengrui	Antibody	Hypercholesterolemia	Phase III
CVI-LM001	CVI Pharmaceuticals	Small molecule	Primary hyperlipidemia	Phase II
AK102	Akeso	Antibody	HeHF, hypercholesterolemia	Phase II
MIL86	Mabworks	Antibody	Hypercholesterolemia	Phase I
DC371739	Joyo Pharma	Small molecule	Hypercholesterolemia, combined dyslipidemia	Phase I
SAL003	Salubris	Antibody	Hypercholesterolemia	Phase I
B1655	Tasly	Antibody	Hypercholesterolemia	Phase I

Source: Insight, CMBIS

### IBI362 (OXM3): a potential FIC weekly GLP-1/GCGR dual agonist

Oxyntomodulin (OXM), along with GLP-1, is a polypeptide secreted from intestinal L-cells. In addition to activating the classical GLP-1 receptor, it also has the effect of activating the GCGR, which is expected to bring additional benefits of appetite suppression and energy expenditure. Comparing with activating GLP-1 R only, IBI362 may activate GLP-1/Glucagon receptor simultaneously as a weekly OXM analog. The ratio of activation between GLP-1 and glucagon receptor by IBI362 was optimized compared with that of nature OXM.

**Figure 65: GLP-1R and GCGR dual co-agonist mechanism of IBI362**



Source: Company presentation, CMBIS

In Aug 2019, Innovent entered into a licensing agreement with Eli Lilly for the development and potential commercialization of OXM3 in China (IBI362). In parallel, Eli Lilly is developing OXM3 outside China. Innovent aims to develop IBI362 as a potential first-in-class weekly GLP-1/GCGR dual agonist, targeting broad indications including obesity, diabetes and NASH.

### **IBI362 showed superior efficacy and safety in clinical studies**

In 2020, Innovent completed the patient enrolment of a phase 1b clinical trial in China to evaluate the safety and tolerability of IBI362 in overweight or obese subjects (CIBI362B101). In Jun 2021, Innovent has finished the first obesity/overweight subject dosed in a phase 2 clinical trial of IBI362 (NCT04904913), which is a randomized, double-blind, placebo-controlled phase 2 study to assess the efficacy and safety of IBI362 in overweight or obese subjects in China with primary to evaluate the change from baseline in body weight at week 24. Furthermore, in Jan 2021, Innovent completed the patient enrolment of a phase 1b clinical trial in China to evaluate the safety and tolerability of IBI362 in diabetic patients (CIBI362A101).

In Jun 2021, the results of this phase 1 trial in overweight or obese Chinese participants were presented in an e-poster at the American Diabetes Association (ADA) 81<sup>st</sup> Scientific Sessions. Twelve participants in each of the three cohorts were randomized 2:1 to receive 1.0-2.0-3.0 mg (cohort 1), 1.5-3.0-4.5 mg (cohort 2) or 2.0-4.0-6.0 mg (cohort 3) IBI362 or placebo for 12 weeks. As for safety, no adverse event leading to dose interruption or dose reduction of the study drug, no serious adverse event, no hypoglycemic event and no pancreatitis was reported. No participant discontinued the study due to a safety reason. Gastrointestinal adverse events and decreased appetite were the most common adverse events. As for efficacy, at week 12, reductions in mean body weight from baseline were 3.80 kg (4.81%), 5.77 kg (6.40%) and 5.12 kg (6.05%) for participants receiving IBI362 in cohort 1, 2 and 3, respectively, compared with a 0.37 kg (0.60%) increase in participants receiving placebo. Meanwhile, waist circumference, body mass index, blood pressure and lipid profile were also improved in participants receiving IBI362. Such preliminary clinical results are so encouraging that more inspiring data are expected in the subsequent phase 2 clinical study (NCT04904913) in subjects with overweight or obesity, which has finished the first patient dosed on 15 Jun 2021 in China.

As a dual Glucagon and GLP-1 receptor agonist, which is an engineered analog of Oxyntomodulin, IBI362 showed superior effect among marketed anti-hyperglycemia agents. In terms of A1c decrease, OXM3 is even more effective than GLP-1 compounds, and as for weight-reducing effect, OXM3 is significantly better than Met, SGLT-2 and GLP-1 compounds. In addition, OXM3 is also more convenient and user-friendly to patients with a weekly dosing regimen, similar to long-acting GLP-1. Thanks to its dual mechanism to agitate both GLP-1R and GCGR, OXM3's potential indications include NASH, obesity, PCOS and LIPID.

Figure 66: Comparison of marketed anti-hyperglycemia agents

	Insulin Secretagogues	Met	TZD	SGLT-2 inhibitors	AGI	DPP-IV Inhibitors	Insulin	GLP-1 RA	OXM3 GLP-1/GCG R dual agonist
MOA	Increase Insulin secretion	Improve insulin resistance (liver)	Improve insulin resistance (Peripheral tissue)	Increase glucose excretion,	Decrease glucose absorption	Increase endogenous level of GLP-1	Supplement exogenous insulin	Supplement exogenous GLP-1	Supplement exogenous OXY
Efficacy (A1c decrease)	++	++	+	+	+	+	+++	++/+++	+++
Hypoglycemia risk	++	+/-	+/-	+/-	+/-	+/-	+++	+/-	+/-
Weight	↑	↓	↑	↓	+/-	+/-	↑ ↑	↓ ↓	↓ ↓ ↓
CV benefit	—	++	—	++	+/-	+/-	—	++	++ ??
Dosing	Daily	Daily	Daily	Daily	Bid/Tid	Daily	Daily (Tid-Qd)	Daily to Weekly	Weekly
Administration	oral	oral	oral	oral	oral	oral	IH	IH	IH
Glucose plus NASH/Obesity/PCOS/LIPID	X	√	X	√	X	X	X	√	√

Source: Company presentation, CMBIS

### Large sales potential given the significant unmet clinical demand

Novel antidiabetic drugs, represented by GLP-1 receptor agonists, have additional benefits such as weight loss, cardiovascular risk reduction, and kidney protection besides effective glycemic control. IBI362 is a dual agonist of GLP-1R and GCGR, and the synergistic effect of dual target activation may achieve more significant benefits of lowering blood glucose, body weight reduction, improvement of hepatic fat metabolism and potential cardiorenal improvement than GLP-1R. IBI362 is the first GLP-1/GCGR dual receptor agonist entering into clinical stage in China.

The prevalence of diabetes among adults in China is 11.6%. To be specific, 1 in 10 adults suffers from diabetes in average, of which type 2 diabetes accounts for about 90% of the total number of diabetic patients, and the number of patients is still increasing.

Obesity has become a global health concern, and is an important cause of several chronic diseases including diabetes, cardiovascular disease, liver disease, respiratory and sleeping disorders and cancer. Approximately 50% of type 2 diabetes cases, 30% of ischemic cardiovascular and cerebrovascular diseases and 10%-40% of cancers are caused by being obese or overweight. Currently, China has the largest number of overweight and obese people in the world. Nevertheless, there is lack of effective therapies to treat overweight and obese patients.

### IBI302, a potential first in class VEGF/Complement bispecific fusion protein

Anti-VEGF therapy is currently the standard treatment for neovascular age-related macular degeneration (nAMD, 新生血管性年龄相关性黄斑变性) which is also named as wet AMD. However, there are still some patients who do not respond well to long-term anti-VEGF therapy and even develop geographic atrophy and fibrosis.

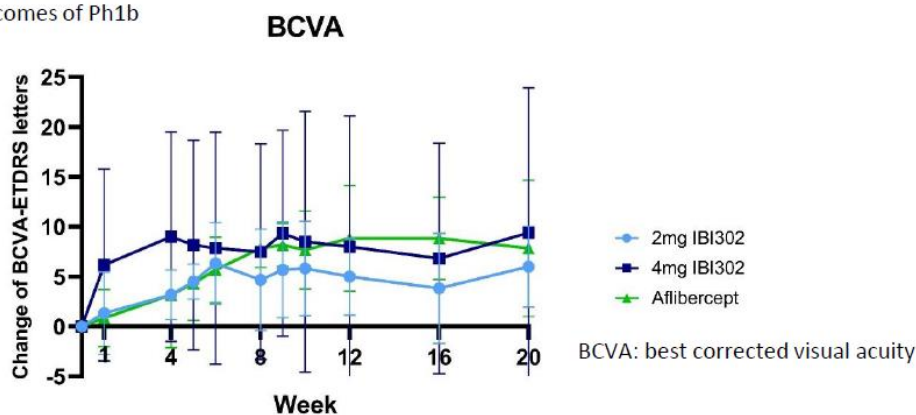
As the world's first bispecific fusion protein targeting VEGF and complement, IBI302 can simultaneously inhibit the proliferation of VEGF-mediated signaling pathway and reduce the inflammatory response mediated by complement activation. Innovent owns the global rights in IBI302. The N-terminus can bind to the VEGF family, block VEGF-mediated signaling pathway, inhibit vascular epithelium proliferation and angiogenesis, and reduce vasopermeability and leakage. The chronic inflammatory response related to complement activation is the key mechanism in the early stage of

AMD. The C-terminus of IBI302 can inhibit the activation of the classic pathway and alternative pathway of complement through the specific binding of C3b and C4b, and reduce the inflammatory response mediated by the complement, so as to achieve the purpose of treating and controlling AMD.

In Nov 2020, the results of a phase I single-dose escalation clinical trial of IBI302 in nAMD patients is released in e-poster at 2020 American Academy of Ophthalmology. A total of 31 subjects were enrolled. All subjects received a single intravitreal injection of IBI302. No serious adverse event or dose limiting toxicity was reported. The study demonstrated good safety and tolerability of IBI302. One week after administration, improved vision and reduction of retinal edema were observed. By 28 days after administration, all 31 patients' best corrected visual acuity increased by 6 letters on average compared to baseline; the average central retinal thickness decreased by 141.2 microns compared to baseline, and the efficacy of some patients lasted until 6 weeks after administration.

**Figure 67: Primary outcomes of IBI302 phase 1b trial**

Primary outcomes of Ph1b



Source: Company presentation, CMBIS

In Apr 2021, Innovent announced that the first patient has been dosed in a phase 2 clinical trial for IBI302 (CTR20210618). This is a randomized, double-blind, multicenter, active-controlled study in subjects with active subfoveal or parafoveal choroidal neovascularization secondary to nAMD.

### IBI302 to become a potential better treatment for nAMD

To date, three anti-VEGF drugs have been approved for the treatment of nAMD in China, including Novartis' Lucentis (ranibizumab), Chengdu Kanghong's Langmu (conbercept) and Bayer's Eylea (aflibercept).

In addition, Lucentis, Eylea were approved for the treatment of nAMD in US, while Avastin is also used off-label for this disease. In 2019, the US FDA approved Beovu (Brolucizumab), a low molecular weight, single-chain antibody fragment VEGF inhibitor being developed by Novartis for the treatment of exudative (wet) age-related macular degeneration (AMD), diabetic macular oedema and macular oedema secondary to retinal vein occlusion.

All currently approved anti-VEGF antibody drugs are mono-specific antibodies and they may only be able to relieve the symptoms of nAMD but may not tackle the root cause of the disease. In comparison, IBI302 targets both VEGF and complement proteins and, therefore, is potentially capable of curing the disease in addition to relieving the symptoms. In addition, we believe that IBI302 also has the potential for meeting the unmet medical needs for the treatment of certain other ocular disease indications such as dry AMD, for which the root cause is also believed to be complement proteins.



**Figure 68: Competitive landscape of VEGF biologics for ophthalmic diseases in China**

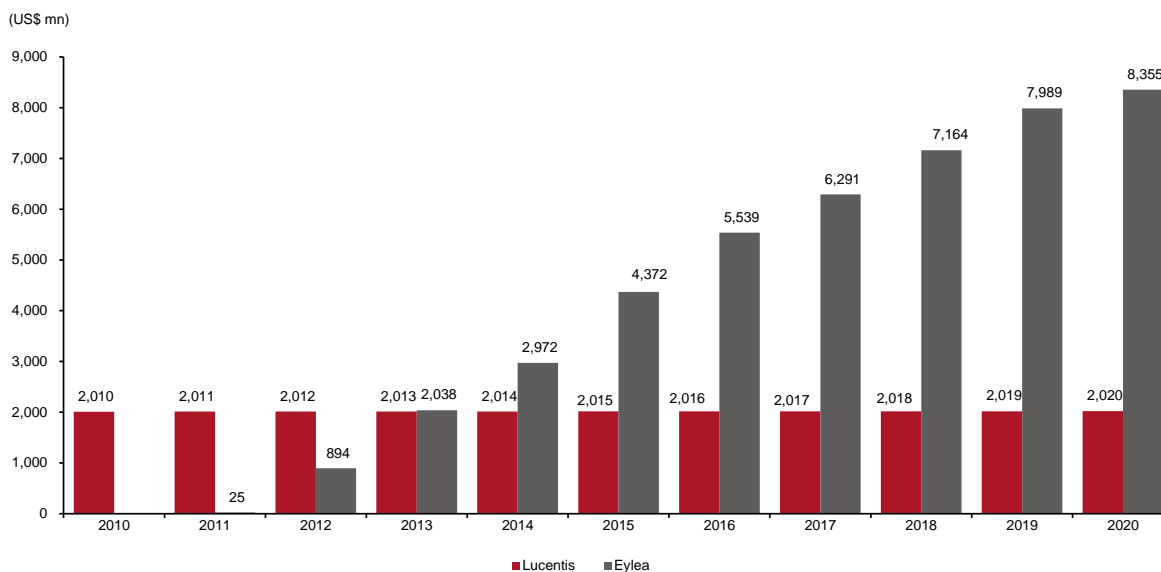
Candidates	Companies	Targets	Format	Progress	Indications
Ranibizumab	Novartis	VEGFA	Monoclonal antibody	Approved in Dec 2011	nAMD, DME, mCNV, retinal vein occlusion
Conbercept	Kanghong pharmaceutical	VEGFA, VEGFB, VEGFC, VEGFR	Fusion protein	Approved in Nov 2013	nAMD, mCNV
Aflibercept	Bayer	VEGFA, VEGFB	Fusion protein	Approved in Feb 2018	nAMD, DME
Faricimab	Roche	VEGFA, ANG-2	Bispecific antibody	Phase 3	nAMD, DME
LY09004 (Aflibercept biosimilar)	Luye Pharma	VEGFA, VEGFB	Fusion protein	Phase 3	nAMD
QL1207 (Aflibercept biosimilar)	Qilu Pharma	VEGFA, VEGFB	Fusion protein	Phase 3	nAMD
QL1205 (Ranibizumab biosimilar)	Qilu Pharma	VEGFA	Monoclonal antibody	Phase 3	nAMD
TAB014	TOT Biopharm	VEGF	Monoclonal antibody	Phase 3	nAMD
Brolucizumab	Novartis	VEGFA	Monoclonal antibody	Phase 3	nAMD, DME
<b>IBI302</b>	<b>Innovent</b>	<b>VEGF, Complement factor</b>	<b>Bispecific fusion protein</b>	<b>Phase 2</b>	<b>nAMD</b>
RC28-E	Remegen	VEGF, FGF	Bispecific antibody	Phase 2	nAMD, mCNV
BAT 5906	Bio-Thera	VEGF	Monoclonal antibody	Phase 2	nAMD, DME
601A	3SBio	VEGF	Monoclonal antibody	Phase 2	DME, mCNV
HB002	HuaBo Biopharm	VEGF, VEGFR	Fusion protein	Phase 2	nAMD

Source: Insight, Companies' data, CMBIS; Note: nAMD = neovascular age-related macular degeneration, DME = Diabetic macular edema, mCNV = Myopic Choroidal Neovascularization

Age-related macular degeneration (AMD) is a chronic progressive disease involving the retina in the macular area, resulting in central visual impairment. It is currently the leading cause disease of blindness in the elderly. In the developed countries or regions, the prevalence of AMD among people over 80 years-old can reach more than 30%. AMD can be divided into dry AMD and nAMD according to clinical manifestations and pathological types. As a main type of AMD, nAMD accounting for 15% to 20% of all AMD patients. But it is the most important cause of irreversible loss of central vision in AMD patients over 65 years of age. AMD has now leapt to the third leading cause of blindness in China with increasing incidence by years. It is generally recognized that angiogenesis induced by increased VEGF expression is the main cause of nAMD. In addition, the inflammatory response mediated by abnormal activation of complement is also considered to be an important cause of AMD, though the mechanism of action in AMD is not fully elucidated. Although anti-VEGF agents confer visual benefits and alter the course of nAMD, the current frequent mode of administration (every 4 or 8 weeks) increases the burden of medication for patients. Besides, the visual benefit of anti-VEGF drug therapy is lost by years with prolonged treatment. In about two-thirds of patients with more than 7 years of follow-up, the visual benefit conferred by anti-VEGF therapy is greatly lost. Some patients on long-term anti-VEGF therapy progress to macular atrophy or fibrosis.

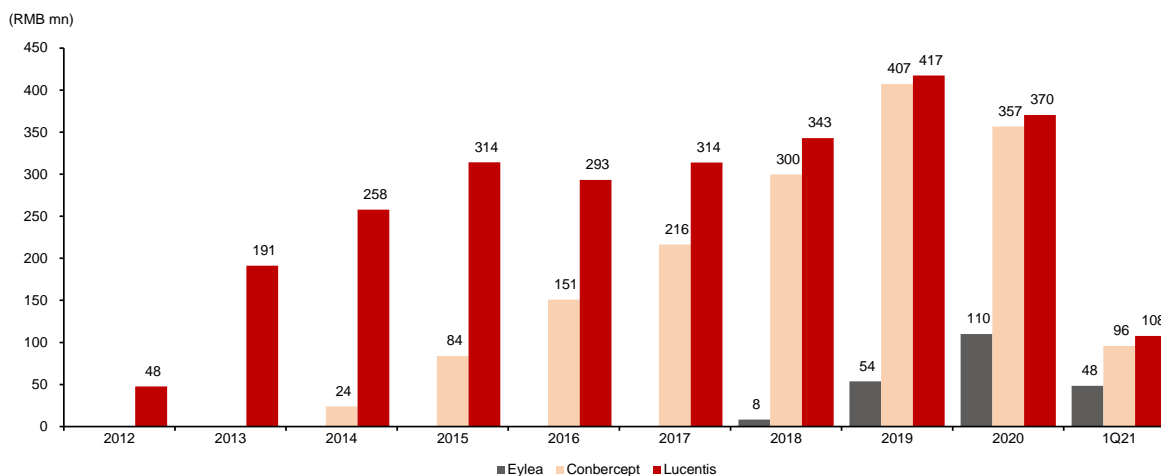
According to a study published in 2004 in the journal Ophthalmology, approximately 1.2mn people in the US suffer from nAMD. F&S estimates that the prevalence of nAMD in China was 3.4mn in 2017 and will reach 4.8mn in 2030.

**Figure 69: Aggregate worldwide sales of Lucentis and Eylea (2010-2020)**



Source: Evaluate Pharma, CMBIS

**Figure 70: Historical sales of Conbercept, Lucentis and Eylea in China (sample hospitals)**

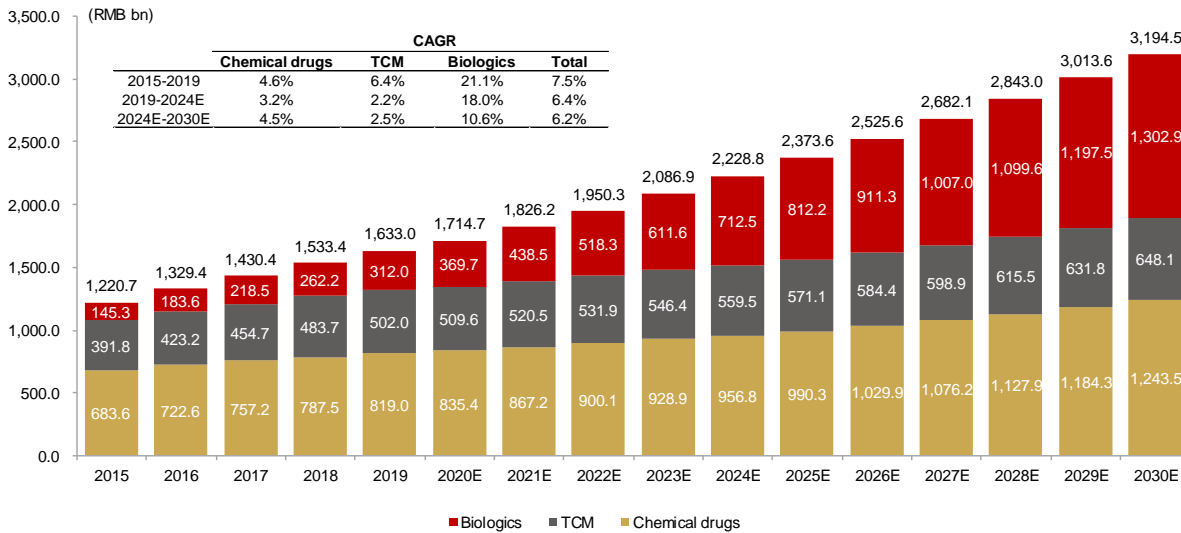


Source: PDB, CMBIS

## Innovative therapies playing more important role in China

Chinese pharmaceutical market has been growing fast in past years. F&S forecasts that size of Chinese pharmaceutical market will grow from RMB1,633.0bn in 2019 to RMB2,228.8bn in 2024E indicating a 6.4% CAGR between 2019 and 2024. The market will further reach RMB3,194.5bn in 2030E, implying a 6.2% CAGR during 2024 and 2030.

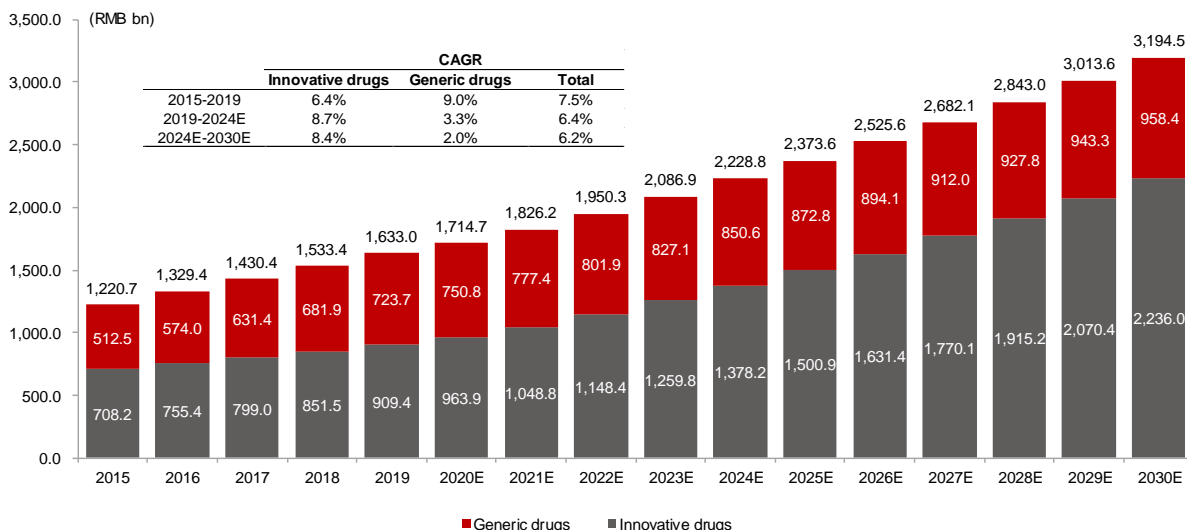
**Figure 71: Size of China pharmaceutical market (2015-2030E)**



Source: F&S, CMBIS

The proportion of innovative drugs in China has been increasing fast in recent years. Driven by favorable policies in innovative drug registration and NRDL inclusion, F&S forecast innovative drugs to account for 70% of total Chinese pharmaceutical market in 2030 vs 56% in 2019.

**Figure 72: Split of China pharmaceutical market (2015-2030E)**

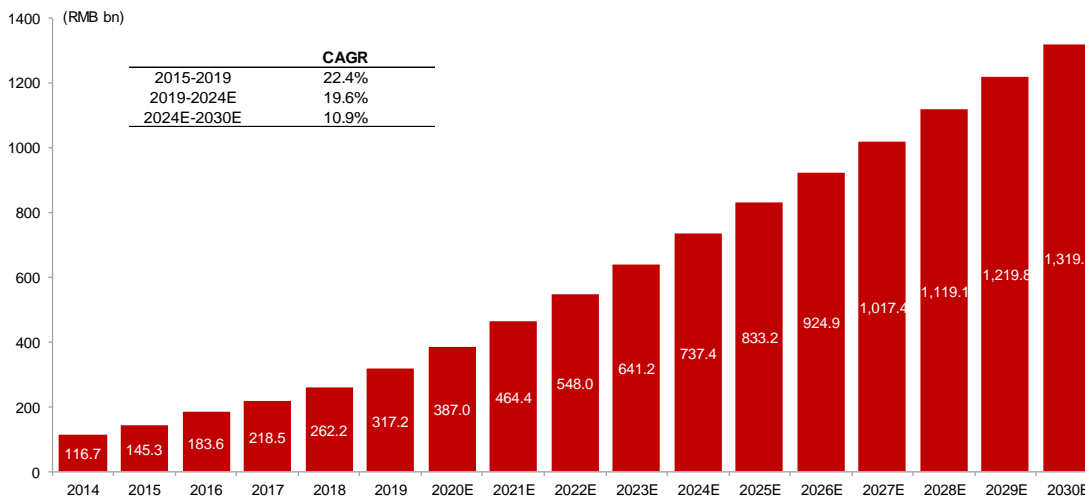


Source: F&S, CMBIS

## Fast-growing biologics market in China

Driven by unmet needs of the cancer patient population, increasing healthcare expenditures, favorable government policies, approval of new biologics therapies and increased investment in research and development, China's biologics market has experienced rapid growth in the past few years, and will continue its robust growth in the future. F&S forecasts China's biologics market to grow from RMB262.2bn in 2018 to RMB641.2bn in 2023 at a CAGR of 19.6% from 2018 to 2023 and further reach RMB1,319.8bn in 2030 at a CAGR of 10.9% from 2023 to 2030.

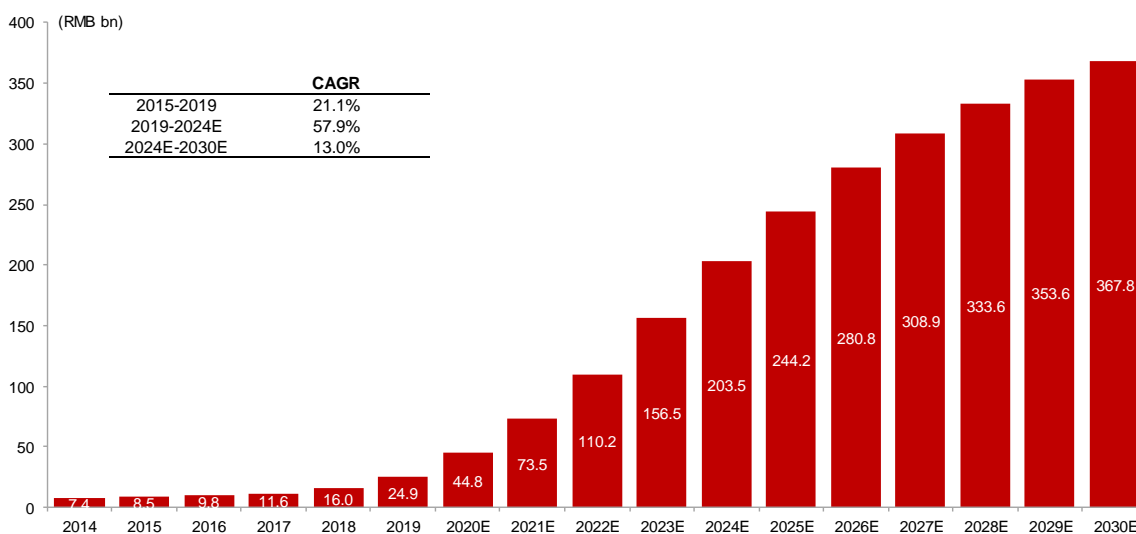
**Figure 73: Size of China biologics market (2014-2030E)**



Source: F&S, CMBIS

According to F&S, as of 2018, monoclonal antibodies (including fusion proteins) market accounted for 55.3% of the global biologics market while the ratio was 6.1% in China. With the inclusion of more mAbs into the NRDL, the sales revenue of China's mAbs market is expected to grow to RMB367.8bn in 2030, representing a CAGR of 13.0% from 2023 to 2030.

**Figure 74: Size of China mAb market (2014-2030E)**

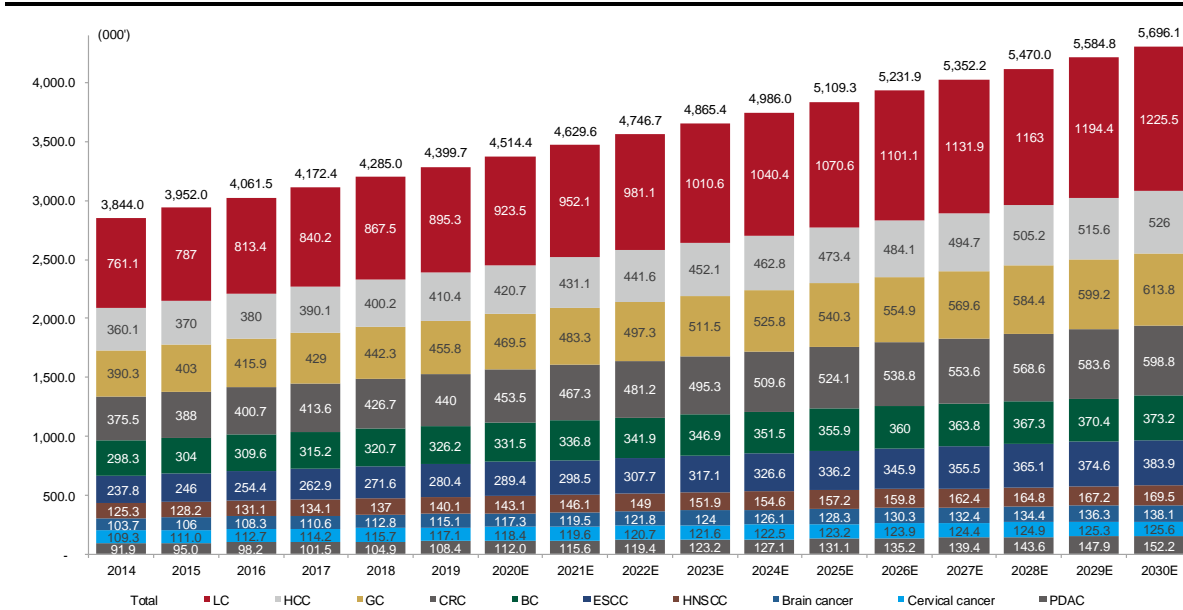


Source: F&S, CMBIS

## Sizable Chinese oncology market

Due to increasing stress in life and work, and existence of unhealthy living habits, cancer incidence in China shows an increasing trend as a whole, growing from 3.8mn in 2014 to 4.4mn in 2019 and will reach 5.7mn in 2030. Among all types of cancer in China, NSCLC has the highest incidence. In 2019, there were 895.3 thousand lung cancer incidence in China, of which 761.0 thousand, or approximately 85%, were recorded as NSCLC. Besides, digestive system cancers such as gastric cancer, colorectal cancer, liver cancer, and esophagus cancer also ranked high among all types of cancer in China in terms of incidence in 2019, indicating vast market potential.

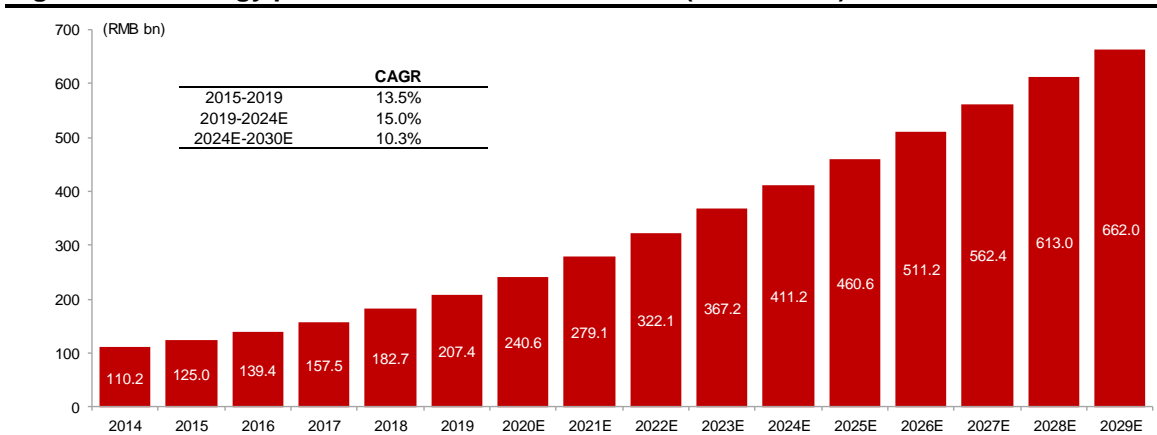
**Figure 75: Incidence by cancer types in China (2014-2030E)**



Source: F&S, CMBIS

According to F&S, the oncology pharmaceutical market in China will grow from RMB182.7bn in 2019 to RMB367.2bn in 2024 and further reach RMB662.0bn in 2030. The key growth drivers include significant unmet clinical demands, increase in patients' affordability and willingness to pay for treatment, favorable government policies to support the development of innovative pharmaceuticals, as well as inclusion of oncology pharmaceuticals in the NRDL.

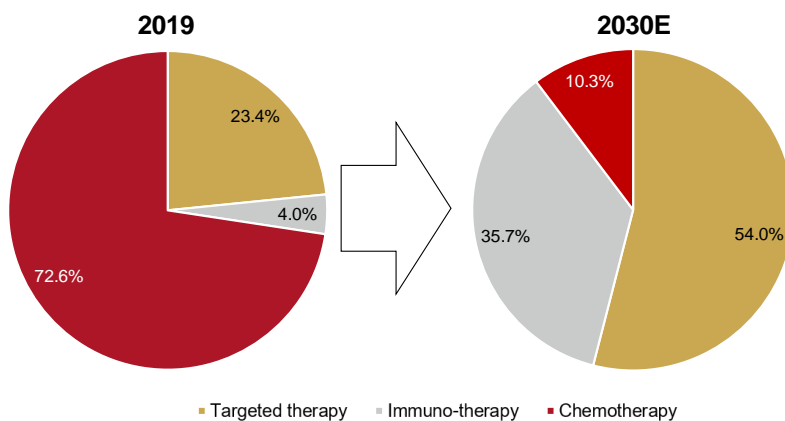
**Figure 76: Oncology pharmaceutical market in China (2015-2030E)**



Source: F&S, CMBIS

In China, pharmaceuticals used for cancer treatment mainly consist of chemotherapy pharmaceuticals, targeted therapy pharmaceuticals, and immuno-oncology therapy pharmaceuticals, among which chemotherapy pharmaceuticals dominated the entire oncology pharmaceutical market with a market share of 72.6% in 2019, while targeted therapy pharmaceuticals and immune -oncology therapy pharmaceuticals accounted for 23.4% and 4.0% of the oncology pharmaceutical market, respectively.

**Figure 77: China oncology pharmaceutical market split (2019 vs 2030E)**



Source: F&S, CMBIS

## Financial analysis

### Strong growth in coming years

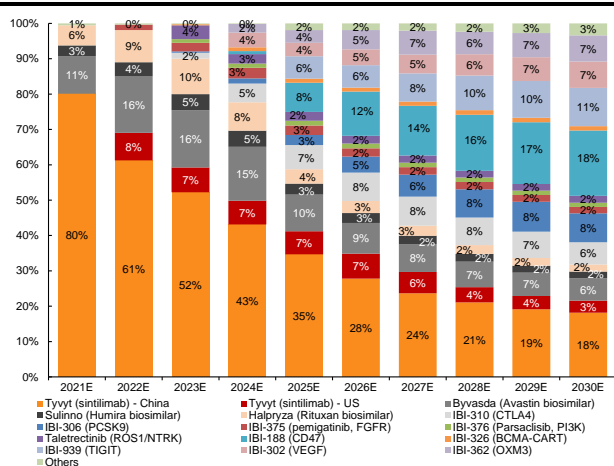
We forecast total revenue to reach RMB3,579mn/ RMB5,747mn/ RMB8,192mn in FY2021E/22E/23E, representing a YoY change of -7%/61%/43%, respectively. We forecast Tyvyt to contribute 80% of Innovent's total revenue in FY21E while the three biosimilars accounting for 20% of the total revenue.

Figure 78: Innovent revenue forecasts (2020-26E)

(YE 31 Dec) (RMBmn)	2020	2021E	2022E	2023E	2024E	2025E	2026E
Tyvyt (sintilimab) - China	2,290	2,867	3,521	4,279	4,926	5,525	5,780
YoY	125%	25%	23%	22%	15%	12%	5%
Tyvyt (sintilimab) - US	0	0	448	576	766	1,045	1,470
YoY				29%	33%	36%	41%
Byvasda (Avastin biosimilar)	50	377	916	1,322	1,738	1,653	1,800
YoY		656%	143%	44%	31%	-5%	9%
Sulinno (Humira biosimilar)	10	111	231	375	523	493	581
YoY		993%	108%	62%	40%	-6%	18%
Halpryza (Rituxan biosimilar)	19	203	523	822	918	648	712
YoY		983%	157%	57%	12%	-29%	10%
IBI-310 (CTLA4)	0	0	0	139	606	1,090	1,667
YoY					335%	80%	53%
IBI-306 (PCSK9)	0	0	0	30	164	452	946
YoY					450%	176%	109%
IBI-375 (pemigatinib, FGFR)	0	0	88	198	342	432	480
YoY				126%	72%	27%	11%
IBI-376 (Parsaclisib, PI3K)	0	0	0	87	139	215	281
YoY					60%	54%	31%
Taletrectinib (ROS1/NTRK)	0	0	0	321	304	393	460
YoY					-5%	29%	17%
IBI-188 (CD47)	0	0	0	0	98	1,320	2,595
YoY						1245%	97%
IBI-326 (BCMA-CART)	0	0	0	23	123	179	238
YoY					425%	46%	33%
IBI-939 (TIGIT)	0	0	0	0	0	1,011	1,311
YoY							30%
IBI-302 (VEGF)	0	0	0	0	472	608	936
YoY						29%	54%
IBI-362 (OXM3)	0	0	0	0	279	576	1,135
YoY						107%	97%
Others	1,475	20	20	20	20	300	390
<b>Total risk adjusted revenue</b>	<b>3,844</b>	<b>3,579</b>	<b>5,747</b>	<b>8,192</b>	<b>11,420</b>	<b>15,940</b>	<b>20,782</b>
YoY	267%	-7%	61%	43%	39%	40%	30%

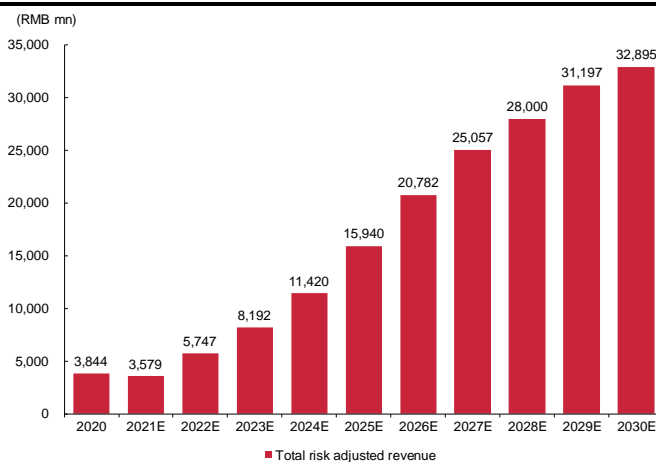
Source: Company data, CMBIS estimates; Note: Sales of three biosimilars in FY20 were CMBIS estimates

Figure 79: Revenue breakdown



Source: Company data, CMBIS estimates

Figure 80: Total risk-adjusted revenue forecasts



Source: Company data, CMBIS estimates

Innovent recorded attributable net loss of RMB1,720mn/ RMB998mn in FY19A/20A. We expect its net loss to be RMB1,399mn/ RMB857mn/ RMB125mn in FY21E/22E/23E.

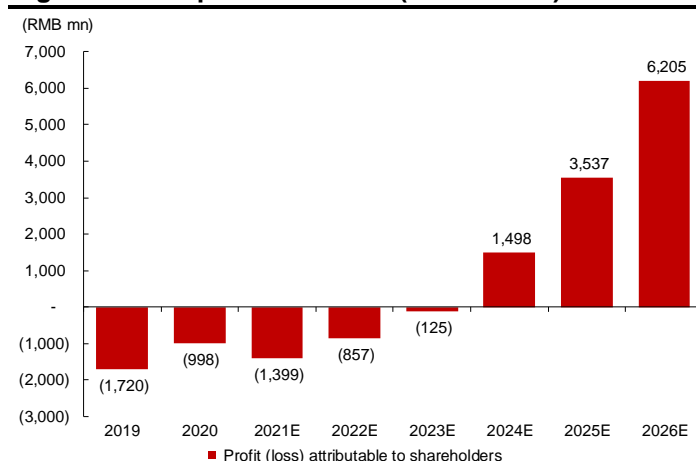
Thanks to the economy of scale, we forecast selling and distribution expenses ratio to decrease from 40.0% in FY21E to 36% in FY23E and administrative expense ratio to be 14%/11%/10% in FY21E/22E/23E.

**Figure 81: P&L forecasts**

(YE 31 Dec) (RMB mn)	2019	2020	2021E	2022E	2023E	2024E	2025E
<b>Revenue (risk-adjusted)</b>	<b>1,048</b>	<b>3,844</b>	<b>3,579</b>	<b>5,747</b>	<b>8,192</b>	<b>11,420</b>	<b>15,940</b>
YoY	N/A	266.9%	-6.9%	60.6%	42.5%	39.4%	39.6%
<b>Gross profit</b>	<b>923</b>	<b>3,456</b>	<b>3,042</b>	<b>4,885</b>	<b>6,922</b>	<b>9,592</b>	<b>13,390</b>
GPM	88.1%	89.9%	85.0%	85.0%	84.5%	84.0%	84.0%
Other income	144	247	278	295	289	309	367
% of revenue	13.8%	6.4%	7.8%	5.1%	3.5%	2.7%	2.3%
Other gains and losses	15	(480)	-	-	-	-	-
% of revenue	1.4%	-12.5%	0.0%	0.0%	0.0%	0.0%	0.0%
R&D expenses	(1,295)	(1,851)	(2,200)	(2,500)	(2,800)	(2,512)	(2,391)
% of revenue	-123.6%	-48.2%	-61.5%	-43.5%	-34.2%	-22.0%	-15.0%
Administrative expenses	(255)	(437)	(500)	(632)	(819)	(1,028)	(1,275)
% of revenue	-24.4%	-11.4%	-14.0%	-11.0%	-10.0%	-9.0%	-8.0%
Selling and marketing expenses	(693)	(1,341)	(1,432)	(2,184)	(2,949)	(3,883)	(5,101)
% of revenue	-66.1%	-34.9%	-40.0%	-38.0%	-36.0%	-34.0%	-32.0%
Finance costs, net	(59)	(68)	(51)	(30)	(31)	(31)	(31)
% of revenue	-5.7%	-1.8%	-1.4%	-0.5%	-0.4%	-0.3%	-0.2%
<b>Profit (loss) before tax</b>	<b>(1,720)</b>	<b>(859)</b>	<b>(1,399)</b>	<b>(857)</b>	<b>(125)</b>	<b>1,763</b>	<b>4,162</b>
PBT margin	-164.2%	-22.3%	-39.1%	-14.9%	-1.5%	15.4%	26.1%
Income tax	-	(140)	-	-	-	(264)	(624)
% tax rate	0.0%	-3.6%	0.0%	0.0%	0.0%	-2.3%	-3.9%
<b>Profit (loss) for the year</b>	<b>(1,720)</b>	<b>(998)</b>	<b>(1,399)</b>	<b>(857)</b>	<b>(125)</b>	<b>1,498</b>	<b>3,537</b>
Minority interests	-	-	-	-	-	-	-
<b>Profit (loss) attributable to shareholders</b>	<b>(1,720)</b>	<b>(998)</b>	<b>(1,399)</b>	<b>(857)</b>	<b>(125)</b>	<b>1,498</b>	<b>3,537</b>
NPM	-164.2%	-26.0%	-39.1%	-14.9%	-1.5%	13.1%	22.2%
YoY	N/A	N/A	N/A	N/A	N/A	N/A	136.1%

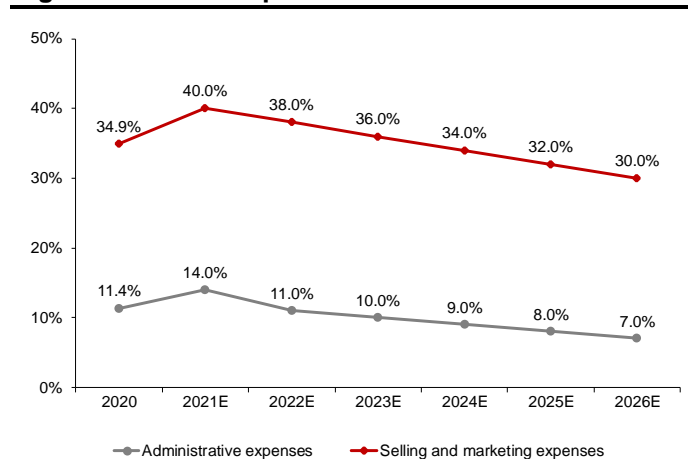
Source: Company data, CMBIS estimates

**Figure 82: Net profit forecasts (2018-2026E)**



Source: Company data, CMBIS estimates

**Figure 83: SG&A expense ratio forecasts**



Source: Company data, CMBIS estimates



## Financial Statements

### Income statement

YE 31 Dec (RMB mn)	FY19A	FY20A	FY21E	FY22E	FY23E
<b>Revenue</b>	<b>1,048</b>	<b>3,844</b>	<b>3,579</b>	<b>5,747</b>	<b>8,192</b>
Cost of sales	(125)	(388)	(537)	(862)	(1,270)
<b>Gross profit</b>	<b>923</b>	<b>3,456</b>	<b>3,042</b>	<b>4,885</b>	<b>6,922</b>
Administrative expenses	(255)	(437)	(500)	(632)	(819)
R&D expenses	(1,295)	(1,851)	(2,200)	(2,500)	(2,800)
Selling and marketing expenses	(693)	(1,341)	(1,432)	(2,184)	(2,949)
Other income	144	247	278	295	289
Other gains and losses	15	(480)	0	0	0
<b>Operating profit</b>	<b>(1,161)</b>	<b>(406)</b>	<b>(811)</b>	<b>(136)</b>	<b>643</b>
Listing expenses	0	0	0	0	0
Finance costs, net	(59)	(68)	(51)	(30)	(31)
Royalties and other related	(500)	(384)	(537)	(690)	(737)
<b>Pre-tax profit</b>	<b>(1,720)</b>	<b>(859)</b>	<b>(1,399)</b>	<b>(857)</b>	<b>(125)</b>
Income tax	0	(140)	0	0	0
Minority interests	0	0	0	0	0
<b>Net profit (Net loss)</b>	<b>(1,720)</b>	<b>(998)</b>	<b>(1,399)</b>	<b>(857)</b>	<b>(125)</b>

### Cash flow summary

YE 31 Dec (RMB mn)	FY19A	FY20A	FY21E	FY22E	FY23E
<b>Profit before tax</b>	<b>(1,720)</b>	<b>(859)</b>	<b>(1,399)</b>	<b>(857)</b>	<b>(125)</b>
Depreciation and	86	86	94	100	105
Changes in working capital	(141)	(334)	158	(310)	(362)
Tax paid	14	(140)	0	0	0
Others	97	939	357	416	538
<b>Net cash from operating</b>	<b>(1,664)</b>	<b>(308)</b>	<b>(790)</b>	<b>(651)</b>	<b>156</b>
Capex	(366)	(489)	(200)	(200)	(200)
Placement of term deposits with maturity dates over 3 months	(4,264)	(7,126)	0	0	0
Other investing activities	2,061	2,431	178	195	189
<b>Net cash from investing activities</b>	<b>(2,569)</b>	<b>(5,185)</b>	<b>(22)</b>	<b>(5)</b>	<b>(11)</b>
Net proceeds from shares issued	2,169	4,657	3,877	0	0
New borrowings raised	43	372	0	0	0
Repayment of borrowings	(10)	(17)	(700)	0	0
Other financing activities	(93)	(100)	(51)	(30)	(31)
<b>Net cash from financing activities</b>	<b>2,109</b>	<b>4,912</b>	<b>3,125</b>	<b>(30)</b>	<b>(31)</b>
<b>Net change in cash</b>	<b>(2,124)</b>	<b>(580)</b>	<b>2,314</b>	<b>(686)</b>	<b>114</b>
Fx Changes	25	(569)	0	0	0
Cash at the beginning of the	4,525	2,426	7,764	10,078	9,391
<b>Cash at the end of the year</b>	<b>2,426</b>	<b>1,276</b>	<b>10,078</b>	<b>9,391</b>	<b>9,506</b>

### Balance sheet

YE 31 Dec (RMB mn)	FY19A	FY20A	FY21E	FY22E	FY23E
<b>Non-current assets</b>	<b>1,775</b>	<b>2,368</b>	<b>2,474</b>	<b>2,574</b>	<b>2,669</b>
PP&E	1,345	1,584	1,707	1,825	1,938
Right-of-use assets	92	327	309	292	274
Intangible assets	0	33	33	33	33
Deposits for acquisition of PP&E	85	272	272	272	272
Other non-current assets	254	152	152	152	152
<b>Current assets</b>	<b>5,455</b>	<b>9,467</b>	<b>11,678</b>	<b>11,409</b>	<b>12,019</b>
Inventories	359	706	588	709	870
Trade receivables	248	475	490	787	1,122
Deposits, prepayments and other receivables	152	165	165	165	165
Other financial assets	463	357	357	357	357
Cash and bank balances	4,233	7,764	10,078	9,391	9,506
<b>Current liabilities</b>	<b>1,044</b>	<b>1,486</b>	<b>1,542</b>	<b>1,649</b>	<b>1,783</b>
Borrowings	17	255	255	255	255
Lease liabilities	16	16	16	16	16
Trade payables	84	121	176	283	417
Other payables and accrued	885	974	974	974	974
Contract liabilities	42	120	120	120	120
<b>Non-current liabilities</b>	<b>1,431</b>	<b>1,569</b>	<b>870</b>	<b>871</b>	<b>872</b>
Contract liabilities	582	588	588	588	588
Borrowings	808	925	225	225	225
Lease liabilities	25	10	11	12	13
Government grants	17	46	46	46	46
<b>Total net assets</b>	<b>4,756</b>	<b>8,780</b>	<b>11,740</b>	<b>11,463</b>	<b>12,034</b>
Minority interest	0	0	0	0	0
<b>Shareholders' equity</b>	<b>4,756</b>	<b>8,780</b>	<b>11,740</b>	<b>11,463</b>	<b>12,034</b>

### Key ratios

YE 31 Dec (RMB mn)	FY19A	FY20A	FY21E	FY22E	FY23E
<b>Profit &amp; loss ratios (%)</b>					
Gross margin	88	90	85	85	85
EBITDA margin	N/A	(21.4)	(40.0)	(16.0)	(2.2)
Net margin	N/A	(26.0)	(39.1)	(14.9)	(1.5)
Effective tax rate (%)	0	(16)	0	0	0
<b>Balance sheet ratios</b>					
Current ratio (x)	5	6	8	7	7
Trade receivables turnover	86	34	50	50	50
Trade payables turnover days	186	96	120	120	120
Total debt to asset ratio (%)	34	26	17	18	18
<b>Returns (%)</b>					
ROE	(36)	(11)	(12)	(7)	(1)
ROA	(24)	(8)	(10)	(6)	(1)
<b>Per share data</b>					
EPS (RMB)	(1.46)	(0.74)	(0.96)	(0.59)	(0.09)
DPS (RMB)	0.0	0.0	0.0	0.0	0.0

Source: Company data, CMBIS estimates

## Valuation

### Initiate at BUY with TP of HK\$120.91

We expect Innovent's to turn profitable from FY24E and to realize net profit of RMB1,498mn in FY24E. To factor in the potential contribution from innovative drug pipelines, we use DCF model to value the Company. We derive our target price of HK\$120.91 based on a 15-year DCF valuation (WACC: 9.05%, terminal growth rate: 4.0%).

**Figure 84: Risk-adjusted DCF valuation (terminal growth rate: 4.0%)**

DCF Valuation (in Rmb mn)	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
EBIT	(1,526)	(1,021)	(283)	1,585	3,926	6,958	9,998	12,420	15,231	16,548	17,625	17,507	17,826	18,254	18,701
Tax rate	0%	0%	0%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
EBIT*(1-tax rate)	(1,526)	(1,021)	(283)	1,347	3,337	5,914	8,498	10,557	12,946	14,066	14,981	14,881	15,152	15,516	15,896
+ D&A	94	100	105	110	114	119	123	127	131	135	138	142	145	148	151
- Change in working capital	158	(310)	(362)	(390)	(428)	(454)	(586)	(403)	(438)	(233)	143	112	(37)	(62)	(66)
- Capx	(200)	(200)	(200)	(200)	(200)	(200)	(200)	(200)	(200)	(200)	(200)	(200)	(200)	(200)	(200)
<b>FCFF</b>	<b>(1,474)</b>	<b>(1,431)</b>	<b>(741)</b>	<b>866</b>	<b>2,823</b>	<b>5,379</b>	<b>7,835</b>	<b>10,081</b>	<b>12,439</b>	<b>13,768</b>	<b>15,062</b>	<b>14,935</b>	<b>15,060</b>	<b>15,401</b>	<b>15,781</b>
<b>Terminal value</b>															<b>325,001</b>
PV of enterprise (RMB mn)	136,789														
Net debt (RMB mn)	(9,570)														
Equity value (RMB mn)	146,359														
Equity value (HK\$ mn)	176,336														
No. of outstanding shares (mn)	1,458														
<b>DCF per share (HK\$)</b>	<b>120.91</b>														
<b>Terminal growth rate</b>	<b>4.0%</b>														
<b>WACC</b>	<b>9.05%</b>														
Cost of Equity	12.5%														
Cost of Debt	4.5%														
Equity Beta	0.9														
Risk Free Rate	3.0%														
Market Risk Premium	10.5%														
Target Debt to Asset ratio	30.0%														
Effective Corporate Tax Rate	15.0%														

Source: CMBIS estimates

**Figure 85: Sensitivity analysis**

		WACC				
		8.05%	8.55%	9.05%	9.55%	10.05%
Terminal growth rate	3.0%	135.15	120.42	108.22	97.96	89.23
	3.5%	144.75	127.80	113.99	102.55	92.93
	4.0%	156.71	136.79	120.91	107.96	97.23
	4.5%	172.05	148.01	129.34	114.45	102.31
	5.0%	192.41	162.38	139.86	122.36	108.40

Source: CMBIS estimates

Figure 86: Peers valuation table

Company	公司名称	Ticker	Rating	Current	Target	Mkt cap	PS(x)	
				Price (HK\$)	Price (HK\$)		FY21E	FY22E
Innovent	信达生物	1801 HK	BUY	84.55	120.91	123,312	23.37	14.58
InnoCare	诺诚健华	9969 HK	BUY	29.00	Reviewing	43,491	63.84	68.03
Kintor	开拓药业	9939 HK	BUY	79.95	92.08	30,988	652.82	3.01
Henlius	复宏汉霖	2696 HK	BUY	34.85	60.61	18,941	10.27	5.49
Ascentage	亚盛医药	6855 HK	BUY	53.80	66.04	13,618	162.28	28.05
Genor	嘉和生物	6998 HK	BUY	16.58	26.49	8,186	125.27	20.72
BeiGene	百济神州	6160 HK	N/A	190.40	NR	228,661	25.96	22.67
ZaiLab	再鼎医药	9688 HK	N/A	1239.00	NR	117,592	103.09	42.59
Shanghai Junshi	君实生物	1877 HK	N/A	58.35	NR	64,765	12.19	12.66
Remegen	荣昌生物	9995 HK	N/A	99.95	NR	48,959	187.99	44.17
AkesoBio	康方生物	9926 HK	N/A	52.45	NR	42,855	70.05	19.80
AlphaMab	康宁杰瑞	9966 HK	N/A	26.05	NR	24,379	572.40	133.52
CStone	基石药业	2616 HK	N/A	17.26	NR	20,422	64.07	17.56
Everest Medicine	云顶新耀	1952 HK	N/A	65.10	NR	19,381	2179.41	59.39
JacoBio	加科思	1167 HK	N/A	21.10	NR	16,300	N/A	N/A
<b>Peers average:</b>							<b>325.36</b>	<b>36.74</b>

Source: Bloomberg (as at 21 Jul 2021), CMBIS

## Investment risks

- 1) Clinical risks: Any failure on Innovent's pipeline's ongoing trials on different indications might induce lead to failure on approval.
- 2) Regulatory approval risks: The Company's ability to generate revenue will depend primarily on the successful regulatory approvals of its pipeline assets.
- 3) Competition risk: It faces intense competition from competitors' PD-1/L1, both in mono therapy and combo therapy. It also faces competition from other novel biologics, including bsAbs and biosimilar drugs.

## Appendix

### Strong management team

**Figure 87: Directors and management profile**

Name	Position	Roles and Responsibilities
Dr. Michael Yu (俞德超)	Co-founder, CEO	Responsible for the overall strategic planning and business direction of the Group and management of the Company
Dr. Yongjun liu (刘勇军)	President	Responsible for group's global R&D, portfolio strategy, business development as well as international operation
Min Liu (刘敏)	Chief Commercial Officer	Responsible for company commercial operations including marketing, sales and market access
Ronald Ede (奚浩)	Executive Director, CFO	Responsible for finance, investor relations, fund, channel management and information technology of the Group
Vivian Zhang (张倩)	Chief People Officer	Responsible for management of CEO office, public relationship, human resources, administrative affairs and other related functions
Dr. Changshou Gao (高长寿)	Chief Technology Officer, Senior Vice President	Responsible for Innovent Academy and global research center.
Dongming Wang (王董明)	Senior Vice President	Responsible for group quality management
Blake Salisbury	Vice president of Business development	Responsible for BD activities

Source: Company data

**Dr. De-Chao Michael Yu** is a co-founder, an executive Director, the Chairman of the Board and Chief Executive Officer of the Company. Dr. Yu is responsible for the overall strategic planning and business direction of the Group and management of the Company. Dr. Yu received his doctoral degree in Molecular Genetics from the Chinese Academy of Sciences (Shanghai, China) and completed his post-doctoral training at the University of California San Francisco (San Francisco, USA). Prior to founding Innovent in 2011, Dr. Yu was President, CEO and a member of the Board of Directors of Chengdu Kanghong Biotech from 2006. Previously, Dr. Yu was Vice President of Research and Development at Applied Genetic Technology Corporation (Nasdaq: AGTC) and Calydon which was acquired by Cell Genesys (Nasdaq: CEGE) in 2001. After the acquisition he worked at Cell Genesys for more than three years. He has aspired to develop and commercialize high quality biopharmaceuticals that are affordable to ordinary people.

Dr. Yu has engaged in innovative research on biopharmaceuticals for more than 20 years, who has invented three Class I new drugs and has promoted their development and commercialization. Dr. Yu invented the world's first commercialized oncolytic virus-based immunotherapeutic product, Oncorine (recombinant human type-5 adenovirus injection), creating a precedent for the use of viruses to treat tumors. Dr. Yu co-invented and led the development of China's first monoclonal antibody-like new drug with global intellectual property rights, Langmu (Conbercept eye injection) which has changed the history of zero domestically developed medicine for Chinese patients with blindness caused by fundus diseases. Dr. Yu also co-invented and led the development of Tyvyt which is domestically-developed innovative PD-1 inhibitor with international quality and has been approved for marketing in China for relapsed or refractory classical Hodgkin's lymphoma (r/r cHL) on Dec 24, 2018.

Dr. Yu is an inventor of over 60 issued patents and patent applications, and has published more than 50 SCI scientific articles and book chapters. He was recognised as “Top Ten Persons in Innovation in China” in 2014, “The E&Y Entrepreneur of the Year in China” in 2015 and “Distinguished Entrepreneur of Jiangsu Province” in 2016. In 2017, Dr. Yu was selected as “Person of the Year in Innovation for Science and Technology in 2016”, “2017 China Person of the Year in Pharmaceutical Economics” and “The Most Influential Person of the Year in Life Science in China in 2017”. In 2018, Dr. Yu was awarded as the First Prize of “The Seventh National Overseas Returnee Contributions Awards” etc.

**Dr. Yong Jun Liu** joined Innovent as the President in Oct 2020, mainly responsible for group's global R&D, portfolio strategy, business development as well as international operation. Dr. Liu received his MD's degree in internal medicine from Bethune Medical University in 1984 and Ph.D. degree in Immunology from University of Birmingham, UK in 1989, and completed postgraduate training in the same laboratory at University of Birmingham.

As a world-renowned scientist in immunology, oncology and translational medicine, Dr. Liu has over 30 years' experiences in both academic institutions and top global pharmaceutical companies. He joined multinational pharmaceutical company Schering-Plough in 1991 as a Senior Scientist at Schering-Plough Lyon France. In 1997, he moved to the DNAX Research Institute, a biotech company owned by Schering-Plough in Palo Alto, California, as a Principal Staff Member. In 2002, Dr. Liu was recruited by the University of Texas (UT), MD Anderson Cancer Center, as the Vivian Smith Distinguished Chair Professor, Chairman of the Department of Immunology and the founding Director of the Center for Cancer Immunology Research (CCIR). In 2011, Dr. Liu was recruited by the Baylor Research Institute as the Chief Scientific Officer and the Director of the Baylor Immunology Research Institute. After more than 10 years at the academia, Dr. Liu was recruited by Medimmune, the biopharmaceutical subsidiary of AstraZeneca, as Chief Scientific Officer and global Head of Research in 2014. Before joining Innovent, Dr Liu served as the global Head of Research at Sanofi from 2016 to 2020.

Dr. Liu has remarkable academic achievements and rich experience in research institutions. As one of the top cited scientists in Immunology with over 94,000 citations, Dr. Liu published over 260 scientific papers in Nature, Science and other top academic journals. These studies provide a number of key targets for drug development in the area of inflammation, autoimmune diseases, allergy and oncology, such as thymic stromal lymphopoietin (TSLP), OX40 (CD134), plasma cell like dendritic cells (pDCs).

**Mr. Ronald Hao Xi Ede, CFO**, is responsible for finance, investor relations, fund, channel management and information technology of the Group. Mr. Ede received his bachelor of business administration degree from University of Hawaii in Dec 1984 and master of business administration degree from University of Washington in Dec 1988. Mr. Ede is a fellow member of the Institute of Singapore Chartered Accountants and an A-Share independent director certified by the Shenzhen Stock Exchange.

Prior to joining the Group, between 2011 and 2016, Mr. Ede was the chief financial officer of Biosensors International Ltd. Between 2009 and 2011, Mr. Ede was the executive director and chief financial officer of Mindray Medical International Limited.

Mr. Ede is an independent non-executive director for Mindray Medical International Limited (a listed company on the Shenzhen Stock Exchange with stock code: 300760) since 2006, and Dawnrays Pharmaceutical (Holding) Ltd. (a company listed on the Hong Kong Stock Exchange with stock code: 2348) since 2015, respectively.

**Dr. Changshou Gao** is the **CTO** of Innovent, mainly responsible for Innovent Academy and global research center. Dr. Gao received his Master degree in Shanghai Institute of Biochemistry, Chinese Academy of Sciences and Ph.D. degree in Chemistry and Molecular Biology from the Scripps Research Institute (La Jolla, California).

Dr. Gao is a well-recognized innovative scientist with about 20 years of biopharmaceutical research and drug development experience and extensive track record in lead antibody discovery and early drug development. Prior to joining Innovent, Dr. Gao was senior director of the Antibody Discovery & Protein Engineering Department of MedImmune/AstraZeneca. Dr. Gao has broad experience on antibody discovery/engineering, protein scaffolds, bispecific antibodies, antibody drug conjugates, large scale antibody transient expression, targeted nanoparticles, PROTAC, AAV mediated gene therapy, and new technology development for the next generation of biologics. He has advanced/contributed more than 20 therapeutic antibodies, including antibody drug conjugates and bispecific antibodies, covering oncology, immunology, infectious disease, cardiovascular, Renal, and metabolic diseases, to clinical trials.

Dr. Gao also has 30 years of academic excellence with publications in major journals (h-index=32, over 3300 citations) and invention on 38 issued patents or patent applications.

**Mr. Min Liu, CCO**, is in charge of company commercial operations including marketing, sales and market access at Innovent. He graduated with a BS in Biochemistry from Wu Han University and earned his MBA from Harvard Business School. He has over 20 years of experience in P&L management, building strategy, developing people, and leading large teams at multinational pharmaceutical companies. Before joining Innovent he was the Vice President of Business Unit Oncology 2 in Roche China and a member of Roche Global Oncology Franchise's Leadership Team.

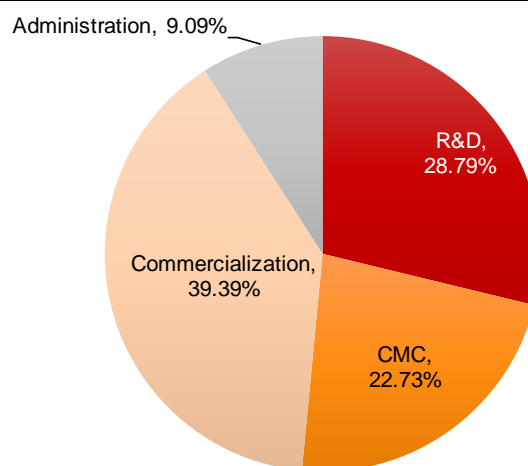
**Mr. Blake Salisbury** is responsible for **BD** activities at Innovent. He received his MBA from Thunderbird Graduate School of Global Management. He has 27 years of experience in pharma/biotech, primarily in business development (20 years), but also in sales, marketing, and pricing. Prior to joining Innovent, Blake spent almost 24 years with Eli Lilly and Company where he closed over 50 transactions of various types.

**Figure 88: Employee structure (as of 31 Dec 2020)**

Function	# of employees	% of Total
Research & Development	950	28.79%
Manufacturing	750	22.73%
Sales & marketing	1,300	39.39%
Others (including Operational and management)	300	9.09%
<b>Total</b>	<b>3,300</b>	<b>100%</b>

Source: Company data, CMBIS

**Figure 89: Staff No. breakdown (as of 31 Dec 2020)**



Source: Company data, CMBIS

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