OVERVIEW OF OUR COMPANY

Our mission is to create a world-class China-based biopharmaceutical company that develops and commercializes high quality drugs that are affordable to ordinary people. We were founded in 2011 by our visionary leader, Dr. De-Chao Michael Yu, a highly accomplished scientist, innovator and entrepreneur. Dr. Yu invented the world's first oncolytic virus-based immunotherapeutic product, Oncorine, and also co-invented and led the development of the first domestic innovative fully human antibody-like therapeutic approved for marketing in China, Conbercept. We are committed to innovation in drug development and have instituted global quality standards for every aspect of our Company's business and operations.

China's biologics market has experienced rapid growth in the past few years, more so than the global biologics market, and we believe it will continue its robust growth in the future, driven by the unmet needs of the cancer patient population, increasing healthcare expenditures, favorable government policies, the approval of new biologics therapies and increased investment in research and development. According to Frost & Sullivan, a leading global market research and consulting firm, China's biologics market grew from RMB86.2 billion in 2013 in terms of market size to RMB218.5 billion in 2017, representing a CAGR of 26.2% during the period.

To capitalize on this tremendous market opportunity, we have developed our fullyintegrated platform which boasts advanced research, discovery, development, manufacturing and commercialization capabilities. These capabilities have enabled us to build a robust pipeline of innovative and commercially promising monoclonal antibodies and other biologics in the fields of oncology, ophthalmology, and autoimmune and metabolic diseases. The full integration of our platform enables smooth collaboration between different functional groups at key points in the lifecycle of a drug candidate with the aim of increasing both the speed of development and the likelihood of success while at the same time reducing the cost of development. This platform is the engine that drives our business and allows us to manage the risks of drug development.

Leveraging our platform, we have built up a pipeline of 17 antibody drug candidates in the last seven years, led by our four core products that are in late-stage clinical development in China, including sintilimab (IBI-308), our novel PD-1 antibody; IBI-305, our bevacizumab (Avastin) biosimilar; IBI-301, our rituximab (MabThera/Rituxan) biosimilar; and IBI-303, our adalimumab (Humira) biosimilar. In addition, out of our pipeline of 17 antibody drug candidates, six are in clinical development in China, including two designated as Category 1 drug candidates, which are sintilimab and IBI-306, and four designated as Category 2 drug candidates, including IBI-310, IBI-301, IBI-303 and IBI-305. Moreover, four other drug candidates in our pipeline, IBI-302, IBI-307, IBI-101 and IBI-188, received IND approval in December 2016, June 2018, June 2018 and August 2018, respectively.

	6 W 4			Commercial	Status				
	Candidate/ Reference Drug	Target(s)	Therapeutic Area: Disease Indications***	Rights	Pre-clinical IND (Filed) (Accepted) Phase 1 Phase 2 Phase 3 (Filed)				
	sintilimab (IBI-308)*	PD-1	Oncology: rlr Hodgkin's lymphoma, 1L and 2L melanoma, refractory gastrointestinal cancers, 2L NSCLC, 2L esophagael cancer, 1L and 2L squamous NSCLC, 1L non-squamous NSCLC, rlr NK/T-cell lymphoma, 2L ESCC, 1L gastric cancer, solid tunors, and esophageal carcinoma	Worldwide ⁽²⁾	NDA filed for th Hodgkin's lymphoma: Apr 3, 2018				
	IBI-306	PCSK9	Metabolic: homozygous familial hyperlipidemia; statin intolerant high CV risk patients	China, Hong Kong, Taiwan	IND approved: Sep 8, 2017				
	IBI-310 ⁽¹⁾	CTLA-4	Oncology: melanoma and renal cell carcinoma	Worldwide	IND approved: Feb 13, 2018				
	IBI-302	VEGF/Complement proteins	Ophthalmology: wet AMD	Worldwide	IND approved: Dec 9, 2016				
	IBI-307	RANKL	Metabolic: osteoporosis and lytic bone lesions associated with cancer metastasis	Worldwide	IND approved: Jun 15, 2018				
	IBI-101	OX40	Oncology: advanced solid tumors, hepatitis B	Worldwide	IND approved: Jun 15, 2018				
Novel	IBI-188	CD47	Oncology: B-cell lymphoma, ovarian cancer, colorectal cancer	Worldwide	IND approved: Aug 22, 2018				
	IBI-110	LAG-3	Oncology: NSCLC, melanoma, mBrCA, advanced tumors	Worldwide					
	IBI-939	TIGIT	Oncology: advanced solid tumors	Worldwide					
	IBI-318	PD-1/undisclosed target	Oncology: advanced tumors (undisclosed target)	China, Hong Kong, Macau ⁽³⁾					
	IBI-319	PD-1/undisclosed target	Oncology: advanced tumors (undisclosed target)	China, Hong Kong, Macau ⁽³⁾					
	IBI-322	PD-L1/CD47	Oncology: PDL1/CD47 coexpressing tumors, M1 macrophage signature tumors	Worldwide					
	IBI-315	PD-1/HER2	Oncology: Her2 + cancers, mBrCA, gastric cancer, NSCLC	**					
	IBI-323	LAG-3/PD-LI	Oncology: PDL1+ tumors with "hot tumor" phenotype	Worldwide					
	rituximab (IBI-301)/ Rituxan*	CD20	Oncology: non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis	Worldwide ⁽²⁾	IND approved: Sep 13, 2014				
Biosimilar	adalimumab (IBI-303)/ Humira*	TNF-α	Autoimmune: rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis and psoriasis	Worldwide	IND approved: Dec 28, 2015				
	bevacizumab (IBI-305)/ Avastin*	VEGF-A	Oncology: r/r NSCLC and metastatic CRC	Worldwide	IND approved: May 10, 2016				

The following chart shows the robust pipeline of both early-stage and late-stage antibody drug candidates that we are developing in China in different therapeutic areas:

Abbreviations: 1L = first-line; 2L = second-line; AMD = age-related macular degeneration; CRC = colorectal cancer; CV = cardiovascular; EGFR = epidermal growth factor receptor; ESCC = esophageal squamous cell carcinoma; HCC = hepatocellular carcinoma; NHL = non-Hodgkin's lymphoma; NK/T-cell lymphoma = natural killer/T-cell lymphoma; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; r/r = relapsed, refractory; SCLC = small-cell lung cancer; TKI = tyrosine kinase inhibitor.

- * denotes a core product.
- ** collaboration with Hanmi, subject to confidentiality terms prohibiting the disclosure of confidential information.
- *** We also plan to develop sintilimab in combination with (i) IBI-310 for the treatment of melanoma, SCLC and RCC, (ii) each of IBI-101, IBI-188, IBI-110 and IBI-939 for the treatment of advanced solid tumors, (iii) IBI-305 for the treatment of HCC and EGFR-TKI failure NSCLC, and (iv) IBI-301 for the treatment of B-cell NHL. We also plan to develop IBI-188 in combination with IBI-301 for the treatment of B-cell NHL.
- (1) We are developing IBI-310 as an innovative drug candidate in accordance with NMPA regulations because ipilimumab has not been approved for marketing in China even though IBI-310 has the same amino acid sequence as ipilimumab.
- (2) We and Eli Lilly will co-promote sintilimab (IBI-308) and rituximab (IBI-301) in China, Hong Kong and Macau.
- (3) Eli Lilly may opt in to co-commercialize IBI-318 and IBI-319 with us in China, Hong Kong and Macau.

We have three bi-specific monoclonal antibody candidates based on sintilimab (IBI-308) in co-development with Eli Lilly, two of which, IBI-318 and IBI-319, are under development in China. See "–Collaboration Agreements–Collaboration with Eli Lilly–Addendum to the Exclusive License and Collaboration Agreement for China" for details.

In addition to developing our pipeline drug candidates in China, we have obtained FDA approval for our IND applications for sintilimab (IBI-308) and IBI-188 and plan to initiate a multi-center Phase 1b/2 clinical trial for sintilimab (IBI-308) and a Phase 1a clinical trial for IBI-188 in the U.S.

For the years ended December 31, 2016 and 2017 and the six months ended June 30, 2017 and 2018, our research and development expenses were RMB384.7 million, RMB611.9 million, RMB225.4 million and RMB420.0 million, respectively. As of the Latest Practicable Date, with respect to our four core product candidates, we owned three issued Chinese patents and three pending Chinese patent applications, two pending U.S. patent applications, and four pending PCT applications, among others.

OUR STRENGTHS

Fully-integrated biological therapeutics platform

In the seven years since our inception in 2011, we have built up a pipeline of 17 monoclonal antibody drug candidates, including four core product candidates that are in late-stage clinical development in China. We have succeeded in developing our pipeline quickly and efficiently because we have built a fully-integrated, end-to-end biological therapeutics platform that encompasses all the key biologic drug development functionalities, including discovery, process development, analytical sciences, quality control and assurance, clinical development, manufacturing, and commercialization. This enables us to identify and address potential clinical, manufacturing and commercial issues early in the development process so we can direct our efforts towards molecules with the best potential to become clinically active, cost-effective and commercially viable drugs. Our platform also allows us to carry out process validation and product manufacturing, maintain consistent quality control, and redeploy resources quickly to prioritize our most promising projects. Our platform also gives us the flexibility to pursue in-license strategies to maximize the value of our facilities and products. We continue to increasingly benefit from the scalability and cost efficiency of our platform as we expand our manufacturing capacity and build up our sales and marketing team in anticipation of our first wave of drug candidates gaining NMPA approval and entering the commercial phase.

Potentially best-in-class innovative PD-1 monoclonal antibody with NDA accepted and priority review status granted by the NMPA

Sintilimab is an innovative fully human PD-1 monoclonal antibody and one of the first PD-1 monoclonal antibodies to have a new drug application (NDA) accepted in China with priority review status. The indication for this NDA is r/r Hodgkin's lymphoma. PD-1/PD-L1 antibodies and other immuno-oncology drugs have revolutionized treatment of many cancers and demonstrated significant clinical benefits over chemotherapy and other therapies in many types of cancers. According to Frost & Sullivan, PD-1/PD-L1 antibodies had sales of US\$10.1 billion worldwide in 2017; however, in China, there is no approved PD-L1 antibody and there are only two approved PD-1 antibodies, i.e., Bristol-Myers Squibb's PD-1 antibody Opdivo

(nivolumab), which was approved by the NMPA on June 15, 2018 for the treatment of locally advanced or metastatic NSCLC after prior platinum-based chemotherapy in adult patients without EGFR or ALK genomic tumor aberration, and Merck's Keytruda (pembrolizumab), which was approved by the NMPA on July 26, 2018 for the treatment of adult patients with unresectable or metastatic melanoma following failure of one prior line of therapy. We are developing sintilimab to treat multiple types of cancers and are currently conducting clinical trials with sintilimab both as a monotherapy and in combination with other therapies. In particular, part of sintilimab forms the anti-PD-1 portion of three bi-specific antibody drug candidates currently under our pre-clinical development, including IBI-318, IBI-319 and IBI-315.

Sintilimab has demonstrated an objective response rate (ORR) of 79.2% (week 24 data) and a complete response (CR) rate of 17.7% (week 15 data) in our registration clinical trial in 96 patients in China with relapsed/refractory classical Hodgkin's lymphoma and a safety and toxicity profile comparable to existing approved PD-1 antibodies. We believe that sintilimab has the potential to be a best-in-class PD-1 antibody given its biochemical and biological properties. For example, based on biochemical assays, sintilimab binds 10-fold and 50-fold more tightly to its target (referred to as high affinity) than pembrolizumab (sold under the trade name Keytruda by Merck) and nivolumab (sold under the trade name Opdivo by Bristol-Myers Squibb), respectively, and, based on *in vivo* pharmacodynamic comparison data, sintilimab also occupies more of the available PD-1 binding sites at a given drug concentration (referred to as target occupancy) than nivolumab. We expect that these characteristics of sintilimab will lead to better clinical efficacy at the same or lower dosage level and at the same or lower frequency of administration in comparison with existing approved PD-1 antibodies. We will co-promote and co-brand sintilimab per the agreement with Eli Lilly in China and, subject to receipt of NMPA approval, we plan to launch sintilimab in 2019.

Three biosimilar drug candidates in Phase 3 clinical trials in China

We are currently conducting Phase 3 clinical trials in China for three biosimilar drug candidates, all of which have significant commercial potential. The reference drugs for each of them have numerous approved indications:

- <u>**IBI-305**</u> is an anti-VEGF monoclonal antibody and our biosimilar product candidate to bevacizumab (Avastin). Bevacizumab has been approved by the FDA for the treatment of metastatic colon cancer, lung cancers, kidney cancers, ovarian cancers and glioblastoma, and it has been approved in China for advanced relapsed/refractory NSCLC and metastatic CRC. Avastin had worldwide sales of US\$6.8 billion in 2017, according to the Frost & Sullivan Report.
- <u>**IBI-301**</u> is an anti-CD20 monoclonal antibody and our biosimilar product candidate to rituximab (MabThera/Rituxan). Rituximab has been approved by the FDA for the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis, granulomatosis with polyangiitis and pemphigus vulgaris, and it has been approved in China for non-Hodgkin's lymphoma. Rituxan had worldwide sales of US\$7.5 billion in 2017, according to the Frost & Sullivan Report.

• <u>**IBI-303**</u> is an anti-TNF- α monoclonal antibody and our biosimilar product candidate to adalimumab (Humira). Adalimumab has been approved by the FDA for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis and psoriasis, and it has been approved in China for rheumatoid arthritis, ankylosing spondylitis and psoriasis. Humira had worldwide sales of US\$18.9 billion in 2017, according to the Frost & Sullivan Report.

Our IND applications for IBI-305, IBI-301 and IBI-303 were approved by the NMPA in May 2016, September 2014 and December 2015, respectively, in each case in accordance with the biosimilar regulatory development pathway based on the demonstrated similarity to their respective reference products in the CMC and pre-clinical studies. We have not had material communications with the NMPA since the approval of our IND applications and we are not aware of any material concern from the NMPA in connection with these three biosimilar drug candidates. Based on our internal review of the relevant clinical trial progress and preliminary clinical observations, we expect to submit NDAs to the NMPA for IBI-305 and IBI-301 in the first quarter of 2019 and in the fourth quarter of 2019, respectively. For IBI-303, we had a pre-NDA meeting with the NMPA on September 10, 2018, and based on internal review of the clinical trial progress, we expect to submit an NDA to the NMPA in the fourth quarter of 2018. The market size of biosimilars in China is expected to grow at a CAGR of 70.9% from RMB1.2 billion in 2017 to RMB16.9 billion in 2022, according to the Frost & Sullivan Report. We believe there is potential for biosimilar drugs in China to surpass the sales of the innovator drugs because of their greater affordability and because the biosimilars will be marketed to a much larger population than the innovator drugs have historically targeted.

Robust pipeline of innovative monoclonal antibody and bi-specific antibody drug candidates

In addition to our four core products, we have a robust pipeline of innovative monoclonal antibody drug candidates targeting diseases with largely unmet patient needs and significant total addressable markets, including bi-specific antibody products that bind to two different targets simultaneously. This pipeline includes two drug candidates that are currently in clinical development in China and being pursued under China's innovative drug registration pathway, and it also includes four drug candidates for which IND applications have been approved in China, including IBI-302:

IBI-306 is a fully human monoclonal antibody drug candidate that we are developing for the treatment of hyperlipidemia which is characterized by high levels of lipids in the blood. It binds to a protein known as PCSK9 and is similar to evolocumab (sold under the trade name Repatha by Amgen) and alirocumab (sold under the trade name Praluent by Sanofi). These anti-PCSK9 antibody drugs have been a significant advance in the treatment of high blood cholesterol and had aggregate worldwide sales of US\$490 million in 2017, according to the Frost & Sullivan Report. Currently Repatha (evolocumab) is the only one marketed PCSK inhibitor in China, which received the approval by the NMPA for the treatment of hypercholesterolemia in August 2018. We are conducting a Phase 1 clinical trial of IBI-306 in China.

- **IBI-310** is a fully human monoclonal antibody drug candidate that we are developing for the treatment of a variety of cancers. It binds to an immune checkpoint known as cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) which down-regulates T-cell immune response to cancer cells. In addition to its potential as a monotherapy, it also can potentially be used in combination therapy with an anti-PD-1 antibody in the treatment of certain cancers. Ipilimumab, the only approved CTLA-4 antibody drug, had worldwide sales of US\$1.2 billion in 2017, according to the Frost & Sullivan Report. There are currently no CTLA-4 inhibitors approved in China. We are conducting a Phase 1 clinical trial of IBI-310 in China.
- <u>**IBI-302**</u> is a fully human bi-specific antibody-like drug candidate that we are developing for the treatment of ocular diseases including a type of age-related macular degeneration (AMD) called wet AMD. The current biological treatment for wet AMD include ranibizumab, aflibercept and conbercept. Conbercept achieved China sales of RMB617 million in 2017, according to the Frost & Sullivan Report. We believe that IBI-302 has the potential to be a best-in-class wet AMD therapeutic by simultaneously targeting two aspects of the disease, angiogenesis (which is the growth of blood vessels) and inflammation, while the current standard of care pharmaceuticals for wet AMD only target angiogenesis. Our IND application for IBI-302 was approved by the NMPA in December 2016. We plan to conduct a multi-center Phase 1 clinical trial of IBI-302 in China. We expect to start and complete this trial in 2019.

We also have a strong lineup of innovative drug candidates currently in pre-clinical stage, including two mono-specific antibody drug candidates against novel targets, and five bi-specific antibody drug candidates, including an anti-CD47/PD-L1 bi-specific antibody. We anticipate advancing four of these pre-clinical candidates into clinical stage in the next 12 months. See "– Our Drug Candidates" for details.

State-of-the-art manufacturing facilities designed to, built to and operating at international standards

From our inception, we have focused on constructing manufacturing facilities that meet rigorous international standards. We have undergone ordinary course, comprehensive annual audits of our production facility to evaluate compliance with industry GMP and quality compliance standards. Without exception, all of the IND registration batches for the ten INDs approved by the NMPA and for the IND approved by the FDA and all of the clinical trial material for the clinical trials of our other drug candidates in the pipeline have been produced at our existing facilities. Our current production facilities for biologics, with three 1,000L disposable bioreactors, satisfy the product validation prerequisite for the approval of innovative drug candidates under current regulations in China and give us flexibility in arranging production schedules while maintaining quality consistency. We expect our existing facilities to be able to support our commercial manufacturing needs for the first two products through 2020. We are currently installing six 3,000L bioreactors, which are designed to be commissioned and validated for GMP compliance in 2019. Additionally, we have also completed the construction of a building shell to host four 15,000L bioreactors in the near future.

Strategic partnerships with leading global companies, such as Eli Lilly and Adimab

Eli Lilly has been our strategic partner since the early days of our Company. Our strategic alliance with Eli Lilly was formalized in 2015 and is comprised of licensing, co-development and co-branding arrangements in China for sintilimab (IBI-308), our PD-1 antibody, and IBI-301, our rituximab (MabThera/Rituxan) biosimilar. In addition, we and Eli Lilly have agreed to collaborate in the discovery, development and commercialization of three PD-1-based bi-specific antibodies, including IBI-318 and IBI-319. We believe that these collaboration agreements demonstrate the quality of our team and its accomplishments. We also cooperate with other strategic partners, such as Adimab, with whom we have an agreement to co-discover monoclonal antibodies. We believe we offer a strong value proposition for potential international strategic partners that includes our technical knowledge, speed, flexibility and lower cost structure.

Senior management with a proven track record of success, led by our founder, the co-inventor and developer of the first domestic innovative fully human antibody-like drug in China

Our leader, Dr. De-Chao Michael Yu, invented and owns world's first oncolytic virus-based immunotherapeutic product, Oncorine. Dr. Yu also co-invented and led the development of Conbercept, the first domestic innovative fully human antibody-like therapeutic approved for marketing in China. Dr. Yu has more than 20 years of experience in key research and development and other management positions at Calydon, Cell Genesys, Applied Genetic Technology Corporation (where he was vice president of research and development) and Chengdu Kanghong Biotech (where he was the CEO and President). Dr. Yu was recruited to return to China as part of a national government initiative to attract leading overseas Chinese scientists. He has advised the government on key regulatory reforms in the pharmaceutical field. For example, Dr. Yu co-authored a proposal with 22 academic researchers in 2014. Dr. Yu currently serves as the Chairman of the Board of the Chinese Antibody Society, a Deputy Director of the National Technical Committee on Biochemistry Products and Testing Technology of the Standardization Administration of China, a Deputy Director of the Drug Research and Development Special Committee of China Pharmaceutical Innovation and Research Development Association, a Deputy Director of the Committee of the Cancer Immunology and Cancer Biotherapy of the Chinese Society for Immunology, a Managing Director of the Chinese Association for Medicinal Biotechnology, a Standing Committee Member of the Special Committee of Gene Therapy Society of the Chinese Association of Medicinal Biotechnology, a member of the Special Committee for Precision Medicine of the China Medicinal Biotech Association and a member of the Special Committee of Cancer Biotherapy of the China Anti-cancer Association. These roles give him keen insight into the regulatory environment in China. Dr. Yu is supported by a senior management team with biologics industry experience at leading international pharmaceutical companies such as Abbvie, Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Genentech, Novartis, Pfizer, and Roche.

Our shareholders consist of well-known global and Chinese institutional investors and biotech-focused investment funds, including but not limited to Eight Roads, F-Prime, Lilly Asia Ventures, Temasek, State Development & Investment Corporation, Legend Capital, Hillhouse Capital, Ping An, China Life, Taikang, Shanghai Milestone, Capital Group Private Markets, Cormorant Asset Management, Rock Springs and Ally Bridge Group.

OUR STRATEGIES

Expedite regulatory approval and commercialization of our lead product candidates

The NDA for our PD-1 antibody, sintilimab (IBI-308), was accepted by the NMPA on April 16, 2018 and was granted priority review status on April 23, 2018. We plan to focus our resources on rapidly delivering sintilimab to patients. We are currently building and expect to have a 250-member commercialization team by the time we receive marketing approval for sintilimab in China. We plan to double that size to a 500-member commercialization team in anticipation of the increased market demand for sintilimab and prior to the commercial launch of our first biosimilar drug candidate in China. We recently hired a chief commercial officer, Mr. Min Liu, to manage our sales, marketing and market access operations. Mr. Liu was formerly a member of Roche Global Oncology Franchise Leadership Team and vice president and head of one of Roche's two oncology business units in China in charge of leading the marketing and sales efforts for products in the fields of lung cancer, gastrointestinal cancer and hematology. In his role as our chief commercial officer, Mr. Liu is supported by key commercialization leadership members who have substantial experience and a strong performance track record commercializing those biological drug products relevant to our pipeline drug candidates at leading multinational and domestic pharmaceutical companies. We believe that our experienced commercialization team is highly competitive and can leverage our co-branding arrangement with Eli Lilly for sintilimab and IBI-301 in China, tapping into Eli Lilly's in-depth knowledge of, and long-term institutional relationships in, the China market to strengthen our competitive position in the market.

Rapidly advance our clinical programs for pipeline products

We plan to maximize the commercial potential of our PD-1 antibody, sintilimab, by exploring additional indications, such as hepatic cellular cancer, colorectal cancer, renal cell cancer, and gynecological cancer, among others. These will be in addition to our current studies for sintilimab in patients with classical Hodgkin's lymphoma, melanoma, gastrointestinal cancer, gastric cancer, esophageal cancer, NSCLC, and NK/T-cell lymphoma. At the same time, we are working to advance the other six drug candidates that we currently have in clinical development to the market approval stage as rapidly as possible. We will also continue to develop products from our pre-clinical pipeline with the aim of advancing one or more additional new products into clinical trials each year. We will devote particular attention to the discovery and development of bi-specific drugs that we believe will be more effective and have fewer side-effects than existing therapies. In addition, we plan to conduct more clinical trials for combination treatments based on sintilimab, particularly where we can combine another drug candidate in our pipeline with sintilimab. We plan to leverage our experience in designing clinical studies, our local knowledge and our extensive collaboration with investigators to develop new drug candidates in the fields of oncology, ophthalmology, and autoimmune and metabolic diseases.

Continue to enhance our fully-integrated platform

We will continue to invest in building out our fully-integrated monoclonal antibody therapeutics platform, not only in manufacturing and commercialization but also in discovery and development. We are actively hiring new personnel in many functional departments across our Company. By September 2019, we expect to have completed installation of six new 3,000L stainless steel bioreactors that will be in full operation at our main campus in Suzhou and we have additional space set aside for the installation of four new 15,000L stainless steel bioreactors and for the further expansion of our research facilities. We are currently building and expect to have a 250-member commercialization team by the time we receive marketing approval for marketing and sales of sintilimab in China. We plan to double that size to a 500-member commercialization team in anticipation of the increased market demand for sintilimab and prior to the commercial launch of our first biosimilar drug candidate in China.

Maximize the value of our fully-integrated platform through a global strategy of organic growth and collaboration

We intend to maximize the value of our fully-integrated platform by manufacturing our products for sale through our strategic partners outside of China and selectively in-licensing drug products for sale both inside and outside China. We have built our manufacturing facilities and our quality system at international standards and we plan to seek certification from the FDA and the EMA that we comply with cGMP requirements. We are building a team in the United States to conduct clinical trials of selected drug candidates, beginning with sintilimab, which has been approved for Phase 1b/2 clinical trials by the FDA based on data from our clinical trial results in China. We are preparing to submit more IND applications for additional innovative drug candidates globally, and we also intend to enrich and supplement our pipeline through collaboration, in-licensing and acquisition.

OUR DRUG CANDIDATES

Leveraging our fully-integrated platform, we are developing 17 monoclonal antibody drug candidates, including seven in clinical development, addressing major unmet or under-served medical needs in China. We believe that some of these innovative compounds have the potential to be best-in-class monotherapies or an important component of combination therapies with other oncology drugs.

	Can didata (Commercial	Status					
	Reference Drug	Target(s)	Therapeutic Area: Disease Indications***	Rights	Pre-clinical	IND (Filed) (Accepted)	Phase 1	Phase 2	Phase 3	NDA (Filed)
	sintilimab (IBI-308)*	PD-1	Oncology: r/r Hodgkin's lymphoma, 1L and 2L melanoma, refractory gastrointestinal cancers, 2L NSCLC, 2L esophagael cancer, 1L and 2L squamous NSCLC, 1L non-squamous NSCLC, r/r NK/T-cell lymphoma, 2L ESCC, 1L gastric cancer, solid tumors, and esophageal carcinoma	Worldwide ⁽²⁾				 NDA filed for t/t	Hodgkin's lymph	oma: Apr 3, 2018
	IBI-306	PCSK9	Metabolic: homozygous familial hyperlipidemia; statin intolerant high CV risk patients	China, Hong Kong, Taiwan		IND approved: Sep 8, 2017				
	IBI-310 ⁽¹⁾	CTLA-4	Oncology: melanoma and renal cell carcinoma	Worldwide		IND approved: Feb 13, 201	8			
	IBI-302	VEGF/Complement proteins	Ophthalmology: wet AMD	Worldwide	IND	approved: Dec 9, 2016	ŕ			
Novel	IBI-307	RANKL	Metabolic: osteoporosis and lytic bone lesions associated with cancer metastasis	Worldwide	IND approved: Jun 15, 2018 IND approved: Jun 15, 2018 IND approved: Aug 22, 2018			 		
	IBI-101	OX40	Oncology: advanced solid tumors, hepatitis B	Worldwide				1		
	IBI-188	CD47	Oncology: B-cell lymphoma, ovarian cancer, colorectal cancer	Worldwide				1		
	IBI-110	LAG-3	Oncology: NSCLC, melanoma, mBrCA, advanced tumors	Worldwide				1		
	IBI-939	TIGIT	Oncology: advanced solid tumors	Worldwide				l I		
	IBI-318	PD-1/undisclosed target	Oncology: advanced tumors (undisclosed target)	China, Hong Kong, Macau ⁽³⁾						
	IBI-319	PD-1/undisclosed target	Oncology: advanced tumors (undisclosed target)	China, Hong Kong, Macau ⁽³⁾				 		
	IBI-322	PD-L1/CD47	Oncology: PDL1/CD47 coexpressing tumors, M1 macrophage signature tumors	Worldwide				' 		
	IBI-315	PD-1/HER2	Oncology: Her2 + cancers, mBrCA, gastric cancer, NSCLC	**				I I	 	
	IBI-323	LAG-3/PD-LI	Oncology: PDL1+ tumors with "hot tumor" phenotype	Worldwide				 		
	rituximab (IBI-301)/ Rituxan*	CD20	Oncology: non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis	Worldwide ⁽²⁾	_	IND approved: Sep 13, 201	4	1		
Biosimilar	adalimumab (IBI-303)/ Humira*	TNF-α	Autoimmune: rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis and psoriasis	Worldwide	_	IND approved: Dec 28, 201	5	-		
	bevacizumab (IBI-305)/ Avastin*	VEGF-A	Oncology: r/r NSCLC and metastatic CRC	Worldwide		IND approved: May 10, 20	16			

The following table summarizes the development status in China of our pipeline antibody candidates as of the Latest Practicable Date:

Abbreviations: 1L = first-line; 2L = second-line; AMD = age-related macular degeneration; CRC = colorectal cancer; CV = cardiovascular; EGFR = epidermal growth factor receptor; ESCC = esophageal squamous cell carcinoma; HCC = hepatocellular carcinoma; NHL = non-Hodgkin's lymphoma; NK/T-cell lymphoma = natural killer/T-cell lymphoma; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; r/r = relapsed, refractory; SCLC = small-cell lung cancer; TKI = tyrosine kinase inhibitor.

- * denotes a core product.
- ** collaboration with Hanmi, subject to confidentiality terms prohibiting the disclosure of confidential information.
- *** We also plan to develop sintilimab in combination with (i) IBI-310 for the treatment of melanoma, SCLC and RCC, (ii) each of IBI-101, IBI-188, IBI-110 and IBI-939 for the treatment of advanced solid tumors, (iii) IBI-305 for the treatment of HCC and EGFR-TKI failure NSCLC, and (iv) IBI-301 for the treatment of B-cell NHL. We also plan to develop IBI-188 in combination with IBI-301 for the treatment of B-cell NHL.
- (1) We are developing IBI-310 as an innovative drug candidate in accordance with NMPA regulations because ipilimumab has not been approved for marketing in China even though IBI-310 has the same amino acid sequence as ipilimumab.
- (2) We and Eli Lilly will co-promote sintilimab (IBI-308) and rituximab (IBI-301) in China, Hong Kong and Macau.
- (3) Eli Lilly may opt in to co-commercialize IBI-318 and IBI-319 with us in China, Hong Kong and Macau.

We have three bi-specific monoclonal antibody candidates based on sintilimab (IBI-308) in co-development with Eli Lilly, two of which, IBI-318 and IBI-319, are under development in China. See "-Collaboration Agreements - Collaboration with Eli Lilly - Addendum to the Exclusive License and Collaboration Agreement for China" for details.

In addition to developing our pipeline drug candidates in China, we have obtained FDA approval for our IND applications for sintilimab (IBI-308) and IBI-188 and plan to initiate a multi-center Phase 1b/2 clinical trial for sintilimab (IBI-308) in the U.S.

Subject to applicable legal and contractual obligations, we consciously prioritize, and from time to time re-prioritize, our pipeline drug candidates for development based on numerous commercial considerations such as existing resources, changing epidemiology and estimated commercialization prospects.

Our Most Advanced Drug Candidate: sintilimab (IBI-308)

Sintilimab (IBI-308) is an innovative fully human PD-1 monoclonal antibody against the programmed death-1 molecule (PD-1). We are developing sintilimab as a monotherapy in relapsed/refractory classical Hodgkin's lymphoma, first-line and second-line melanoma, gastrointestinal cancers, NSCLC, second-line esophageal cancer, second-line squamous NSCLC, and NK/T-cell lymphoma. We are also developing sintilimab in combination with chemotherapy for first-line non-squamous NSCLC, first-line squamous NSCLC, and first-line gastric cancer.

Mechanism of Action

PD-1 is a protein on the surface of T-cells and is one of the proteins referred to as an "immune checkpoint" inhibitor. The normal function of PD-1 is to turn off the T-cell mediated immune response as part of the process that stops a healthy immune system from attacking other cells in the body. When PD-1 attaches to certain proteins called the PD-1 ligand 1 (PD-L1) or the PD-1 ligand 2 (PD-L2) on the surface of a normal cell or a cancer cell, the T-cell turns off its ability to kill the cell. Some cancer cells produce large amounts of PD-L1 and PD-L2 to help these cancer cells evade T-cell attacks. Sintilimab binds to PD-1 and blocks it from binding to both PD-L1 and PD-L2, which allows the T-cells to kill cancer cells. The following diagram illustrates the mechanism of action of sintilimab.

In the diagram below, a T-cell interacts with a tumor cell via an antigen on the surface of the tumor cell. Under normal conditions, the T-cell would recognize the tumor antigen as being foreign and kill the tumor cell. In the top panel of the diagram, however, the tumor cell also expresses PD-L1 on its surface. PD-L1 can bind to the checkpoint receptor, PD-1, and in doing so, turn off the T-cell. In this manner the tumor cell can evade the immune system. As shown in the lower panel of the diagram, sintilimab binds to PD-1 on the surface of the T-cell and blocks the ability of PD-L1 to activate the checkpoint. The T-cell then initiates cell killing.

Mechanism of action of sintilimab (IBI-308)



Based on Francisco, Loise M., Peter T. Sage, and Arlene H. Sharpe. "The PD-1 Pathway in Tolerance and Autoimmunity." Immunological Reviews 236 (2010): 219-242. PMC. Web. 1 Aug. 2018.

Market Opportunity and Competition

We believe there is a significant commercial opportunity in China for PD-1 or PD-L1 antibody drugs. According to the Frost & Sullivan Report, the incidence of all cancers in China increased from 3.7 million in 2013 to 4.2 million in 2017. Among all types of cancers, the incidence of lung cancer, colorectal cancer and esophageal cancer grew the fastest during this period. Driven by a combination of factors such as unhealthy lifestyle and pollution, it is estimated that the incidence of all cancers in China will reach 4.8 million in 2022. Among all types of cancers, lung, stomach, liver, colorectal, breast and esophageal cancers are the six most common cancers in China and respectively accounted for 863,900, 454,500, 489,100, 411,100, 299,600 and 285,300 of the total incidence in China in 2017.

Currently available clinical data suggest that some of the most prevalent cancers in China, such as lung, stomach, liver, colorectal and esophageal cancers, are responsive to the PD-1/PD-L1 class of drugs. Taking into account the other cancer types (such as bladder, melanoma and kidney cancers) that are also responsive to the PD1-/PD-L1 class, the overall annual incidence of the aforementioned eight types of cancers in China is approximately 3.0 million in 2017.

In China, according to the Frost & Sullivan Report, only two PD-1 antibodies have been approved for marketing: Bristol-Myers Squibb's Opdivo (nivolumab), which was approved by the NMPA on June 15, 2018 for the treatment of locally advanced or metastatic NSCLC after prior platinum-based chemotherapy in adult patients without EGFR or ALK genomic tumor aberration, and Merck's Keytruda (pembrolizumab), which was approved by the NMPA on July 26, 2018 for the treatment of adult patients with unresectable or metastatic melanoma

following failure of one prior line of therapy; there is no approved PD-L1 antibody yet. CDE released guidance in February 2018 on the requirements for NDA submissions of PD-1/PD-L1 drug candidates, specifically for data from single-arm trials on refractory/recurrent advanced cancers without standard-of-care therapies. A pre-NDA meeting is required before the NDA submission, and a rolling NDA submission will be accepted for PD1-/PD-L1 therapies. Besides us, several companies also have anti-PD-1 drug candidates with an NDA application under review by the NMPA for the first indications, including Hengrui's SHR-1210 (camrelizumab), Junshi's JS-001 (toripalimab), and BeiGene's BGB-A317 (tislelizumab). There are also several anti-PD-1/PD-L1 drug candidates in late-stage clinical development in China, including Roche's Tecentriq (atezolizumab), CStone's CS1001, Alphamab/3DMed's KN035, AstraZeneca/MedImmune's Imfinzi (durvalumab) and Merck KGaA/Pfizer's Bavencio (avelumab). According to the Frost & Sullivan Report, the market size for PD-1/PD-L1 antibodies in China is expected to grow to RMB98.4 billion in 2030.

According to the Frost & Sullivan Report, the worldwide sales for Opdivo (nivolumab) and Keytruda (pembrolizumab) in 2017 were US\$5.8 billion and US\$3.8 billion, respectively. The two approved PD-1 antibodies (Keytruda and Opdivo) and the three approved PD-L1 antibodies (Tecentriq, Bavencio and Imfinzi) in the aggregate had worldwide sales of US\$10.1 billion in 2017, which grew at a CAGR of 412.2% from 2014. With the increase in approved cancer indications for PD-1/PD-L1 antibody drugs and the launch of combination therapies including PD-1/PD-L1 antibodies, it is expected that the sales for this class will continue to grow over the next ten years and will reach US\$78.9 billion in 2030. See "Industry Overview – Overview of PD-1 and PD-L1 Antibodies Market" for further information on the market opportunities for PD-1/PD-L1 antibody drugs.

Competition in the oncology therapeutic area to which sintilimab (IBI-308) belongs is extremely fierce given the abundance of existing competing drugs and drug candidates that continue to increase competition in the market. The following table sets forth comparisons between IBI-308 and its competitive drug candidates in China which are approved to market or in late stage clinical trials:

Generic (Brand) Name/	~	Filing Status in	-	Mechanism	Lead/Proposed	Retail Price	
Drug Code	Company	China	Date*	of Action	Indications	(RMB)	NRDL/PRDL
Sintilimab (IBI-308)	Innovent	NDA submission	2018/4/19	Anti-PD-1	R/r Hodgkin's lymphoma	N.A.	N.A.
Nivolumab (Opdivo)	BMS	Marketed	2018/6/15	Anti-PD-1	Locally advanced or metastatic NSCLC	9,260/100 mg, 4,591/40 mg	No
Pembrolizumab (Keytruda) ⁽¹⁾	Merck	Marketed	2018/7/26	Anti-PD-1	Locally advanced or metastatic melanoma	17,918/100 mg	No
Camrelizumab (SHR-1210)	Hengrui	NDA submission	2018/4/23	Anti-PD-1	Classical Hodgkin's lymphoma	N.A.	N.A.
JS-001	Junshi	NDA submission	2018/3/20	Anti-PD-1	Unresectable local progression or metastatic melanoma	N.A.	N.A.
Tislelizumab (BGB-A317)	Beigene	NDA submission	2018/9/6	Anti-PD-1	Classical Hodgkin's lymphoma	N.A.	N.A.

Comparison Between Sintilimab (IBI-308) and its Approved or Late-Stage Competitors in China

Source: Frost & Sullivan

Abbreviation: NRDL = national reimbursement drug list of China; PRDL = provincial reimbursement drug list; "No" means that the drug is not list in the NRDL or the PRDL even though it is marketed; "N.A." means, with respect to retail price, not available, and with respect to NRDL/PRDL, not applicable because the drug candidate is not marketed yet.

- * for a marketed product, it refers to the NMPA approval date; for a clinical stage product, it refers to the date when the information about clinical trials is published for the first time (首次公示日期); for a product with NDA submitted and the NDA result pending, it refers to the date of NDA submission.
- ⁽¹⁾ Merck has publicly announced its patient assistance program for Keytruda, subject to its right to cancel at anytime, which provides the patients for certain indications and with proven financial difficulties with free Keytruda for a certain period of time.

Current PD-1 Therapies and Limitations

Immunotherapy has become a lifesaving therapy for some patients with previously incurable cancers. Some types of cancers are exquisitely sensitive to immunotherapy with antibodies that bind to immune checkpoint proteins, and in so doing, stimulate the immune system to attack cancer cells. In patients with melanoma, Hodgkin's disease and Merkel cell carcinoma, the majority have demonstrated substantial clinical benefit from treatment with these new types of therapy.

Two PD-1 antibodies, pembrolizumab and nivolumab, have been approved outside China for the treatment of several types of cancer, including melanoma, non-small cell lung cancer (NSCLC), Hodgkin's lymphoma, gastric cancer, microsatellite instability high (MSI-H) cancers, head and neck cancer, urothelial cancer, MSI-H/dMMR colorectal cancer, liver cancer, kidney cancer, bladder cancer, cervical cancer and primary mediastinal large B-cell lymphoma. One PD-1 antibody, nivolumab, has been approved in China for the treatment of locally advanced or metastatic NSCLC. In addition, three PD-L1 monoclonal antibodies, atezolizumab, avelumab and durvalumab, have been approved by the FDA for the treatment of a few types of cancers: metastatic NSCLC, locally advanced or metastatic urothelial carcinoma, and metastatic Merkel cell carcinoma. Unfortunately, less than 20% of all cancer patients have a clinically meaningful response to these approved PD-1 or PD-L1 antibody therapies.

The clinical efficacy of an antibody drug depends upon several factors. The most important factor is the ability of the antibody to bind to the target with sufficient strength and duration. The currently approved antibodies against PD-1, pembrolizumab and nivolumab, have biological characteristics that could be enhanced, such as binding affinity and durations of target engagement.

Advantages

Sintilimab (IBI-308) has the potential to be a global best-in-class PD-1 antibody, based on characteristics that were designed into sintilimab that improve the biological properties compared to other well-studied PD-1 antibody drugs such as pembrolizumab and nivolumab. We believe sintilimab potentially has the following competitive advantages:

Higher binding affinity for PD-1

A major contributor to the action of an antibody in the body is how the antibody engages the target, including how tightly the antibody binds its antigen and how long the antibody stays bound to the antigen.

In vitro studies have shown that the binding affinity of sintilimab for PD-1 is approximately 10- and 50-fold higher compared to that of pembrolizumab and nivolumab, respectively. This higher binding affinity allows sintilimab to bind more tightly to PD-1 on lymphocytes and to better compete against the binding of PD-L1 and PD-L2 on tumor cells. The following table shows the *in vitro* equilibrium binding characteristics of sintilimab, pembrolizumab and nivolumab. A lower dissociation constant (K_d) indicates higher binding affinity.

K _d hPD-1 (10 ⁻¹¹ M)
1.20
13.0
64.0

Sintilimab (IBI-308) has higher binding affinity for human PD-1 than pembrolizumab and nivolumab

Abbreviations: M = mole (unit for amount of substance); K_d = dissociation constant; hPD-1 = human PD-1.

Prolonged binding for PD-1

The binding affinity of an antibody consists of two opposing factors: the on-rate which is the rate at which the antibody (sintilimab) binds to the antigen (PD-1); and the off-rate which is the rate at which the antibody releases the antigen. Pembrolizumab has a comparably fast off-rate, and hence, after binding to PD-1 on lymphocytes, pembrolizumab can dissociate from PD-1, leaving the lymphocyte's PD-1 free to bind to PD-L1 or PD-L2 on tumor cells. Sintilimab was engineered to slow down its dissociation from PD-1 and thereby prolong the duration of its binding to PD-1 so as to allow more robust and longer inhibition of the PD-1 signal as compared to pembrolizumab. The following graphs show the side-by-side comparison of the binding kinetics of pembrolizumab and sintilimab.

Sintilimab (IBI-308) has a slower off-rate than pembrolizumab



Abbreviations: RU = resonance units.

Improvements in the binding affinity and in binding kinetics lead to more robust activity of sintilimab in *ex vivo* mixed lymphocyte reactions, which is a measure of the ability of human lymphocytes to recognize foreign cells and become activated. The degree of lymphocyte activation is measured by the induction of cytokines such as interferon- γ and interleukin-2 (IL-2). As shown in the figure below, sintilimab leads to greater induction of IL-2 and interferon- γ than nivolumab or pembrolizumab, respectively.

Sintilimab outperforms both nivolumab and pembrolizumab in mixed lymphocyte reaction cytokine induction



Abbreviations: IL-2 = interleukin-2; IFN- γ = interferon- γ ; IgG = immunoglobulin G.

In another laboratory study, the ability of sintilimab to change the types of tumor infiltrating T lymphocytes (TILs) in human xenographs was compared directly against that of pembrolizumab and nivolumab. A proximate measure of blockade of PD-1 action in tumors is $CD8/T_{reg}$, which is the ratio of cytotoxic T lymphocytes (CD8) to T_{reg} lymphocytes. While each PD-1 antibody increased the ratio of $CD8/T_{reg}$ lymphocytes, at the equivalent dose levels, sintilimab led to more robust changes, as shown in the figure below. This increase in $CD8/T_{reg}$ ratio is a beneficial change in the immune status within the tumors.

Tumor infiltrating lymphocytes in a syngeneic murine model of cancer



Abbreviations: T_{reg} = Regulatory T-cell; h-IgG = human immunoglobulin G.

Another measure of the improvement in immune status induced by PD-1 blockage is the shrinkage of tumors in animal models. In our case, mice studies we conducted using the H292 humanized Winn mouse model. As illustrated in the following diagram, sintilimab was shown to be 100-fold more potent than nivolumab in terms of tumor shrinkage in immunocompromised mice that are injected with human NSCLC cells. Notably, at the highest dose level of 10 mg/kg which is the standard dose level for nivolumab, treatment with sintilimab led to complete regression of tumors.

Winn model demonstrating immune-based efficacy of sintilimab



Abbreviations: h-IgG = human immunoglobulin G; PBMC = peripheral blood mononuclear cells.

PD-1 antibodies function by binding to PD-1 on the surface of T lymphocytes and blocking PD-1 binding to PD-L1 and PD-L2 on the surface of cancer cells. The binding of PD-1 antibodies to PD-1 is called receptor occupancy and is a measure of the fraction of PD-1 that is blocked on the surface of T lymphocytes which can be measured using standard flow cytometry methodology. A higher fraction of occupied receptor for a longer period of time may potentially result in better clinical efficacy. We compared the receptor occupancy of PD-1 in patients during and after they are given sintilimab to the published receptor occupancy for nivolumab. As shown in the left panel of the following figure, sintilimab had greater than 95% receptor occupancy for the full duration of a cycle of therapy at the 3 mg/kg dose level. In comparison, published data show that, at the same 3 mg/kg dose level, nivolumab (indicated in the figure by its former name MDX-1106) had a receptor occupancy that falls within the range of approximately 75% to 80% throughout the cycle of therapy, as shown in the right panel of the following figure.



Receptor occupancy in patients after a single dose of anti-PD-1 antibodies

Note: MDX-1106 is the original name for nivolumab. Source for nivolumab (MDX-1106) data: Julie R. et al. JCO 2010: 3167-3174.

In addition to achieving a higher level of PD-1 receptor occupancy, sintilimab also proved to be able to maintain that level for a long period of time. Indeed, in Hodgkin's lymphoma patients given multiple cycles of sintilimab at 200 mg flat dose level, the PD-1 receptor occupancy in peripheral blood lymphocytes is greater than 95% for at least 180 days, as shown in the graph below.



PD-1 receptor occupancy by sintilimab after multiple doses in patients

Abbreviations: PD-1 RO = PD-1 receptor occupancy; IV = intravenous.

Safety profile consistent with pembrolizumab with no unexpected adverse events

Longer and more robust receptor occupancy prolongs PD-1 blockade in patient lymphocytes and could allow for stronger efficacy. One concern could be that better PD-1 blockade could result in a higher frequency and intensity of adverse events in patients.

Fortunately, with sintilimab, this does not appear to be the case. 567 patients have been treated with sintilimab as of the Latest Practicable Date and the results from our clinical studies, albeit not head-to-head comparisons, have demonstrated that the safety profile of sintilimab is similar to that of pembrolizumab with no unexpected adverse events. In most of these clinical studies, the dose level and frequency of administration of sintilimab is identical to that of pembrolizumab, i.e., 200 mg flat dose given intravenously every three weeks. As shown in the following tables, in all categories of adverse events collected in our ongoing trials in 371 patients, sintilimab has numerically lower frequency of adverse events than reported in the pembrolizumab reference safety dataset.

Adverse events in the sintilimab safety data set (371 patients) in comparison to pembrolizumab safety data set.

Index	Sintilimab N=371
Adverse Events (AE)	88.1%
Treatment emerged adverse events (TEAE)	85.2%
TEAEs related to IBI308 (TRAE)	80.9%
≥ grade 3 TEAE	24.3%
≥ grade 3 Treatment related AE (TRAE)	21.8%
Serious adverse events (SAE) during treatment	17.3%
SAE related to drug	6.5%
AE leading to permanent withdrawal	6.2%

Adverse events in the sintilimab safety data set

Adverse events in the pembrolizumab safety data set

Index	Pembrolizumab N=2799*
Adverse Events (AE)	97.4%
Treatment emerged adverse events (TEAE)	97.4%
TEAEs related to drug (TRAE)	73.7%
≥ grade 3 TEAE	45.5%
≥ grade 3 Treatment related AE (TRAE)	13.8%
Serious adverse events (SAE) during treatment	37.2%
SAE related to drug	10.0%
AE leading to permanent withdrawal	11.9%

* Pooled data from reference safety data set for Pembrolizumab. Pembrolizumab safety profile is presently based on 2,799 patients, including 1,232 NSCLC patients from studies KEYNOTE-001 and KEYNOTE-010 and 1,567 melanoma patients from studies KEYNOTE-001, KEYNOTE-002 and KEYNOTE-006.

Efficacy observed in clinical studies

Improved biochemical properties, more robust receptor occupancy, and longer blockade of PD-1 on lymphocytes, not only lead to more robust pre-clinical tumor efficacy of sintilimab, but could also lead to more robust clinical benefit for patients. While there is no head-to-head clinical trial comparison of the various PD-1 antibodies, sintilimab, nivolumab and pembrolizumab have all completed Phase 2 trials in relapsed/refractory classical Hodgkin's lymphoma. Sintilimab has demonstrated robust clinical efficacy in this patient population. As judged by an independent radiological review committee, 79.2% of the 96 patients treated with sintilimab in our registration trial achieved a best overall objective response (week 24 data), 17.7% of the patients achieved a best complete response (week 15 data), and the disease control rate is 97.9% (week 24 data). The efficacy results from our registration trial for sintilimab are summarized in the following table.

Efficacy analysis of sintilimab in relapsed/refractory classical Hodgkin's lymphoma 24 weeks after initiation of therapy

	Patients, N (%)						
Parameter	IRRC Review	Investigator Review					
CR	17 (17.7%)	17 (17.7%)					
PR	59 (61.5%)	60 (62.5%)					
SD	18 (18.8%)	19 (19.8%)					
PD	2 (2.1%)	0 (0%)					
ORR (CR+PR) (95% CI)	79.2% (69.7-86.8%)	80.2% (70.8-87.6%)					
DCR (CR+PR+SD) (95% CI)	97.9% (92.7-99.7%)	100% (96.2-100%)					

Abbreviations: N = sample size (96 patients); IRRC = independent radiological review committee; IWG 2007 = International Working Group 2007; CR = complete response rate; PR = partial response rate; SD = stable disease; PD = progressive disease; ORR = objective response rate; DCR = disease control rate; CI = confidence interval.

Note: The 24-week response measurement does not include PET scans. Hence, IWG complete response cannot be assessed at this time point and the complete response rate (CR) in the table is week 15 data. Partial responses increased at 24 weeks due to four patients with stable disease achieving partial response. The objective response rate therefore increased to 79.2%.

These important clinical parameters achieved from treatment with sintilimab are numerically similar to the results achieved from treatment with nivolumab or pembrolizumab, as shown in the table below. Although the patient populations are all relapsed/refractory classical Hodgkin's lymphoma, the standard of care across geographies is not identical. Brentuximab vedotin is not available in China and autologous stem cell transplantation is less common in China than in the United States and the European Union. In addition, the timing of response measurements is different across studies.

Parameter		Nivolumahi	Pembrolizumab ²						
		ASCT+BV (N=80)	Cohort A:Cohort B:ASCT+BVBV(N=69)(N=81)		Cohort C: ASCT (N=60)	Total (N=210)			
	CR	7 (8.8%)	15 (21.7%)	20 (24.7%)	12 (20.0%)	47 (22.4%)			
	PR	46 (57.5%)	36 (52.2%)	32 (39.5%)	30 (50.0%)	98 (46.7%)			
	SD	18 (22.5%)	11 (15.9%)	10 (12.3%)	10 (16.7%)	31 (14.8%)			
IWG 2007 Standard	PD	6 (7.5%)	5 (7.2%)	17 (21.0%)	8 (13.3%)	30 (14.3%)			
	unreadable	3 (3.8%)	2 (2.9%)	2 (2.5%)	0	4 (1.9%)			
	ORR (CR+PR)	66.3%	73.9%	65.2%	70.0%	69.1%			
	DCR (CR+PR+SD)	88.8%	89.8%	76.5%	86.7%	83.9%			

Efficacy analysis of nivolumab and pembrolizumab in relapsed/refractory classical Hodgkin's lymphoma

Abbreviations: IWG 2007 = International Working Group 2007; ASCT = autologous stem cell transplantation; BV = brentuximab vedotin; CR = complete response rate; PR = partial response rate; SD = stable disease; PD = progressive disease; ORR = objective response rate; DCR = disease control rate.

- 1. Younes et al, Lancet Oncol., 17(9) 1283-94, 2016. "Best overall response was defined as the best response designation recorded between the date of the first dose and the date of initial objectively documented progression per the 2007 International Working Group criteria or the date of subsequent therapy, whichever occurred first."
- 2. Chen et al, JCO., 35(19) 2125-2132, 2017. "ORR was defined as the proportion of patients who achieved CR or partial response using RRC criteria17 at any time during the study. Best overall response was defined as best ORR during the period between the first dose and the first documented PD, death, or, in the absence of PD, last efficacy assessment before subsequent therapy."

Summary of Registration Trial Results

We have completed a multi-center, single arm, open-label, registration trial in China to evaluate the efficacy and safety of sintilimab in 96 patients with relapsed/refractory classical Hodgkin's lymphoma, which is the largest clinical study in China for this indication. The primary endpoint is objective response rate (ORR) and the secondary endpoint is complete response rate (CR). Trial response data was assessed and confirmed by an independent radiological review committee (IRRC) according to IWG 2007 criteria. Patients were evaluated by PET after completing a 15-week course of treatment with sintilimab at the dose level of 200 mg every three weeks. As confirmed by the IRRC, for patients in the trial, the best objective response rate was 79.2% (week 24 data), the best complete response rate was 17.7% (week 15 data), and the disease control rate was 97.9% (week 24 data).

The following graph shows the best objective response in each of the 96 patients as measured by the percentage of change from baseline in target lesion based on CT scans and PET scans. By IWG 2007 (International Working Group 2007) criteria for assessing objective response in Hodgkin's lymphoma, patients whose tumor do not completely resolve based on size of the tumors but become PET scan negative (blue bars) are complete responses.



Best response in relapsed/refractory classical Hodgkin's lymphoma patients

Abbreviations: CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease.

The safety profile of sintilimab is consistent with the expected safety profile of a PD-1-specific antibody such as those of nivolumab and pembrolizumab that does not involve side effects such as skin capillary hemangioma. In these 96 patients, every patient experienced at least one treatment emergent adverse event (TEAE), 92.7% of which were assessed as treatment related by the investigator. The majority of the TEAEs were grade 1 to 2. 25.0% of the TEAEs were grade 3 to 4. No grade 5 TEAE occurred. The most common treatment related adverse event (AE) was fever, which affected 40.6% of the patients during the study. Serious AE (SAEs) of any cause were reported in 14.6% of the patients, with the most common being pneumonia (3.1%), lung infection (2.1%), infectious pneumonia (2.1%), upper respiratory tract infection (2.1%) and infusion-related reaction (2.1%). Treatment related SAEs occurred in 11 patients (11.5%). Adverse events that led to permanent treatment discontinuation occurred in three out of 96 patients, including one patient with grade 2 pneumonia, one patient with grade 4 liver dysfunction, and one patient with grade 3 pneumonia and grade 4 platelet count decreased. 52 of the 96 patients reported immune related adverse events (irAE), including hypothyroidism (19.8%), serum thyrotropin increased (16.7%) and free thyroxine decreased (11.5%). Three patients experienced irAEs above grade 3, including one patient with grade 3 alanine aminotransferase increase, one patient with grade 4 liver dysfunction, and one patient with grade 3 pneumonia and grade 3 platelet count decrease. Immune pneumonitis is a PD-1 class specific adverse event. No fatalities and no unusual or unexpected safety signals, which are signals not related to the PD-1 class of drugs, have been observed in this study.

The adverse events observed from 96 patients in this trial are summarized in the following table.

Index	Sintilimab
Number	N=96
Adverse Events (AE)	100%
Treatment emerged adverse events (TEAE)	100%
≥ Grade 3 TEAE	25.0%
Drug related TEAE	92.7%
≥ grade 3 drug related TEAE	17.7%
TEAE leading to treatment termination	3.1%
Critical TEAE	84.4%
Serious adverse events (SAE)	14.6%
Drug related SAE	11.5%
AE leading to death	0

The preliminary results from this study were published on the official website of the American Society of Clinical Oncology, or ASCO, on May 16, 2018. The updated and final results from this study were presented at the 2018 ASCO Annual Meeting in Chicago in a poster session on June 4, 2018 (Abstract No. 7536).

We submitted our original NDA for sintilimab for the treatment of relapsed/refractory classical Hodgkin's lymphoma on December 1, 2017, which was accepted by the NMPA on December 7, 2017. In light of the new guidance released in February 2018 by the Center for Drug Evaluation, or CDE, under the NMPA, we resubmitted our NDA for sintilimab for the treatment of relapsed/refractory classical Hodgkin's lymphoma on April 3, 2018, which was accepted by the NMPA on April 16, 2018. We became one of the first companies to have an NDA for a PD-1/PD-L1 product accepted by the NMPA and we were granted priority review status on April 23, 2018. We have not had material communications with the NMPA since our submission of the NDA and we are not aware of any material concern that has resulted from the NMPA's review of the NDA for sintilimab. As such, relapsed/refractory classical Hodgkin's lymphoma is expected to be the first cancer indication for which sintilimab will be approved for marketing.

Clinical Development Plan

Since beginning clinical trials in October 2016 to the Latest Practicable Date, we have treated 567 patients with sintilimab. Based on these trials, we believe that sintilimab demonstrates anti-tumor activity across multiple tumor types and has an acceptable safety profile. In addition to our completed registration trial in China to evaluate sintilimab in patients with relapsed/refractory classical Hodgkin's lymphoma, we are executing a broad development program targeting an array of cancer indications including several registration trials for sintilimab, both as a monotherapy and as part of a combination therapy, and both in China and in the U.S., which is intended to support our regulatory submissions for multiple indications both in China and globally.

		Status					
	Mono-/Combo-Therany	IND	Phase 1				NDA
Indication	(other components)	(Accepted)	1a	1b	Phase 2	Phase 3	(Filed)
China							
r/r classical Hodgkin's lymphoma	Mono						•
2L squamous NSCLC	Mono					O	
1L non-squamous NSCLC	Combo (pemetrexed and platinum)					Ð	
1L squamous NSCLC	Combo (gemcitabine and platinum)					O	
EGFR+ TKI failure NSCLC	Combo (IBI-305)					٢	
1L hepatocellular carcinoma	Combo (IBI-305)					•	
1L gastric cancer	Combo (capecitabine and oxaliplatin)					٥	
1L esophageal carcinoma	Combo (paclixel and cisplatin)					٢	
2L ESCC	Mono				0		
r/r NK/T-cell lymphoma	Mono				0		
2L NSCLC	Mono			Ð			
1L/2L melanoma	Mono			Ð			
Refractory gastrointestinal cancer	Mono			O			
2L neuroendocrine tumor	Mono			O			
1L non-squamous NSCLC	Combo (pemetrexed and platinum)			•			
1L squamous NSCLC	Combo (gemcitabine and cisplatin)			•			
1L gastric cancer Combo (capecitabine and oxaliplatin)				O			
Refractory solid tumors	Mono		O				
U.S.							
Solid tumors	Mono			۲			
Late stage endometrial carcinoma	Mono			۲			

The chart below shows the indications for which we are currently evaluating sintilimab in clinical trials:

Notes:

- 1. Abbreviations: r/r = relapsed, refractory; 2L = second-line; 1L = first-line; NK/T-cell lymphoma = natural killer/T-cell lymphoma; ESCC = esophageal squamous cell carcinoma; NSCLC = non-small cell lung cancer; EGFR = epidermal growth factor receptor; TKI = tyrosine kinase inhibitor.
- 2. Symbols: \bullet = completed; \bullet = in progress; \bullet = to be initiated within next quarter.
- 3. Some indications may not require every clinical trial indicated on this chart to be completed prior to the filing of an NDA.

China

We have conducted a multi-center Phase 1a (dose escalation) study in China to evaluate the safety and efficacy of sintilimab as a monotherapy in cancer patients with no available standard of care therapy. We enrolled 12 patients and studied four Q3W dose strengths: 1 mg/kg, 3 mg/kg, 200 mg flat dose and 10 mg/kg. Four drug-related SAEs were observed, but no dose limiting toxicity was observed. Three patients are still on treatment and two partial responses (PRs) have been observed. Based on the results of this study, 200 mg flat dose was selected for further study.

NSCLC

We are conducting a multi-center Phase 3 clinical trial in China of sintilimab as a second-line monotherapy in patients with advanced or metastatic squamous NSCLC. This trial is designed as a superiority trial comparing sintilimab with standard of care chemotherapy using docetaxel. We have enrolled 119 patients in 34 trial sites as of June 7, 2018 and plan to enroll a total of 266 patients in this trial. The primary endpoint of this trial is overall survival.

We are conducting a multi-center Phase 1b (dose expansion) study in China to evaluate the safety and efficacy of sintilimab at 200 mg Q3W dose level in combination with pemetrexed and platinum in patients with first-line non-squamous NSCLC. As of June 28, 2018, we recruited 21 patients, exceeding our planned sample size of 20 patients at 4 trial sites. As of the same date, the combination demonstrated an ORR of 68.4%, based on data from 19 patients with at least one radiological assessment among the 21 patients. The study also demonstrated a safety profile for sintilimab that is consistent with the expected safety profile of a PD-1-specific antibody. Based on the results of this Phase 1b study, we have initiated a randomized, double-blinded, multi-center Phase 3 study in China to evaluate the safety and efficacy of sintilimab in combination with pemetrexed and platinum-based chemotherapy in patients with first-line non-squamous NSCLC. The primary endpoint of this Phase 3 study is progression free survival. We plan to enroll a total of 378 patients in this Phase 3 study.

We are conducting a Phase 1b (dose expansion) study in China to evaluate the safety and efficacy of sintilimab at 200 mg flat dose level every 3 weeks in combination with gemcitabine and cisplatin in patients with first-line squamous NSCLC. The endpoints of this trial are dose-limiting toxicity, tumor response, and clinical and laboratory adverse events. As of June 7, 2018, we recruited 18 out of 20 planned patients at 3 trial sites. The study demonstrated a safety profile for sintilimab that is consistent with the expected safety profile of a PD-1-specific antibody. Based on the results of this study, we plan to initiate a randomized Phase 3 clinical trial for the same combination therapy in China.

We are conducting a multi-center Phase 1b (dose expansion) study in China to evaluate the safety and efficacy of sintilimab at 200 mg Q3W dose level as a monotherapy in patients with second-line NSCLC. At the data cutoff of June 7, 2018, we completed patient enrollment, recruiting 37 patients at 6 trial sites and exceeding the planned sample size of 20 patients. As of September 1, 2018, 34 patients received at least one radiological assessment, of whom the ORR was 17.6% and the medium average survival was 13.8 months.

We are conducting a multi-center Phase 1b (dose expansion) study in China to evaluate the safety and efficacy of sintilimab at 200 mg Q3W dose level as a monotherapy in patients with neuroendocrine tumors for whom the standard therapy failed. As of September 1, 2018, we recruited 25 patients. Based on data from 22 patients who had at least one radiological assessment, the ORR was 22.7%. Furthermore, out of the 22 patients, 19 patients were with poorly differentiated neuroendocrine carcinoma and data from them demonstrated an ORR of 26.3%.

We plan to initiate a multi-center Phase 3 clinical trial in China to evaluate the efficacy of sintilimab in combination with our IBI-305 on patients with NSCLC or hepatocellular carcinoma. The relevant IND application was approved on September 18, 2018.

Esophageal Cancer

We have initiated a multi-center Phase 2 clinical trial in China of sintilimab as a second-line monotherapy in patients with advanced or metastatic esophageal squamous cell carcinoma. This trial is designed as a superiority trial comparing sintilimab with standard of care chemotherapy using paclitaxel or irinotecan. We have enrolled 139 patients in 26 trial sites as of June 7, 2018 and plan to enroll a total of 180 patients at 35 sites in this trial. The primary endpoint of this trial is overall survival.

NK/T-Cell Lymphoma

We have initiated a multi-center, single arm, Phase 2 study in China to evaluate the efficacy and safety of sintilimab in patients with relapsed/refractory extranodal NK/T-cell lymphoma (ENKTL) to assess the response to sintilimab treatment in ENKTL patients. Patients are dosed 200 mg every three weeks. We have enrolled 28 patients at 6 sites at the data cutoff of June 7, 2018, and plan to enroll a total of 60 patients in this trial. The primary endpoint of this trial is objective response rate.

Melanoma

We are conducting a multi-center Phase 1b (dose expansion) study in China to evaluate the safety and efficacy of sintilimab at 200 mg Q3W dose level as a monotherapy in patients with locally advanced, relapsed or metastatic melanoma. The endpoints of this trial are dose-limiting toxicity, tumor response, and clinical and laboratory adverse events. At the data cutoff of June 7, 2018, we completed patient enrollment, recruiting 22 patients and exceeding the planned sample size of 20 patients.

Gastrointestinal Cancer

We are conducting a multi-center Phase 1b (dose expansion) study in China to evaluate the safety and efficacy of sintilimab at 200 mg Q3W dose level as a monotherapy in patients with refractory gastrointestinal cancers. The endpoints of this trial are dose-limiting toxicity, tumor response, and clinical and laboratory adverse events. At the data cutoff of June 7, 2018, we completed patient enrollment, recruiting 87 patients at 4 trial sites and exceeding the planned sample size of 50 patients.

Gastric Cancer

We are conducting a multi-center Phase 1b (dose expansion) study in China to evaluate the safety and efficacy of sintilimab at 200 mg Q3W dose level in combination with capecitabine (Xeloda) and oxaliplatin (Eloxatin) in patients with first-line gastric cancer. The endpoints of this trial are dose-limiting toxicity, tumor response, and clinical and laboratory adverse events. At the data cutoff of June 7, 2018, we recruited 4 out of 20 planned patients and opened one trial site.

United States of America

We have begun the process of seeking FDA marketing authorization for sintilimab. The FDA approved our IND application for sintilimab in January 2018, and based on the strength of our pre-clinical data and clinical data from trials conducted in China we will not be required to conduct a dose finding Phase 1 study in the U.S. We plan to initiate a multi-center Phase 1b/2 clinical trial in the U.S. in 60 patients with solid tumors for whom no standard of care approved therapies exist. The study will investigate the role of tumor mutational burden as related to response to PD-1 blockade. A second cohort in the study will investigate the clinical activity in 20 patients with late stage endometrial carcinoma who have no available approved therapy.

Licenses, Rights and Obligations

We co-discovered sintilimab through our collaboration with Adimab as described under "– Collaboration Agreements – Collaboration with Adimab" below. We will co-promote sintilimab with Eli Lilly in China pursuant to an exclusive license and collaboration agreement as described under "– Collaboration Agreements – Collaboration with Eli Lilly" below.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET SINTILIMAB SUCCESSFULLY.

Our Phase 3 Biosimilar Drug Candidates

Biosimilars are biologics similar to approved branded reference products. Unlike generics, biosimilars are not identical to their reference products and in some aspects have minor differences. The Biosimilars Guideline in China adopts an approach focused on stepwise development that involves demonstration of structural similarity and functional equivalence and yet stops short of providing sufficient details to be regarded as overarching guidelines and standards the compliance with which can be readily ascertained. Therefore, we have looked to and substantially followed the technical standards and guiding principles adopted by the US FDA for biosimilars, which we believe the NMPA may aim to emulate in the implementation of the regulatory approval pathway for biosimilars in China. In so doing, we believe that we have imposed standards above and beyond those provided in the Biosimilars Guideline. For instance, under the Biosimilars Guideline, the standards for clinical study data to substantiate bioequivalence between a biosimilar drug candidate and its reference product may be relaxed to the extent that results from pre-clinical studies have demonstrated sufficient similarity and also that results from clinical pharmacology studies suggest similarity in endpoints in clinical confirmation studies. Such relaxed standards are not available under the US FDA's biosimilar regulatory pathway and BLA requirements. We have not elected to and do not expect to take advantage of such relaxed standards for the assessment of applicable endpoints in clinical confirmation studies. In addition, we have voluntarily conducted Phase 1 clinical trials for some of our biosimilar drug candidates as discussed below, even though such early-stage trials are not required under the Biosimilars Guideline, as they are required under the US FDA's biosimilar regulatory pathway and BLA requirements. The goal of a biosimilar clinical development program is to confirm similarity with the reference product based on (1)

analytical studies for functional and structural characterization at various stages of the manufacturing process, (2) pre-clinical animal studies, (3) a clinical pharmacology study (a human pharmacokinetic/pharmacodynamic equivalence study), and (4) a confirmatory comparative pivotal clinical study in a representative indication evaluating safety, efficacy and immunogenicity. Consistent with this approach, we apply our integrated platform to the following four key steps of biosimilar development that are designed to provide the analytical, pre-clinical and clinical basis to establish biosimilarity and support regulatory approvals for our biosimilar drug candidates:

Step 1: CMC and Analytical Characterization. The amino acid sequence of a biosimilar drug candidate must precisely match that of its reference product. We validate the amino acid sequence of all biosimilar drug candidates through enzymatic digestion and peptide mapping using liquid chromatography-mass spectroscopy/mass spectroscopy (LC-MS/MS). We establish master cell banks and working cell banks for our biosimilar drug candidates and demonstrate their quality and stability in accordance with the ICH guidelines. We develop, scale up and implement a process to manufacture our biosimilar drug candidates in our GMP facility in order to ensure the manufactured products are suitable for use in clinical trials.

Once a biosimilar drug candidate has been manufactured, we use a variety of analytical characterization techniques and *in vitro* studies comparing our biosimilar drug candidate with its reference product to ensure that our biosimilar drug candidate closely matches the primary structure, higher order structure, product purity and impurities, charge and glycan heterogeneity, biological activity, Fc functions and other general properties of the reference product, as the results from such comparisons may be predictive of clinically relevant differences in PK, PD, efficacy, safety and immunogenicity between our biosimilar drug candidate and its reference product. These techniques and studies include but are not limited to differential scanning calorimetry (DSC), cation-exchange chromatography (CEX-HPLC), high performance liquid chromatography with fluorescence detection (UHPLC-FLD), size exclusion chromatography (SEC-HPLC), capillary electrophoresis sodium dodecyl sulfate (CE-SDS), cell-based potency, ELISA blinding potency, and Bio-layer Interferometry (BLI).

Step 2: Pre-clinical Studies. After we demonstrate the *in vitro* biosimilarity, we compare our biosimilar drug candidate with the reference product in relevant animal models using the intended dosage form and route of administration prior to performing human clinical trials, since PK, PD and safety observations from these studies may be predictive of the human clinical trial experience. In general, two studies are required in relevant animal models to provide sufficient pre-clinical rationale to advance to the clinical pharmacology study.

Step 3: Clinical Pharmacology Study. An essential regulatory requirement is the completion of a clinical study in a sufficient number of human subjects directly comparing our biosimilar drug candidate and its reference product to establish PK/PD similarity. Bioequivalence is generally measured by three defined parameters as follows:

- C_{max}: maximum measured serum concentration;
- AUC_{0-t}: area under the concentration-time curve from the first time point measured (0) to the last time point measured (t); and

• AUC_{0-inf}: area under the concentration-time curve from the first time point measured (0) extrapolated to infinity.

The area under the curve, or the AUC, is a measure of how much of a drug is in a patient's system over a given time period. In order to calculate the AUC, the concentration of the drug in blood serum or plasma is plotted over time starting at the time the drug is administered and ending when the last time point is collected (AUC_{0-t}) or when the serum or plasma concentration would be below the level of detection or zero (AUC_{0-inf}) , and then the area under this curve is calculated. To be deemed bioequivalent, for each parameter, the ratio of the biosimilar drug candidate and the reference product shall fall between 80% and 125%, with the identical match being at 100%.

Step 4: Clinical Confirmation Studies. The final step to support regulatory approval for a biosimilar drug candidate is a single Phase 3 confirmatory safety and efficacy study in a therapeutic indication for which the reference product has been approved. The objective of this study is to demonstrate biosimilarity between the two molecules with respect to both safety and efficacy. Trial endpoints include considerations such as the number of subjects, statistical significance, confidence intervals and accumulated safety database size. We currently do not have safety data relating to our biosimilar product candidates available because our clinical confirmation studies are double blind trials which are still ongoing. Only upon the closure of such trials the safety data will be "unblinded" and cleansed and become available.

IBI-305 is our biosimilar product candidate to bevacizumab, which is sold under the trade name Avastin (阿瓦斯汀) in China.

Mechanism of Action

Bevacizumab is a recombinant fully-humanized monoclonal antibody that decreases the growth of blood vessels (this growth is referred to as angiogenesis) by inhibiting vascular endothelial growth factor A (VEGF-A). VEGF-A is a protein that stimulates angiogenesis which in turn promotes the growth of certain solid tissues, including solid tumors.

As illustrated by the following graph, VEGF-A can bind with VEGFR-2 and activate the downstream pathway to angiogenesis. Anti-VEGF monoclonal antibody such as bevacizumab can bind with VEGF, including VEGF-A, and thus block the angiogenesis pathway and depress the growth of solid tumors.



Source: Frost & Sullivan analysis

Market Opportunity and Competition

Non-small cell lung cancer (NSCLC) is a subset of lung cancer. According to the Frost & Sullivan Report, in China, NSCLC patients increased from 0.6 million in 2013 to 0.7 million in 2017, representing a CAGR of 3.5%, and are expected to reach 0.8 million in 2022 at a CAGR of 2.7% from 2017 to 2022 and reach 1.1 million in 2030 with a CAGR of 3.1% from 2023 to 2030.

Avastin is the best-selling drug among all anti-VEGF monoclonal antibodies. According to the Frost & Sullivan Report, worldwide sales of Avastin were US\$6.8 billion in 2017 and are estimated to remain near US\$7 billion in 2018.

Bevacizumab has been approved for advanced relapsed/refractory NSCLC and metastatic CRC in China and has been included in the National Reimbursement Drug List. According to the Frost & Sullivan Report, the China sales of bevacizumab were RMB1.7 billion in 2017 and are expected to reach RMB8.8 billion in 2022 and RMB16.6 billion in 2030. There is one other bevacizumab biosimilar drug candidate for which NDA has been submitted to NMPA. Besides our IBI-305, there are seven other bevacizumab biosimilar drug candidates in Phase 3 clinical trials in China.

Competition in the oncology therapeutic area to which IBI-305 belongs is extremely fierce given the abundance of existing competing drugs and drug candidates that continue to increase competition in the market. The following table sets forth comparisons between IBI-305 and its competitive drug candidates in China which are approved to market or in late stage clinical trials:

Generic		Filing					
(Brand) Name/	rand) Name/ Status in Mechanism Lead/Pro		Lead/Proposed	Retail Price			
Drug Code	Company	China	Date*	of Action	Indications	(RMB)	NRDL/PRDL ⁽¹⁾
IBI-305	Innovent	Phase 3	2016/11/17	Anti-VEGF	R/r NSCLC and	N.A.	N.A.
					metastatic CRC		
Bevacizumab	Roche	Marketed	2010/2/26	Anti-VEGF	Metastatic CRC and	1,998/100 mg	List B
(Avastin)					advanced r/r		
					NSCLC		
HLX04	Henlius	Phase 3	2018/3/18	Anti-VEGF	Metastatic CRC	N.A.	N.A.
QL1101	Qilu	NDA	2018/8/15	Anti-VEGF	NSCLC	N.A.	N.A.
		submission					
GB222	Genor	Phase 3	2017/12/15	Anti-VEGF	NSCLC	N.A.	N.A.
MIL60	Beijing	Phase 3	2017/8/4	Anti-VEGF	A/R non-squamous	N.A.	N.A.
	mAbworks				NSCLC		
LY01008	Shandong	Phase 3	2018/1/28	Anti-VEGF	NSCLC	N.A.	N.A.
	Boan						
BP102	Hengrui	Phase 3	2018/3/27	Anti-VEGF	Non-squamous	N.A.	N.A.
					NSCLC		
TAB008	TOT	Phase 3	2017/5/17	Anti-VEGF	A/R non-squamous	N.A.	N.A.
	Biopharm				NSCLC		
BAT1706	Bio-Thera	Phase 3	2017/10/31	Anti-VEGF	Non-squamous	N.A.	N.A.
	Solutions				NSCLC		

Comparison Between IBI-305 and its Approved or Late-Stage Competitors in China

Source: Frost & Sullivan

Abbreviation: NRDL = national reimbursement drug list of China; PRDL = provincial reimbursement drug list;

"N.A." means, with respect to retail price, not available, and with respect to NRDL/PRDL, not applicable because the drug candidate is not marketed yet.

- * for a marketed product, it refers to the NMPA approval date; for a clinical stage product, it refers to the date when the information about clinical trials is published for the first time (首次公示日期); for a product with NDA submitted and the NDA result pending, it refers to the date of NDA submission.
- (1) Bevacizumab are included in the NRDL List B Catalogue. As Bevacizumab entered into the NRDL List B Catalogue via price negotiation, it will automatically be added into the PRDLs when each provinces and municipalities updates its PRDL according to Notice on Inclusion of 36 Drugs in NRDL List B Catalogue for National Basic Medical Insurance, Work Injury Insurance and Maternity Insurance (《關於將36種藥品納入國家基本醫療保險、工傷保險和生育保險藥品目錄乙類範圍的通知》). As of August 9, 2018, eight provinces and municipalities, including Heilongjiang, Shanghai, Henan, Jilin, Jiangxi, Shandong, Jiangsu and Liaoning, have recently updated their PRDLs to include bevacizumab as a List B drug.

Current Development Status and Data

Step 1: CMC and Analytical Characterization

We have developed, manufactured and characterized a master cell bank and demonstrated its quality and stability in accordance with the ICH guidelines. We have also completed development of a stable and controllable production process for IBI-305 and demonstrated through comprehensive studies that the stability of drug substance and drug product comply with the requirements of clinical research.

We completed extensive analytical characterization and *in vitro* studies comparing IBI-305 to the reference product Avastin.

We have confirmed through Lys-C peptide mapping that the amino acid sequence of IBI-305 is identical to that of the reference product Avastin, which is required for the biosimilar pathway under NMPA regulations. The graph below shows the peptide fingerprint of IBI-305 compared with Avastin. IBI-305 and Avastin were fragmented by endoproteinase Lys-C degradation and the peptides were separated by liquid chromatography-mass spectroscopy/mass spectroscopy (LC-MS/MS). This technology creates a peptide fragment-based fingerprint for proteins. If the fingerprints are identical, it can be inferred that two proteins have identical amino acid primary structure.



The peptide fingerprint of IBI-305 is highly similar to bevacizumab (Avastin)

Abbreviation: mAU = mAnson Unit (a unit of measurement for enzyme activity)

A cell-based potency assay demonstrated that IBI-305 and Avastin have similar *in vitro* potency. As shown in the left hand panel of the following figure, when increasing concentration of IBI-305 and Avastin are incubated in the reporter assay, both antibodies block VEGF induced activation of the reporter gene with identical potency. The right hand panel of the following figure demonstrates that multiple lots of IBI-305 and Avastin have similar potency.



Cell-based potency assay shows similarity in potency between IBI-305 and Avastin

Step 2: Pre-clinical Studies

We have performed comprehensive pre-clinical studies of IBI-305 and the results indicate that IBI-305 has an efficacy, toxicity and PK/PD profile which is similar to that of Avastin.

The figure below demonstrates that, at both 1.5 mg/kg and 5 mg/kg dosage levels, there were no statistical differences in the relative tumor volume between IBI-305 dosed animals and Avastin dosed animals. These results indicate similarity in tumor-suppressive efficacy between IBI-305 and Avastin.

The anti-tumor efficacy of IBI-305 and bevacizumab are similar



The PK profiles of IBI-305 and Avastin are highly similar. As shown in the figure below, there were no statistical differences in drug concentration between IBI-305 dosed animals and Avastin dosed animals at the same time points throughout the study. These results indicate the similarity in the PK profile between IBI-305 and Avastin.



The PK profiles of IBI-305 and Avastin in cynomolgus monkeys are highly similar

We conducted additional toxicology studies in cynomolgus monkey to determine the potential for harmful antibody responses to IBI-305 or other toxic effects in comparison with Avastin. We found no differences between IBI-305 and Avastin in terms of potentially harmful antibody responses or other toxicities.

Step 3: Clinical Pharmacology Study

Our IND application for IBI-305 was approved by the NMPA in May 2016 to follow the biosimilar regulatory development pathway based on the demonstrated similarity to the reference product in the CMC and pre-clinical studies. Since then, we have completed a randomized double-blind parallel controlled clinical trial in China to assess the PK/PD, safety, tolerance and immunogenicity of a single 3 mg/kg dose of IBI-305 compared to Avastin in 100 healthy volunteers. Similar to bevacizumab (Avastin), no serious adverse events were observed in the study for IBI-305. The primary endpoints of AUC_{0-inf} (extrapolated total area under plasma curve to time infinity) and AUC_{0-t} (area under the plasma concentration-time curve), as well as C_{max} (the peak serum concentration that a drug achieves in a test area of the body after drug administration), $t_{1/2}$ (half-life), drug clearance and volume of distribution, were similar for IBI-305 and bevacizumab (Avastin) at a 3 mg/kg dose level. For each of AUC_{0-inf} and AUC_{0-t}, the 90% confidence intervals (90% CI) for the ratio of IBI-305 to bevacizumab (Avastin) were fully contained within 80% to 125%, confirming the bioequivalence between IBI-305 and bevacizumab (Avastin). As shown in the following graph, the PK profile plots demonstrated substantial overlap for the profile of IBI-305 and bevacizumab (Avastin) out to 2,000 hours after a single dose administration in normal volunteers.

We have not seen unexpected adverse events with IBI-305 in this study. Safety data from these small and short clinical pharmacology studies aimed at establishing bioequivalence are not useful, representative or material. The useful or material safety data set only comes from the large and lengthy clinical confirmation studies at Step 4.



The PK profiles of IBI-305 and bevacizumab (Avastin) in normal volunteers are bioequivalent

Step 4: Clinical Confirmation Studies

We are conducting a randomized, double blind, multi-center, Phase 3 study in China to evaluate the efficacy, safety and immunogenicity of IBI-305 in combination with chemotherapy compared to bevacizumab in combination with chemotherapy in patients with advanced or recurrent non-squamous non-small cell lung cancer (non-squamous-NSCLC). The study randomizes 436 patients at a 1:1 ratio to two treatment arms. The primary endpoint of this study is objective response rate. As of June 7, 2018, we opened 42 trial sites and completed patient enrollment. We recruited a total of 450 patients, exceeding our planned 436 patients. Based on internal review of the progress of this trial and preliminary clinical observations, we expect to complete this trial and, if the data successfully demonstrated biosimilarity, to have a pre-NDA meeting with, and submit an NDA to, the NMPA in the first quarter of 2019.

We have not seen unexpected adverse events with IBI-305 in this trial. The aggregate safety data for this trial cannot be disclosed at the date of this prospectus because the trial is double blind and has not been unblinded yet and the trial data base has not been locked. The trial data base is expected to be locked on October 30, 2018. The blinded analysis of the interim trial data shows that the safety profile of IBI-305 is consistent with the reported safety profile for Avastin. We expect the safety data for IBI-305 to become available for disclosure in the first quarter of 2019 and we will promptly disclose such data by way of announcement on the Stock Exchange.

Note: The inset is a log transformation of the PK data to better illustrate the lower ranges of antibody concentration.

Adverse reactions to the reference drug

According to the prescribing information of Avastin, the most common adverse reactions observed in patients receiving Avastin as a single agent or in combination with chemotherapy at a rate > 10%, are epistaxis, headache, hypertension, rhinitis, proteinuria, taste alteration, dry skin, rectal hemorrhage, lacrimation disorder, back pain and exfoliative dermatitis. Across clinical studies, Avastin was discontinued in 8% to 22% of patients because of adverse reactions.

The safety of Avastin was evaluated as first-line treatment in 422 patients with unresectable NSCLC who received at least one dose of Avastin in an active-controlled, open-label, multicenter trial. Only Grade 3-5 non hematologic and Grade 4-5 hematologic adverse reactions were collected. Grade 3-5 non hematologic and Grade 4-5 hematologic adverse reactions occurring at a higher incidence ($\geq 2\%$) in patients receiving Avastin with paclitaxel and carboplatin compared with patients receiving chemotherapy alone were neutropenia (27% vs. 17%), fatigue (16% vs. 13%), hypertension (8% vs. 0.7%), infection without neutropenia (7% vs. 3%), venous thromboembolism (5% vs. 3%), febrile neutropenia (5% vs. 2%), pneumonitis/pulmonary infiltrates (5% vs. 3%), infection with Grade 3 or 4 neutropenia (4% vs. 2%), hyponatremia (4% vs. 1%), headache (3% vs. 1%) and proteinuria (3% vs. 0%).

Licenses, Rights and Obligations

We obtained CHO cell line that expresses IBI-305 from Suzhou-based Alphamab Co. Ltd., or Alphamab. We currently have no material further monetary obligations to Alphamab with respect to IBI-305.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBI-305 SUCCESSFULLY.

IBI-301 is our biosimilar product candidate to rituximab, which is sold under the trade names MabThera (美羅華) in China and MabThera/Rituxan outside China.

Mechanism of Action

Rituximab is a recombinant chimeric monoclonal antibody that binds to the cell surface protein CD20, which is widely expressed on immune system B-cells. Rituximab mediates antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC), and induces programmed cell death, or apoptosis, of CD20 positive cells. These activities result in the elimination of B-cells (including the cancerous ones) from the body.


Mechanisms of action of anti-CD20 mAbs

Source: FDA, Frost & Sullivan analysis

Notes:

CD20 mAbs can induce tumor killing in several ways.

- A. Direct binding of CD20 mAbs initiates the crosslinking of multiple CD20 molecules, resulting in cell-death via induction of non-classical apoptosis;
- B. Activation of complement results in complement-dependent cytotoxicity;
- C. Recognition of opsonized tumor cells by FcγRs expressed on immune effector cells initiates antibodydependent cell-mediated cytotoxicity;
- D. FcyR may only serve as crosslinking platform and thereby enhance antigen signaling in the tumor cells;
- E. Ab-initiated complement activation yields to deposition of complement cleavage fragments, which may enhance tumor killing through recognition by complement receptors (CRs) in a process called complement-enhanced ADCC.

Market Opportunities and Competition

Originally developed by Roche and Genentech, and first approved for marketing in 1997, rituximab is used for treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis, granulomatosis with polyangiitis, idiopathic thrombocytopenic purpura, pemphigus vulgaris and myasthenia gravis. Rituxan reached US\$7.5 billion in worldwide sales in 2017, according to the Frost & Sullivan Report.

According to Frost & Sullivan Report, there were 81,800 new cases of non-Hodgkin's lymphoma in China in 2017, and the incidence is expect to increase to 90,100 in 2022. These

patients currently have only limited treatment options. MabThera was approved for treatment of non-Hodgkin's lymphoma in China and has been listed in National Reimbursement Drug List 2017. Besides our IBI-301, there are one other rituximab biosimilar drug candidate with an NDA under review by the NMPA and two other rituximab biosimilar drug candidates in Phase 3 clinical trials in China.

Competition in the oncology therapeutic area to which IBI-301 belongs is extremely fierce given the abundance of existing competing drugs and drug candidates that continue to increase competition in the market. The following table sets forth comparisons between IBI-301 and its competitive drug candidates in China which are approved to market or in late stage clinical trials:

Generic		Filing					
(Brand) Name/		Status in		Mechanism	Lead/Proposed	Retail Price	
Drug Code	Company	China	Date*	of Action	Indications	(RMB)	NRDL/PRDL ⁽¹⁾
IBI-301	Innovent	Phase 3	2016/08/19	Anti-CD20	DLBCL	N.A.	N.A.
Rituximab	Roche	Marketed	2000/3/15	Anti-CD20	R/r follicular central	2,418/100 mg	List B
(MabThera/					lymphoma, CD20-	8,290/500 mg	
Rituxan)					positive DLBCL		
HLX01	Henlius	NDA	2017/12/11	Anti-CD20	DLBCL	N.A.	N.A.
		submission					
SCT400	SinoCelltech	Phase 3	2016/6/6	Anti-CD20	CD20-positive	N.A.	N.A.
					DLBCL		
Obinutuzumab	Roche	Phase 3	2014/12/30	Anti-CD20	NHL	N.A.	N.A.
(Gazyva)							

Comparison Between IBI-301 and its Approved or Late-Stage Competitors in China

Source: Frost & Sullivan

Abbreviation: NRDL = national reimbursement drug list of China; PRDL = provincial reimbursement drug list;

"N.A." means, with respect to retail price, not available, and with respect to NRDL/PDRL, not applicable because the drug candidate is not marketed yet.

- * for a marketed product, it refers to the NMPA approval date; for a clinical stage product, it refers to the date when the information about clinical trials is published for the first time (首次公示日期); for a product with NDA submitted and the NDA result pending, it refers to the date of NDA submission.
- (1) Rituximab are included in the NRDL List B Catalogue. As Rituximab entered into the NRDL List B Catalogue via price negotiation, it will automatically be added into the PRDLs when each provinces and municipalities updates its PRDL according to Notice on Inclusion of 36 Drugs in NRDL List B Catalogue for National Basic Medical Insurance, Work Injury Insurance and Maternity Insurance (《關於將36種藥品納入國家基本醫療保險、工傷保險和生育保險藥品目錄乙類範圍的通知》). As of August 9, 2018, eight provinces and municipalities, including Heilongjiang, Shanghai, Henan, Jilin, Jiangxi, Shandong, Jiangsu and Liaoning, have recently updated their PRDLs to include rituximab as a List B drug.

Current Development Status and Data

Step 1: CMC and Analytical Characterization

We have developed, manufactured and characterized a master cell bank and demonstrated its quality and stability in accordance with the ICH guidelines. We have also completed development of a stable and controllable production process for IBI-301 and demonstrated through comprehensive studies that the stability of drug substance and drug product comply with the requirements of clinical research.

We completed extensive analytical characterization and *in vitro* studies comparing IBI-301 to Rituxan.

We have confirmed through Lys-C peptide mapping that the amino acid sequence of IBI-301 is identical to that of the reference product (MabThera/Rituxan), which is required for the biosimilar pathway under NMPA regulations. The graph below shows peptide fingerprint of IBI-301 compared with Rituxan. IBI-301 and Rituxan were fragmented by endoproteinase Lys-C degradation and the peptides were separated by liquid chromatography-mass spectroscopy/mass spectroscopy (LC-MS/MS). This technology creates a peptide fragment-based fingerprint for proteins. If the fingerprints are identical it can be inferred that two proteins have identical amino acid primary structure.



The peptide fingerprint of IBI-301 is highly similar to Rituxan

Abbreviation: mAU = mAnson Unit (a unit of measurement for enzyme activity)

One major mechanism of action of rituximab is complement-dependent cytotoxicity (CDC). A cell-based potency assay based on the accurate measurement of CDC demonstrated equivalent *in vitro* potency between IBI-301 and Rituxan. As shown in the left panel of the following figure, when increasing concentrations of the two antibodies are incubated in the reporter assay, the CDC activities as measured by cellular lysis are identical. The right hand panel of the following figure shows that multiple lots of IBI-301 and rituximab (MabThera/Rituxan) have similar potency.

Cell-based potency assay shows similarity in potency for IBI301 and Rituxan



Step 2: Pre-clinical Studies

We have performed comprehensive pre-clinical studies of IBI-301 and the results indicate that IBI-301 has an efficacy, toxicity and PK/PD profile which is similar to that of Rituxan.

The figure below shows that both of IBI-301 and rituximab (MabThera/Rituxan) are effective in the complete and persistent depletion of CD20 positive B cells in the peripheral circulation of monkeys after a single dose of 30 mg/kg. These results indicate similarity in efficacy between IBI-301 and rituximab (MabThera/Rituxan).

Similarity in PD for IBI-301 and Rituxan in Cynomolgus monkeys



The results of our studies also demonstrate the similarity in the PK profiles between IBI-301 and rituximab (MabThera/Rituxan). As shown in the figure below, there are no statistical differences in drug concentration between IBI-301 dosed animals and rituximab (MabThera/Rituxan) dosed animals at the same time points throughout the study. These results indicate the similarity in the PK profile between IBI-301 and rituximab (MabThera/Rituxan).

Similarity in PK profiles for IBI-301 and rituximab (MabThera/Rituxan) in cynomolgus monkeys



Step 3: Clinical Pharmacology Study

Our IND application for IBI-301 was approved by the NMPA in September 2014 in accordance with the biosimilar regulatory development pathway based on the demonstrated similarity to the reference product in the CMC and pre-clinical studies. We are conducting a multi-center clinical trial to assess PK/PD, safety, tolerance and immunogenicity of IBI-301 in CD20 positive B-cell lymphoma patients who obtained complete remission or uncertain complete remission after the prior therapy. The primary endpoints of this study are AUC_{0-inf} (the area under the curve from zero to infinity, which is the definite integral in a plot of drug concentration in blood plasma vs. time) and AUC_{0-t} . As of June 7, 2018, 160 patients at 15 trial sites are enrolled in the trial and 142 of these patients have completed trial procedures. We expect to complete this clinical pharmacology study in the second quarter of 2019.

We have not seen unexpected adverse events with IBI-301 in this study. Safety data from these small and short clinical pharmacology studies aimed at establishing bioequivalence are not useful, representative or material. The useful or material safety data set only comes from the large and lengthy clinical confirmation studies at Step 4.

Step 4: Clinical Confirmation Studies

We are conducting a randomized, double-blind, multi-center, Phase 3 trial in China to evaluate the efficacy, PK/PD, safety and immunogenicity of IBI-301 for the treatment of patients with first-line diffuse large B-cell lymphoma (DLBCL) in combination with standard chemotherapy. The primary endpoint of this trial is objective response rate. As of September 14, 2018, we opened 52 trial sites and completed patient enrollment. We recruited a total of 419 patients in this trial, exceeding our planned 400 patients. Based on internal review of the progress of this trial and preliminary clinical observations, we expect to complete this trial and, if the data demonstrates biosimilarity, to have a pre-NDA meeting with, and submit an NDA to, the NMPA in the fourth quarter of 2019.

We have not seen unexpected adverse events with IBI-301 in this trial. The aggregate safety data for this trial cannot be disclosed at the date of this prospectus because the trial is double blind and is still ongoing. We have not encountered any material inconsistencies with the reported safety profile for Rituxan in the aggregated data from this clinic trial program. We expect the safety data to become available for disclosure in the third quarter of 2019 after trial completion and we will promptly disclose such data by way of announcement on the Stock Exchange.

Adverse reactions to the reference drug

According to the prescribing information of Rituxan, the most common adverse reactions (incidence $\geq 25\%$) observed in clinical trials of patients with non-Hodgkin's lymphoma (NHL) were infusion reactions, fever, lymphopenia, chills, infection and asthenia. In the majority of patients with NHL, infusion reactions consisting of fever, chills/rigors, nausea, pruritus, angioedema, hypotension, headache, bronchospasm, urticaria, rash, vomiting, myalgia, dizziness, or hypertension occurred during the first Rituxan infusion.

The incidence of infusion reactions was highest during the first infusion (77%) and decreased with each subsequent infusion. Serious infections, including sepsis, occurred in less than 5% of patients with NHL in the single-arm studies. The overall incidence of infections was 31% (bacterial 19%, viral 10%, unknown 6%, and fungal 1%). In the patients with DLBCL, viral infections occurred more frequently in those who received Rituxan. In patients with NHL receiving Rituxan monotherapy, NCI-CTC Grade 3 and 4 cytopenias were reported in 48% of patients. These included lymphopenia (40%), neutropenia (6%), leukopenia (4%), anemia (3%), and thrombocytopenia (2%). The median duration of lymphopenia was 14 days (range, 1–588 days) and of neutropenia was 13 days (range, 2–116 days). A single occurrence of transient aplastic anemia (pure red cell aplasia) and two occurrences of hemolytic anemia following Rituxan therapy occurred during the single-arm studies. In studies of monotherapy, Rituxan-induced B-cell depletion occurred in 70% to 80% of patients with NHL. Decreased IgM and IgG serum levels occurred in 14% of these patients.

Licenses, Rights and Obligations

We contracted with Medicilon to obtain CHO cell line that expresses IBI-301. We have no material further monetary and technical obligations to Medicilon with respect to IBI-301. We will co-promote IBI-301 with Eli Lilly in China pursuant to an exclusive license and collaboration agreement as described under "– Collaboration Agreements – Collaboration with Eli Lilly" below.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBI-301 SUCCESSFULLY.

IBI-303 is our biosimilar product candidate to adalimumab, which is sold under the trade name Humira (修美樂) in China.

Mechanism of Action

Adalimumab is a fully human monoclonal antibody that can bind to a protein called tumor necrosis factor- α (TNF- α). As illustrated by the following graph, TNF- α stimulates inflammatory responses, regulates innate immunity and plays an important role in regulation of Th1 immune responses against intracellular bacteria and certain viral infections. Dysregulated TNF- α can also contribute to numerous pathological situations, including various autoimmune and inflammatory diseases. Treatment with adalimumab inhibits the action of TNF- α and ameliorates such diseases.





Source: American College of Radiology, Frost & Sullivan analysis

Market Opportunity and Competition

Adalimumab has been approved by the EMA and the FDA for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis and psoriasis when conventional therapies are not sufficiently effective. Worldwide sales of adalimumab exceeded US\$18.9 billion in 2017. According to the Frost & Sullivan Report, the prevalence of rheumatoid arthritis in China increased from 5.7 million in 2013 to 5.8 million in 2017 and is expected to further increase to 6.0 million by 2022 and 6.2 million by 2030. Also according to the Frost & Sullivan Report, the prevalence of ankylosing spondylitis in China increased from 3.7 million in 2013 to 3.8 million in 2017 and is expected to further increase to 3.9 million by 2022 and 4.1 million by 2030.

Adalimumab (sold under the trade name Humira by AbbVie) and golimumab (sold under the trade name Simponi by Johnson & Johnson) were approved by the NMPA in China as a treatment for rheumatoid arthritis, ankylosing spondylitis and psoriasis. Simponi was also approved in China as a treatment for ulcerative colitis. There are two other adalimumab biosimilar drug candidates for which NDAs have been submitted to NMPA. Besides our IBI-303, there are two other adalimumab biosimilar drug candidates in Phase 3 clinical trials in China.

Competition in the autoimmune therapeutic area to which IBI-303 belongs is extremely fierce given the abundance of existing competing drugs and drug candidates that continue to increase competition in the market. The following table sets forth comparisons between IBI-303 and its competitive drug candidates in China which are approved to market or in late stage clinical trials:

Generic (Brand) Name/ Drug Code	Company	Filing Status in China	Date*	Mechanism of Action	Lead/Proposed Indications	Retail Price (RMB)	NRDL/PRDL
IBI-303	Innovent	Phase 3	2016/9/13	Anti-TNF α	Ankylosing	N.A.	N.A.
Adalimumab (Humira)	AbbVie	Marketed	2010/2/26	Anti-TNF	Rheumatoid arthritis, ankylosing spondylitis, Psoriasis	7,600/40 mg	No
Golimumab (Simponi)	Johnson & Johnson	Marketed	2017/12/28	Anti-TNF	Rheumatoid arthritis, psoriatic arthritis, Ankylosing spondylitis, Ulcerative colitis	5,180/50 mg	No
HLX03	Henlius	Phase 3	2017/11/27	Anti-TNF α	Moderate-severe Plaque psoriasis	N.A.	N.A.
UBP1211	Jiangsu Union	Phase 3	2017/5/27	Anti-TNF α	Rheumatoid Arthritis	N.A.	N.A.
BAT1406	Bio-Thera Solutions	NDA submission	2018/8/27	Anti-TNF α	Ankylosing Spondylitis	N.A.	N.A.
HS016	Zhejiang Hisun	NDA submission	2018/9/14	Anti-TNF α	Ankylosing Spondylitis	N.A.	N.A.

Comparison Between IBI-303 and its Approved or Late-Stage Competitors in China

Source: Frost & Sullivan

Abbreviation: NRDL = national reimbursement drug list of China; PRDL = provincial reimbursement drug list;

"No" means that the drug is not list in the NRDL or the PRDL even though it is marketed;

"N.A." means, with respect to retail price, not available, and with respect to NRDL/PDRL, not applicable because the drug candidate is not marketed yet.

* for a marketed product, it refers to the NMPA approval date; for a clinical stage product, it refers to the date when the information about clinical trials is published for the first time (首次公示日期); for a product with NDA submitted and the NDA result pending, it refers to the date of NDA submission.

Current Development Status and Data

Step 1: CMC and Analytical Characterization

We have developed, manufactured and characterized a master cell bank and demonstrated its quality and stability in accordance with the ICH guidelines. We have also completed development of a stable and controllable production process for IBI-303 and demonstrated through comprehensive studies that the stability of drug substance and drug product comply with the requirements of clinical research.

We completed extensive analytical characterization and *in vitro* studies comparing IBI-303 to the reference product Humira.

We have confirmed through Lys-C peptide mapping that the amino acid sequence of IBI-303 is identical to that of the reference product Humira, which is required for the biosimilar pathway under NMPA regulations. The graph below shows the peptide fingerprint of IBI-303 compared with Humira (adalimumab). IBI-303 and adalimumab were fragmented by endoproteinase Lys-C degradation and the peptides were separated by liquid chromatographymass spectroscopy/mass spectroscopy (LC-MS/MS). This technology creates a peptide fragment-based fingerprint for proteins. If the fingerprints are identical it can be inferred that two proteins have identical amino acid primary structure.

Peptide fingerprint for IBI-303 and Humira are highly similar



Abbreviation: mAU = mAnson Unit (a unit of measurement for enzyme activity)

A cell-based potency assay demonstrated that IBI-303 and Humira have similar *in vitro* potency. As shown in the left hand panel of the following figure, when increasing concentration of IBI-303 and Humira are incubated in the reporter assay, both antibodies neutralize the TNF- α with identical potency, as measured by the viability of a TNF- α dependent cell line. The right hand panel of the following figure demonstrates that multiple lots of IBI-303 and Humira have similar potency.





Step 2: Pre-clinical Studies

We have performed comprehensive pre-clinical studies of IBI-303 in mice with rheumatoid arthritis and the results indicate that IBI-303 has an efficacy, toxicity and PK/PD profile which is similar to that of Humira.

As shown in the following figure, arthritic score curves generated from our studies demonstrated the efficacy similarity between IBI-303 and Humira at two different dose levels.

The efficacy of IBI-303 and adalimumab (Humira) in a human TNF- α dependent mouse model of rheumatoid arthritis is highly similar



We also performed another study in cynomolgus monkeys to characterize and compare the PK profile of IBI-303 against that of Humira. As shown in the figure below, there were no statistical differences in drug concentration between IBI-303 dosed animals and Humira dosed animals at the same time points throughout the study. These results indicate the similarity in the PK profile between IBI-303 and Humira.

IBI-303 and adalimumab (Humira) have highly similar PK profiles after a single dose in cynomolgus monkeys



Step 3: Clinical Pharmacology Study

Our IND application for IBI-303 was approved by the NMPA in December 2015 in accordance with the biosimilar regulatory development pathway based on the demonstrated similarity to the reference product in the CMC and pre-clinical studies. We have substantially completed a randomized double-blind clinical trial in China to assess the bioequivalence, pharmacokinetics, safety and immunogenicity of IBI-303 in comparison with Humira in 183 healthy volunteers. The primary endpoints of the study are C_{max} , AUC_{0-inf} and AUC_{0-i}.

The study procedures have been completed with all trial subjects as of the Latest Practicable Date. We are in the process of analyzing the trial data and we expect to complete analysis of the trial data in the second half of 2018 and to report the results thereafter at a scientific conference or other appropriate forum.

We have not seen unexpected adverse events with IBI-303 in this study. Safety data from these small and short clinical pharmacology studies aimed at establishing bioequivalence are not useful, representative or material. The useful or material safety data set only comes from the large and lengthy clinical confirmation studies at Step 4.

Step 4: Clinical Confirmation Studies

We are conducting a randomized, double blind, multi-center, Phase 3 clinical trial in China to evaluate the safety, efficacy and immunogenicity of IBI-303 compared to Humira at a dose level of 40 mg SC Q2W in adult patients with active ankylosing spondylitis who have had an inadequate response to or are intolerant to one or more nonsteroidal anti-inflammatory drugs. As of June 7, 2018, we have completed enrollment of 438 patients in this trial, exceeding our planned 400 patients. The primary endpoint of the study is ASAS-20 (Assessments in Ankylosing Spondylitis Assessment of Response 20), which is a standard tool to score for response in ankylosing spondylitis patients.

We had a pre-NDA meeting with the NMPA on September 10, 2018, and based on internal review of the progress of this trial, we expect to complete this trial in the second half of 2018 and, if the data from this trial establishes biosimilarity between IBI-303 and Humira, to submit an NDA to the NMPA in the fourth quarter of 2018.

We have not seen unexpected adverse events with IBI-303 in this trial as of the Latest Practicable Date. The aggregate safety data for this trial cannot be disclosed at the date of this prospectus because the trial is double blind and has not been unblinded yet and the trial data base has only recently been locked. The blinded analysis of the interim trial data shows that the safety profile of IBI-303 is consistent with the reported safety profile for Humira. We expect the safety data to become available for disclosure in the fourth quarter of 2018 and we will promptly disclose such data by way of announcement on the Stock Exchange.

Adverse reactions to the reference drug

According to the prescribing information of Humuira, the most common adverse reaction with Humira was injection site reactions. In placebo-controlled trials, 20% of patients treated with Humira developed injection site reactions (erythema and/or itching, hemorrhage, pain or swelling), compared to 14% of patients receiving placebo. Most injection site reactions were described as mild and generally did not necessitate drug discontinuation.

The proportion of patients who discontinued treatment due to adverse reactions during the double-blind, placebo-controlled portion of studies in patients with rheumatoid arthritis (RA) was 7% for patients taking Humira and 4% for placebo-treated patients. The most common adverse reactions leading to discontinuation of Humira in these RA studies were clinical flare reaction (0.7%), rash (0.3%) and pneumonia (0.3%).

In the controlled portions of the 39 global Humira clinical trials in adult patients with Humira targeted indications, such as RA and ankylosing spondylitis, the rate of serious infections was 4.3 per 100 patient-years in 7,973 Humira-treated patients versus a rate of 2.9 per 100 patient-years in 4,848 control-treated patients. Serious infections observed included pneumonia, septic arthritis, prosthetic and postsurgical infections, erysipelas, cellulitis, diverticulitis, and pyelonephritis.

Licenses, Rights and Obligations

We obtained an exclusive license for IBI-303 cell line from Aragen Bioscience. Other than the obligation to pay a US\$30,000 approval milestone, we have no further obligations to Aragen Bioscience. We have the rights to out-license the molecule globally but have not done so as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBI-303 SUCCESSFULLY.

Our Phase 1 Innovative Drug Candidates

IBI-306

IBI-306 is a fully human monoclonal antibody drug candidate that we are evaluating for the treatment of hyperlipidemia which is characterized by high levels of lipids in the blood, including fatty acids, cholesterol and triglycerides.

Mechanism of Action

IBI-306 binds to a protein called proprotein convertase substilisin/kexin type 9 (PCSK9), preventing its interaction with the low-density lipoprotein cholesterol receptor (LDL-R) and restoring the recycling of LDL-R and the uptake of low-density lipoprotein cholesterol (LDL-C). This mechanism of action positions IBI-306 as a potentially important treatment approach for hyperlipidemia, especially for those with ultrahigh cholesterol.

Market Opportunity and Competition

Nowadays, hypercholesterolemia has become a serious issue in China's society. The patients with hypercholesterolemia increased rapidly in recent years due to unhealthy diet and life style and population ageing. The number of hypercholesterolemia patients in China increased at a CAGR of 4.4% from 66.8 million in 2013 to 79.3 million in 2017, and is expected to further increase to 95.9 million in 2022 and 110.5 million in 2030, according to the Frost & Sullivan Report.

FDA has approved two anti-PCSK9 antibodies, including evolocumab (sold under the trade name Repatha by Amgen) and alirocumab (sold under the trade name Praluent by Sanofi). These drugs have been a significant advance in the treatment of high blood cholesterol and had aggregate worldwide sales of US\$490 million in 2017.

Currently Repatha (evolocumab) is the only one marketed PCSK inhibitor in China, which received the approval by the NMPA for the treatment of hypercholesterolemia in August 2018. Besides us, there are three other anti-PCSK9 drug candidates in clinical development in China, including Junshi's JS002, Amgen's Repatha (evolocumab) and Sanofi's Praluent (alirocumab). The table below sets forth the information of the foregoing anti-PCSK9 drug candidates in clinical development in China:

Generic name/ mAb category	Brand name/ Drug Code	Company	Status in China	Date*	Indication
Evolocumab (Fully Human Anti-PCSK-9 mAb)	AMG145	Amgen	Marketed	2018/8/8	Hypercholesterolemia
Alirocumab (Fully Human Anti-PCSK-9 mAb)	SAR236553	Sanofi-aventis	Phase 3 Phase 3	2016/7/6 2016/2/25	Hypercholesterolemia Acute coronary syndrome
Humanized Anti-PCSK-9 mAb	JS002	Shanghai Junshi Biosciences Co., Ltd	Phase 1	2017/11/17	Hypercholesterolemia

Source: Frost & Sullivan

* for a marketed product, it refers to the NMPA approval date; for a clinical stage product, it refers to the date when the information about clinical trials is published for the first time (首次公示日期).

Current Treatments and Limitations

The approved anti-PCSK9 drugs, alirocumab (sold under the trade name Praluent by Sanofi) and evolocumab (sold under the trade name Repatha by Amgen), have limitations in terms of their binding affinity for PCSK9. The ability of an antibody to produce a beneficial effect in a patient depends on its ability to block the target protein. Blocking the target protein depends on several factors including the binding affinity of the antibody for the target, the distribution of the antibody in the body and the duration that the antibody binds the target. We believe that higher binding affinity of IBI-306 for PCSK9 compared with the binding affinity of evolocumab and alirocumab could provide more durable responses in patients at a lower dose strength, which could allow IBI-306 to provide more clinical benefits at lower dosage levels and also at the same dose level achieve both a convenient (shorter and less frequent) dosing schedule and a lower dosage level for patients. In comparison, alirocumab and evolocumab require monthly injections with 2-3 separate injections each dose and the injecting time varies from 40 seconds to 9 minutes depending on the product.

Potential Advantages

Based on initial pre-clinical data, we believe that IBI-306 has the following potential competitive advantages as compared to approved anti-PCSK9 drugs alirocumab and evolocumab:

Higher affinity for human PCSK9

We conducted *in vitro* studies to compare the equilibrium binding affinity of IBI-306 for human PCSK9 with that of alirocumab and evolocumab and the results showed that of IBI-306 is higher than alirocumab and evolocumab. The table below shows equilibrium binding affinity of PCSK9 antibody fragments. The binding affinity of the Fab fragments of 3 PCSK9 antibodies for human PCSK9 is shown. Human PCSK9 is fixed to a Meso Scale Discovery plate binding of the various antibodies to the plate is detected by and electrochemiluminescence. The dissociation constant, K_d , is a ratio of unbound to bound antibody: PCSK9 complexes measured in molar (M) units. The smaller the number, the tighter the antibody binding affinity. In this study IBI-306 binds to PCSK9 approximately 4 times more tightly than evolocumab and 17 times tighter than alirocumab. We believe that IBI-306's higher binding affinity for its target will lead to more clinical benefit at a lower dosage level and a more convenient dosing schedule for the treatment of hyperlipidemia.

IBI306 has higher binding affinity for human PCSK9

Antibody Name	PCSK9 Fab K _d (10 ⁻¹² M)
IB1306	4.2
Alirocumab	72
Evolocumab	16

Abbreviations: Fab = antigen-binding fragment; K_d = dissociation constant.

Longer duration of LDL-C reduction

The results from a monkey study indicate that IBI-306 reduced LDL-C reduction level and has a longer duration of serum LDL-C reduction (from 24 hours through up to 504 hours after administration) than evolocumab (from 24 hours through up to 336 hours after administration) at the same dose level. The chart below shows LDL-C reduction of IBI-306 compared to evolocumab. Normal monkeys were given a single 10 mg/kg dose of IBI-306 or evolocumab. IBI-306 has a long duration of LDL-C reduction most evident from the 500 hour timepoint. We believe that the longer duration will allow us to achieve a more convenient (less frequent) dosing schedule (longer than 6-week dosing) for the treatment of hyperlipidemia.



IBI306 produces a more durable decrease in LDL-C after a single dose in monkeys than does evolocumab

Abbreviation: LDL-C = low-density lipoprotein cholesterol.

Clinical Development Plan

Our IND application for IBI-306 was approved by the NMPA in September 2017. We are conducting a randomized, double-blind, placebo-controlled, single-center Phase 1 clinical trial in China to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and immunogenicity of single ascending doses of IBI-306 in healthy adults. The ascending dose design includes six dose level cohorts: 25 mg, 75 mg, 150 mg, 300 mg, 450 mg and 600 mg. Tolerance and safety data for up to 14 days after dosing from all subjects of the previous cohort will be reviewed before proceeding to the next dose. Total duration of the study per subject is 12 weeks. The first subject was enrolled in November 2017. If this trial is successful, we expect to advance IBI-306 to Phase 2 and 3 clinical trials in China in 2019.

Licenses, Rights and Obligations

We have the rights to develop, manufacture and commercialize IBI-306 in China, Hong Kong and Macau. We obtained the original DNA sequence for IBI-306 from Adimab pursuant to our collaboration agreement with Adimab. See "-Collaboration Agreements-Collaboration with Adimab" below for details of our rights and obligations with respect to IBI-306.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBI-306 SUCCESSFULLY.

IBI-310

IBI-310 is a fully human monoclonal anti-CTLA-4 antibody drug candidate that we are evaluating for treatment of a variety of cancers in China as a monotherapy and potentially in combination with anti-PD-1 monoclonal antibodies, including sintilimab. IBI-310 has the same DNA sequence as ipilimumab (sold under the trade name Yervoy). Ipilimumab has not been approved for marketing in China and we are developing IBI-310 under the novel drug pathway according to the NMPA regulations. We have developed our proprietary cell line for IBI-310.

Mechanism of Action

IBI-310 specifically targets an immune checkpoint called cytotoxic T-lymphocyteassociated protein 4 (CTLA-4), which down-regulates T-cell immune response to cancer cells in a separate pathway from the PD-1/PD-L1 pathway. IBI-310 binds to CTLA-4 to remove the blockade and reactivate the immune response.

Market Opportunity and Competition

Yervoy has been approved as a monotherapy and as part of a combination therapy in melanoma and renal cell carcinoma in the U.S. It is still in clinical development in China.

According to the Frost & Sullivan Report, Yervoy achieved sales of US\$1.2 billion worldwide in 2017. CTLA-4 is an important pathway for a number of diseases. BMS is conducting numerous clinical trials of Yervoy in the U.S. both as a monotherapy and in combination with other therapies such as nivolumab.

Melanoma is mainly caused by intense ultraviolet light exposure. It is less prevalent in China than in the North America or Europe. Also according to the Frost & Sullivan Report, from 2013 to 2017, the number of melanoma patients in China increased from 7,500 to 8,500 in China, and is expected to increase to 9,600 in 2022 and 12,100 in 2030. Besides us, there are three other anti-CTLA-4 drug candidates in clinical development in China. The table below sets forth the information of the foregoing anti-CTLA-4 drug candidates in clinical development in China:

Generic name	Drug Code	Company	Status in China	Date*	Indication
Ipilimumab	BMS-734016	BMS	Phase 3	2015/10/23	Advanced Melanoma
			Phase 3	2014/3/13	SCLC
			Phase 1	2015/10/21	Advanced R/R Nasopharyngeal Carcinoma, Melanoma, NSCLC
			Phase 1, 3	2018/3/20	Combination therapy with Nivolumab for localized renal cell carcinoma etc.
Tremelimumab	-	AstraZeneca	Phase 3	2018/4/27	Stage IV NSCLC
			Phase 3	2018/5/8	Stage IV SCLC
			Phase 1	2017/6/8	Unresectable hepatocellular carcinoma
			Phase 3	2017/1/22	Advanced or metastatic NSCLC
			Phase 1, 2, 3	2017/2/21	Combination therapy with Durvalumab for advanced urothelial carcinoma etc.
Belatacept	KN019	Alphamab Co. Ltd	Phase 1	2018/1/8	Rheumatoid Arthritis

Source: Frost & Sullivan

* refers to the date when the information about clinical trials is published for the first time.

Clinical Development Plan

Our IND application for IBI-310 was approved by the NMPA in February 2018. We are conducting a single-center, open-label, Phase 1 study in China to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and immunogenicity of IBI-310 as a monotherapy and in combination with sintilimab in patients with advanced solid tumors.

Licenses, Rights and Obligations

We own all rights to IBI-310 and have not out-licensed it to any third party as of the Latest Practicable Date.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBI-310 SUCCESSFULLY.

Our IND-Stage Candidates

We have four IND-stage drug candidates as of the Latest Practicable Date:

IBI-302

IBI-302 is a fully human bi-specific antibody-like drug candidate we are developing to treat ocular diseases including a type of age-related macular degeneration (AMD) called wet AMD.

Mechanism of Action

IBI-302 is a bi-specific fusion protein designed with both a VEGF binding domain from VEGFR-1 and VEGFR-2 and a complement binding domain called sCR1 (soluble complement receptor type 1), and the two binding domains are connected by the Fc region of human immunoglobulin, as shown in the diagram below. IBI-302 binds to and inhibits the action of both VEGF and complement proteins, which activates the complement cascade that is part of the immune inflammatory process. Uncontrolled activation of complement and upregulation of VEGF play fundamental roles in AMD. The root cause of wet AMD is believed to be complement proteins as opposed to VEGF.

The Structure and Characteristics of IBI-302



Market Opportunity and Competition

AMD is a medical condition characterized by proliferation of abnormal blood vessels in the retina. Wet AMD, the "wet" form of advanced AMD, is a leading cause of severe vision loss and blindness in people over the age of 50 in the developed world. If untreated, the blood vessel growth and leakage associated with wet AMD can eventually lead to blindness. The majority of patients with wet AMD experience severe vision loss in the affected eye within

approximately two years after diagnosis of the disease. According to a study published in 2004 in the journal *Ophthalmology*, approximately 1.2 million people in the United States suffer from wet AMD. Based on estimates from AMD Alliance International, a non-profit organization focused on AMD awareness, and census growth data, we estimate there are approximately 293,000 new cases of wet AMD each year in the United States. Because the risk of developing wet AMD increases with age, we expect that the overall aging of the population will result in a significant increase in the number of wet AMD cases, both in the United States and worldwide. According to the Frost & Sullivan Report, the prevalence of wet AMD in China was 3.4 million in 2017 and is expected to reach 4.0 million in 2022 and 4.8 million in 2030. We believe that there is a significant commercial demand for the treatment of wet AMD.

Ranibizumab (sold under the trade name of Lucentis by Norvartis), conbercept (sold under the trade name of Langmu by Chengdu Kanghong) and aflibercept (sold under the trade name of Eylea by Bayer) have been approved in China for the treatment of wet AMD, and ranibizumab and conbercept have been included in the National Reimbursement Drug List.

The current biological treatment for wet AMD include ranibizumab, aflibercept and conbercept. According to the Frost & Sullivan Report, conbercept achieved sales of RMB617 million in China in 2017. Besides us, there are four other biologic candidates treating wet AMD in clinical development in China. The table below sets forth the information of the foregoing biologic candidates treating wet AMD in clinical development in China:

Generic name/ mAb category	Brand name/ Drug Code	Company	Status in China	Date*	Indication
Ranibizumab	Lucentis	Norvartis	Marketed	2011/12/31	wet AMD
Aflibercept	Eylea	Bayer	Marketed	2018/2/2	wet AMD
Conbercept	Langmu	Chengdu Kanghong Biotechnologies Co. Ltd	Marketed	2013/11/27	wet AMD, choroid neovascularization
VEGFR-Fc Protein	HB002.1M	Huabo Biopharm Co., Ltd.	Phase 1	2018/1/2	wet AMD
Humanized Anti-VEGF mAb	QL1205	Qilu Pharmaceutical Co., Ltd.	Phase 1	2018/2/5	wet AMD
Humanized Anti-VEGF mAb JY028 Beijing Eastern Biotech, Co., Ltd.		Phase 1	2018/7/2	wet AMD	
Humanized Anti-VEGF mAb	TK001	Jiangsu T-mab BioPharma Co., Ltd	Phase 1	2017/6/16	wet AMD

Source: Frost & Sullivan

* for a marketed product, it refers to the NMPA approval date; for a clinical stage product, it refers to the date when the information about clinical trials is published for the first time (首次公示日期).

Current Treatments and Limitations

The current standard of care for the treatment of wet AMD is administration by intravitreal injection of anti-VEGF drugs as a standalone therapy. The anti-VEGF drugs approved for the treatment of wet AMD in China include Lucentis, Langmu and Eylea. In addition, Lucentis and Eylea were approved for the treatment of wet AMD in U.S., while Avastin is also used off-label for this disease.

According to the American Academy of Ophthalmology, the use of anti-VEGF agents will likely reduce the odds of blindness from wet AMD and could theoretically reduce the rate of blindness by up to 70% over two years. However, longer-term follow-up studies from the population originally treated with regular anti-VEGF agents suggest that these gains in visual acuity are largely lost in two-thirds of patients followed for over seven years.

Advantages

We believe that IBI-302 has the following potential competitive advantages:

Inhibition of two pathways leading to wet AMD

All currently approved anti-VEGF antibody drugs are mono-specific antibodies and they may only be able to relieve the symptoms of wet AMD but may not tackle the root cause of the disease. In comparison, IBI-302 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 IBI-302 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. Furthermore, we believe that IBI-302's bi-specificity allows it to achieve comparable clinical results with a single treatment that would otherwise require two separate treatments (two vitreal injections) with combination therapies that block the same two targets.

We completed *in vitro* studies comparing the cell-based bioactivity of IBI-302 to that of anti-VEGF blockers aflibercept (Zaltrap) and bevacizumab (Avastin) and to complement receptor 1 (CR1). The results of these studies are shown in the following figure. These studies demonstrate two aspects of cell based bioactivity of IBI-302. In the left panel of the following figure, the ability of IBI-302 to inhibit the VEGF induced proliferation of human umbilical vein endothelial cells is shown. The antiproliferative effect induced by VEGF binding is similar to that of Zaltrap, a VEGF receptor trap, and is greater than that of Avastin (a VEGF antibody). In the middle and right panels of the following figure, the ability of IBI-302 to block both the classical and the alternative complement pathway is shown. The potency of IBI-302 in blocking complement cascade induced destruction of red blood cells is as a negative control in these studies demonstrating that an unrelated immunoglobin does not block red cell destruction.



Cell based activity of IBI-302 compared with standards

We also assessed IBI-302 in a Mouse Choroidal Neovascularization model (the Mouse CNV model). Choroidal neovascularization (CNV) is a non-specific response to specific damage of Bruch's membrane (the middle layer of the retina) and is the pathobiology behind wet and dry AMD. The results of the study indicated that IBI-302 was more potent than each of VEGF Inhibitory Domain (VID) and Complement Inhibitory Domain (CID) alone in blocking murine CNV and in reducing both the concentration of VEGF and the concentration of complement proteins. These results indicate an additive effect for VID and CID and demonstrate that IBI-302 is capable of blocking both the complement and the angiogenesis (the growth of blood vessels) pathways in the eye.

In the following figure, the green fluorescent circular lesions represent the MACs (membrane attack complexes) that form in the retina of mice as a result of laser-induced activation of the complement system, and treatment with IBI-302 decreased the dimensions of the MAC more significantly, indicating stronger efficacy, as compared to treatment with either VID or CID alone or to treatment with PBS (phosphate buffer saline) which is used as a control.



Abbreviations: MAC = membrane attack complex; PBS = phosphate buffer saline; VID = VEGF inhibitory domain; CID = complement inhibitory domain.

The following figure shows that, in the same study using the Mouse CNV model, IBI-302 reduces both the concentration of VEGF and the concentration of C3a (a part of the complement protein system known as complement component 3) to a greater extent than each of PBS, VID and CID does.

IBI-302 results in greater reduction of the intraocular concentration of VEGF and complement proteins

Reduction of VEGF concentration

Reduction of C3a concentration



Abbreviations: PBS = phosphate buffer saline; VID = VEGF inhibitory domain; CID = complement inhibitory domain; C3a = a complement peptide formed by the cleavage of complement component 3.

Better efficacy at lower dose level than bevacizumab

We assessed the efficacy of IBI-302 in the Rhesus Monkey Choroidal Neovascularization (CNV) model. Based on the study as shown in the figure below, IBI-302 at a 0.25 mg/eye dose level shows better efficacy than bevacizumab at a 1.25 mg/eye dose level. In this study, the retina of a monkey is damaged with a laser. The retina responds by activation of the complement cascade and the proliferation of endothelial cells, which induces inflammation, angiogenesis and proteolysis. These reactions create the white circular lesions in the retinal photos above. Treatment of the monkey by intraocular injection of IBI-302 or bevacizumab (a VEGF antibody) decreases CNV and IBI-302 is more potent in blocking laser induced CNV than bevacizumab.



Efficacy of IBI-302 in Rhesus Monkey CNV Model

Clinical Development Plan

Our IND application for IBI-302 was approved by the NMPA in December 2016. We plan to conduct a multi-center Phase 1 clinical trial in China to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and immunogenicity of IBI-302 in wet AMD patients. We expect to start and complete this trial in 2019.

Licenses, Rights and Obligations

We have the right to develop, manufacture and commercialize IBI-302 worldwide. We licensed IBI-302 cell line from AP Biosciences, Inc. (formerly known as ProtevoBio Inc.) pursuant to an exclusive license agreement with AP Biosciences, Inc. as described under "– Collaboration Agreements – Exclusive License from Protevo" below.

WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET IBI-302 SUCCESSFULLY.

IBI-307

IBI-307 is a fully human monoclonal antibody drug candidate that we are developing for the treatment of osteoporosis and lytic bone lesions associated with cancer metastasis. It binds to RANKL (RANK ligand), a hormone that controls the activation and survival of osteoclasts, the cells that remodel bone. By blocking the activity of RANKL, bone resorption is inhibited resulting in stronger and denser bones. According to the Frost & Sullivan Report, approved RANKL inhibitors include denosumab of Amgen (sold under the trade names Prolia and XGEVA), which had worldwide sales of US\$3.5 billion in 2017; in contrast, there are currently no RANKL inhibitors approved for marketing in China. We filed an IND application for IBI-307 with the NMPA in November 2017, which was approved on June 15, 2018.

IBI-101

IBI-101 is a fully human monoclonal antibody drug candidate that we are developing to treat cancers and hepatitis B. IBI-101 binds to and stimulates OX40, which should increase the survival and activation of tumor specific T cells. There is currently no OX40 agonist approved globally. We filed an IND application for IBI-101 with the NMPA in January 2018, which was approved on June 15, 2018. We also plan to file an IND application for IBI-101 with the FDA in 2018.

IBI-188

IBI-188 is a fully human monoclonal antibody drug candidate that we are developing for the treatment of cancers. IBI-188 binds to CD47, a surface protein that provides a "do not eat me" signal to macrophages. Cancer cells frequently express CD47 and by doing so evade destruction by macrophage. Our pre-clinical data show that IBI-188 is efficacious for inhibiting tumor growth. We filed an IND application for IBI-188 with the NMPA in June 2018, which was approved on August 22, 2018. We have also begun the process of seeking FDA marketing authorization for IBI-188, our CD47 antibody. The FDA approved our IND application for IBI-188 in September 2018. We plan to initiate a Phase 1a clinical trial (dose escalation) in the U.S. in approximately 17 to 42 patients with cancer. According to Frost & Sullivan, there are no currently approved anti-CD47 therapies, although many companies are currently developing candidates that target CD47 in pre-clinical studies and clinical trials. For example, California-based Forty Seven, Inc. is evaluating its anti-CD47 antibody drug candidate in five ongoing monotherapy Phase 1 and combination therapy Phase 1b/2 trials, in patients with solid tumors, leukemia or lymphoma.

Our Pre-clinical Candidates

In addition to our clinical-stage drug candidates, we are also developing seven pre-clinical-stage drug candidates. Each of these candidates has been approved by our science committee, which reviews all proposals for research programs before they enter discovery and development. Our drug discovery platform has allowed us to maintain and expand a strong pre-clinical-stage drug pipeline in potentially important areas, such as oncology, ophthalmology, cardiovascular and autoimmune diseases. We believe we have the opportunity to combine our sintilimab (IBI-308) with other clinical-stage and pre-clinical candidates in our pipeline to target multiple immuno-oncology checkpoints.

We have seven innovative pre-clinical drug candidates as of the Latest Practicable Date. These include two mono-specific antibody drug candidates with which no competing antibody against the same targets has obtained marketing approval anywhere in the world and also include five bi-specific antibody drug candidates. We anticipate advancing three of our pre-clinical candidates into the clinical stage in the next 12 months.

Mono-specific Antibodies

IBI-110

IBI-110 is a fully human monoclonal antibody drug candidate that we are developing for the treatment of cancers. IBI-110 binds to LAG-3, an immune checkpoint expressed on the surface of T cells, NK cells, B cells and plasmacytoid dendritic cells. 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 with IBI-110 should restore activities of tumor infiltrating T cells, reverse T-cell exhaustion and drive T-cell activation. Our pre-clinical animal study data show that IBI-110 has good *in vivo* anti-tumor efficacy when combined with an anti-PD-1 antibody.

IBI-939

IBI-939 is a fully human monoclonal antibody drug candidate that we are developing for the treatment of cancers. IBI-939 binds to TIGIT. 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. IBI-939 binds to TIGIT and blocks its interaction with CD155, thereby increasing immune activation.

Bi-specific Antibodies

IBI-322

IBI-322 is an anti-CD47/PD-L1 bi-specific antibody that we are developing for the treatment of cancers. IBI-322 simultaneously inhibits both CD47 binding to SIRP α and PD-L1 binding to PD-1. Our pre-clinical studies demonstrate that IBI-322 is effective in inducing

phagocytosis of tumor cells and stimulating T cells activation. Anti-CD47 antibodies tend to attack normal cells. However, IBI-322 molecules preferentially distribute to PD-L1 positive tumor cells and thereby reduce this potential on-target side effect associated with monospecific anti-CD47 antibodies. Our pre-clinical data show that IBI-322 has promising *in vivo* efficacy, tumor-enriched distribution and better safety than a mono-specific anti-CD47 antibody.

The diagram below shows that IBI-322, a bi-specific antibody that contains a binding site for CD47 and a different binding site for PD-L1, has a dual mechanism of action-stimulation of macrophages and blockade of the PD-1 T-cell checkpoint. Macrophages are phagocytes (cells that "eat other cells and pathogens"). CD47 is a protein on the surface of many normal cells that signals to the macrophage: "Don't eat me". The signaling protein on the surface of the macrophage that interacts with CD47 is SIRP α . Tumors often express high levels of CD47 to inhibit macrophage phagocytosis. Also, tumors frequently express high levels of PD-L1, a protein that binds to the checkpoint receptor, PD-1, on surface of T-cell. This binding turns off the ability of a T-cell to kill PD-L1 expressing tumor cells. As is seen in the top panel of the following diagram, tumor cells that express both PD-L1 and CD47 are able to block two different pathways that would normally kill tumor cells. Normal erythrocytes also express CD47 so that high potency binding of an anti-CD47 antibody will cause the macrophage to ingest erythrocytes. The erythrocyte phagocytosis causes significant anemia. IBI-322 has a finely tuned affinity for CD47 and also has the PD-L1 binding component to only target tumor cells that express both PD-L1 and CD47. The bi-specific nature of IBI-322 and the careful tuning of the affinity allow the antibody to spare the erythrocytes which do not express PD-L1.



Based on Yoji Murata, Takenori Kotani, Hiroshi Ohnishi and Takashi Matozaki. "The CD47-SIRP α signalling system: its physiological roles and therapeutic application." J. Biochem. 2014 Jun; 155(6):335-344. Published online 2014 Mar 12. doi:10.1093/jb/mvu017; Francisco, Loise M., Peter T. Sage and Arlene H. Sharpe. "The PD-1 Pathway in Tolerance and Autoimmunity." Immunological Reviews 236 (2010): 219-242. PMC. Web. 1 Aug. 2018.

IBI-318

IBI-318 is a bi-specific antibody incorporating sintilimab anti-PD-1-binding backbone that we are developing in collaboration with Eli Lilly for the treatment of cancers. It simultaneously binds to both PD-1 and an undisclosed target.

IBI-319

IBI-319 is a bi-specific antibody incorporating sintilimab anti-PD-1-binding backbone that we are developing in collaboration with Eli Lilly for the treatment of cancers. It simultaneously binds to both PD-1 and an undisclosed target.

IBI-315

IBI-315 is a bi-specific antibody incorporating sintilimab anti-PD-1-binding backbone that we are developing in collaboration with Hanmi for the treatment of cancers. It simultaneously binds to both HER2 and PD-1.

IBI-323

IBI-323 is an anti-LAG-3/PD-L1 bi-specific antibody that we are developing for the treatment of cancers. IBI-323 simultaneously inhibits LAG-3 binding to MHC Class II and PD-L1 binding to PD-1. IBI-323 also has the potential to further enhance the specific killing activity of T cells by tethering LAG-3 positive T cells with PD-L1 positive tumor cells. Our pre-clinical data show that IBI-323's *in vitro* efficacy and *in vivo* efficacy are both better than a combination therapy of an anti-LAG-3 mono-specific antibody and an anti-PD-L1 mono-specific antibody.

The table below sets forth a comparison of our PD-L1 drug candidates and their competitors drug candidates in China which are approved or in Phase 3 or more advanced clinical trial stage:

Generic (Brand) Name/	~	Filing Status in		Mechanism	Lead/Proposed	Retail Price	
Drug Code	Company	China	Date*	of Action	Indication	(RMB)	NRDL/PRDL
IBI-322	Innovent	pre-clinical	N.A.	Anti-PD-L1/	PDL1/CD47	N.A.	N.A.
				CD47	coexpressing		
					tumors, M1		
					macrophage		
					signature tumors		
IBI-323	Innovent	pre-clinical	N.A.	Anti-LAG-3/	PDL1+ tumors with	N.A.	N.A.
				PD-L1	"hot tumor"		
					phenotype		
Atezolizumab	Roche	Phase 3	2018/7/2	Anti-PD-L1	Advanced or	N.A.	N.A.
					metastatic NSCLC		
					Renal cell carcinoma		
					NSCLC		
					Advanced or		
					metastatic urethral		
					carcinoma		
					Muscular-invasion		
					urethral carcinoma		

Generic		Filing					
(Brand) Name/		Status in		Mechanism	Lead/Proposed	Retail Price	
Drug Code	Company	China	Date*	of Action	Indication	(RMB)	NRDL/PRDL
Durvalumab	Astrazeneca	Phase 3	2017/1/19	Anti-PD-L1	NSCLC	N.A.	N.A.
KN035	Alphamab	Phase 3	2018/4/9	Anti-PD-L1	MSI-H/dMMR CRC	N.A.	N.A.
					Gastric carcinoma		
					Cholangiocarcinoma		
Avelumab	Merck	Phase 3	2018/6/25	Anti-PD-L1	HNSCC	N.A.	N.A.
	KGaA/						
	Pfizer						

Source: Frost & Sullivan

Notes:

Abbreviation: NRDL = national reimbursement drug list of China; PRDL = provincial reimbursement drug list;

- "No" means that the drug is not list in the NRDL or the PRDL even though it is marketed.
- "N.A." means, with respect to date, not applicable because the drug candidate is still in pre-clinical stage; with respect to retail price, not available, and with respect to NRDL/PRDL, not applicable because the drug candidate is not marketed yet.
- * for a marketed product, it refers to the NMPA approval date; for a clinical stage product, it refers to the date when the information about clinical trials is published for the first time (首次公示日期); for a product with NDA submitted and the NDA result pending, it refers to the date of NDA submission.

COLLABORATION AGREEMENTS

Collaboration with Eli Lilly

Beginning in March 2015, we have entered into several agreements with Eli Lilly concerning the development and commercialization of various products. Each of the collaborations that we are currently participating in with Eli Lilly are described as follows:

Exclusive License and Collaboration Agreement for China and Co-Development Agreement for IBI-301 and PD-1 (collectively, the "Lilly China Agreement")

The Lilly China Agreement, which was entered into in March 2015, governs the development and commercialization activities concerning (1) IBI-301, our Rituxan biosimilar, and (2) sintilimab (IBI-308), our PD-1 monoclonal antibody (collectively, the "China Products") in the People's Republic of China, including Hong Kong and Macau, but excluding Taiwan (solely for purposes of this "Collaboration Agreements – Collaboration with Eli Lilly", "China").

Under the Lilly China Agreement, we must use commercially reasonable efforts to develop each of the China Products for certain indications until each of them has achieved regulatory approval or we determine in good faith that regulatory approval for each of them cannot be achieved in a commercially reasonable fashion. We are responsible for developing unique cell lines to express and manufacture each of the China Products and Eli Lilly is responsible for assisting us in those efforts. As part of this effort, we are responsible for the costs of developing the cell lines. These costs include the costs of assistance provided by Eli Lilly at our request, whereby we will pay Eli Lilly for the time Eli Lilly's employees spend on these activities, subject to certain caps. With respect to the development of IBI-301, we are responsible for the development costs associated with developing the IBI-301 in China. With respect to the development of sintilimab, we are responsible for the costs leading up to the filing of the IND in China. Thereafter, we share such development costs for sintilimab with Eli Lilly equally and sintilimab is the only drug candidate among the China Products to which such cost sharing arrangement applies for agreed-upon clinical indications under development. In practice, a joint steering committee established by the parties approves the budget of development costs for sintilimab once a year and reviews such budget every quarter. The shared development costs are subject to the approved budget and generally include direct costs such as raw materials and third-party contractor costs and indirect costs such as staff costs, depreciation and amortization, power and utility cost and shared supporting expenses for research and development. The Company settles Eli Lilly's payment of half of the shared development costs for sintilimab periodically.

We are responsible for all regulatory activities performed under the Lilly China Agreement, including the strategy for filings and label content, leading up to the receipt of regulatory approvals for the China Products in China. Eli Lilly must cooperate with our regulatory efforts.

We and Eli Lilly will co-promote IBI-301 and sintilimab (IBI-308) in China in accordance with the agreement terms. We will share the difference between net sales and expenses (profits if such difference is positive and losses if such difference is negative) pertaining to commercialization of IBI-301 and sintilimab (IBI-308) equally. Under the agreement, expenses mean the commercialization costs and manufacturing costs incurred by either party or its affiliates for the relevant product, whereas net sales means the gross amount invoiced by Eli Lilly or any of its sublicensees to unrelated third parties (excluding any non-end user sublicensee) for sales of the relevant product in China, less certain deductions to the extent included in the gross invoiced sales price for the product or otherwise directly paid or incurred by Eli Lilly or any of its sublicensees with respect to the sales of the product in China. Net sales will be determined from Eli Lilly's (including its affiliates and sublicensees) books and records maintained in accordance with GAAP or similar accounting principles. Eli Lilly will determine net sales by using its then current standard procedures and methodology.

We are responsible, in consultation with Eli Lilly for manufacturing and supplying the China Products to Eli Lilly under the Lilly China Agreement. This responsibility includes the payment of any capital costs necessary for such manufacture. The supply agreement, including the applicable supply prices to be paid to us by Eli Lilly, must be negotiated at least 18 months before the anticipated regulatory approval for a China Product in China. We and Eli Lilly are in the process of negotiating such supply agreement.

Pursuant to this agreement, Eli Lilly provided us with a non-refundable upfront payment of US\$36,000,000 on June 26, 2015 in consideration for its rights and obligations under the agreement and separate from the sharing of development costs for sintilimab as described above. Of this upfront payment amount, US\$5,000,000 was paid to Adimab by Eli Lilly as required by our collaboration with Adimab, which is described below in "– Collaboration Agreement with Adimab". We will also be entitled to milestone payments totaling up to US\$75,000,000 should sintilimab (IBI-308) achieve certain net sales milestones, in addition to the sharing of profits and losses from the commercialization of IBI-301 and sintilimab as described above.

Under the Lilly China Agreement, we and Eli Lilly established a joint steering committee with equal representation from each party to coordinate and oversee development and commercialization activities and decisions for the China Products, including periodic review and approval of the budget of development costs for sintilimab that are subject to equal sharing between us and Eli Lilly. In the event that the joint steering committee cannot agree on a decision, however, we have final decision-making authority concerning the development of the China Products. Neither party has unilateral final-decision making authority concerning either decisions to downsize the development plan for either China Product, or decisions to increase the development activities for sintilimab (IBI-308). Eli Lilly has final decision-making authority on commercialization decisions following regulatory approval of the China Products. Eli Lilly elects not to proceed with commercializing either China Product following regulatory approval, such commercialization rights will revert to us and we do not expect that it would result in any material negative impact on our business.

For risks relating to our collaboration with third parties, see the section headed "Risk Factors – Risks Relating to Our Reliance on Third Parties."

In the development and commercialization of the China Products, both we and Eli Lilly maintain ownership of our respective background intellectual property rights. We will own all intellectual property generated in connection with the development of (i) the China Products and (ii) the unique cell lines for the China Products. We granted Eli Lilly an exclusive license (with the right to sublicense) under certain of our patents, know-how and regulatory approvals to commercialize the China Products in China. We control prosecution and enforcement of the patents developed under the Lilly China Agreement related to IBI-301 and sintilimab. We retain the right to develop, manufacture and to co-promote the China Products. We also provided Eli Lilly a non-exclusive license to certain of our trademarks in connection with Eli Lilly's commercialization of the China Products in China. We similarly received a non-exclusive license to Eli Lilly trademarks with the right to sublicense in connection with our possible commercialization of the China Products.

The initial term of the Lilly China Agreement continues on a product-by-product and region-by-region basis until fifteen years after the first commercial sale in a region of a China Product and the Lilly China Agreement automatically renews thereafter for one-year periods unless Eli Lilly provides written notice of its intent not to further commercialize such China

Product in China at least 180 days prior to the conclusion of the initial term or the then-current renewal term. In addition to certain customary termination rights such as the right to terminate for an uncured material breach by the other party or the other party's insolvency, Eli Lilly has the right to terminate the Lilly China Agreement in its sole discretion by providing 180 days' advance written notice.

With certain limited exceptions, during the initial term of the Lilly China Agreement, neither party may commercialize any monoclonal antibody or fragment of such antibody that targets the same antigens as the China Products in China. We granted Eli Lilly a right of first refusal to exclusively commercialize IBI-301 outside of China in jurisdictions in which IBI-301's any future regulatory approval and related filings are not adequate to support a filing for regulatory approval in any such jurisdiction without significant additional clinical development. If we receive an offer from a third party in connection with the foregoing, we must notify Eli Lilly in writing of such offer and Eli Lilly will have 45 days from receipt of such notice to exercise its right of first refusal. We also granted Eli Lilly a right of first negotiation in connection with the foregoing, which Eli Lilly can exercise within 45 days of receiving written notice from us of our intent to enter into a term sheet or commence negotiations with a third party.

Addendum to the Exclusive License and Collaboration Agreement for China

In October 2015, we and Eli Lilly entered into an addendum to the Lilly China Agreement (the "Lilly China Addendum") whereby the parties agreed to pursue the development of three additional drug candidates consisting of bi-specific PD-1 monoclonal antibodies (the "Bi-Specific PD-1 Products") which include IBI-318 and IBI-319.

Under the Lilly China Addendum, we and Eli Lilly must collaborate on the development of Bi-Specific PD-1 Products. Eli Lilly is responsible for developing the pre-clinical data package concerning various potential Bi-Specific PD-1 Products, and grants us the right to develop Eli Lilly's preferred candidates in China, which include IBI-318 and IBI-319. If we decide to develop an Eli Lilly's preferred Bi-Specific PD-1 Product candidate, Eli Lilly grants to us an exclusive license (with the right to sublicense under certain conditions) under certain Eli Lilly patents and know-how and Eli Lilly's rights in certain patents and inventions jointly owned by us and Eli Lilly related to the Bi-Specific PD-1 Product to develop, manufacture, and commercialize the preferred Bi-Specific PD-1 Product for any use in China. After Phase 1 clinical trials for the preferred Bi-Specific PD-1 Product are completed in China, we must provide all Phase 1 final data for Eli Lilly's evaluation and review, and Eli Lilly will have the right to opt in to the development and commercialization of the preferred Bi-Specific PD-1 Product in China. Unless Eli Lilly exercises such right, we will be responsible for all costs and all decisions regarding such product's development, manufacture and commercialization. In addition, we granted Eli Lilly a right of first negotiation to commercialize a Bi-Specific PD-1 Product in China if we seek a third party partner for such commercialization.

If we decide to develop and commercialize an Eli Lilly's preferred Bi-Specific PD-1 Product candidate, we would owe milestone payments to Eli Lilly totaling up to US\$37,000,000, and would owe Eli Lilly royalties of a low-to-mid-single digit percentage of

net sales. We will also be solely responsible for certain royalty payments owed to Adimab for net sales of such preferred Bi-Specific PD-1 Product, as described in "– Collaboration with Adimab".

If we decide not to develop an Eli Lilly's preferred candidate in China, Eli Lilly may develop that preferred Bi-Specific PD-1 Product. In such an event, we will grant to Eli Lilly an exclusive license under certain of our patents, know-how and jointly owned patents and inventions related to such preferred Bi-Specific PD-1 Product to develop and commercialize such product for any use in China. Eli Lilly will owe us development milestones totaling up to US\$21,000,000, and royalties of net sales. Eli Lilly would be responsible for the aforementioned royalty payments to Adimab in this scenario.

If we opt to develop an Eli Lilly's preferred Bi-Specific PD-1 Product candidate in China, and Eli Lilly opts in to our development and commercialization efforts, then each party will grant the other rights in their patents, know-how, joint patents, and joint inventions related to such preferred Bi-Specific PD-1 Product to develop, manufacture, and commercialize such product in China. The parties would then equally share development costs and revenue. If Eli Lilly opts in, it can either pay us (i) a US\$25,000,000 upfront fee for each Bi-Specific PD-1 Product or (ii) a US\$15,000,000 upfront fee for each Bi-Specific PD-1 Product and up to US\$47,500,000 in milestone payments.

Both parties have agreed that neither party will develop in China a PD-1 bi-specific antibody that targets the same receptor pairs as the Bi-Specific PD-1 Products for a period of time so long as either the Lilly China Agreement and Lilly China Addendum are in effect in relation to a Bi-Specific PD-1 Product in China or we have not elected to exercise our development rights with respect to Eli Lilly's preferred candidate in China.

Exclusive License for PD-1 Outside China and License Agreement for PD-1 Outside China (collectively, the "Lilly Ex-China Agreement")

The Lilly Ex-China Agreement, which was entered into in March 2015, governs the development of cell lines for sintilimab and for Eli Lilly to develop cell lines for bi-specific PD-1 products ("Ex-China Bi-Specific PD-1 Products") (collectively, the "Ex-China PD-1 Products") throughout the world other than in China. This agreement was amended in July 2015, October 2015, December 2017, and most recently in June 2018.

Under the Lilly Ex-China Agreement, as amended, Eli Lilly has full responsibility for the development, regulatory, manufacturing, and commercialization activities concerning the Ex-China Bi-Specific PD-1 Products throughout the world other than in China at its own cost. Eli Lilly is also responsible for developing a cell line for the expression of the Ex-China PD-1 Products.

In December 2017, pursuant to a letter agreement between us and Eli Lilly, Eli Lilly opted not to pursue development of sintilimab as a monotherapy outside China under the Lilly Ex-China Agreement. The development and commercialization rights of sintilimab as a

monotherapy outside China now belong to us. Eli Lilly has retained a limited right to develop sintilimab in combination with one or more active pharmaceutical ingredients controlled by Eli Lilly or its affiliates ("Eli Lilly PD-1 Combination Product") until we enter into an agreement with a third party for the development of sintilimab outside China. If we enter into an agreement with a third party after Eli Lilly has already commenced patient dosing of an Eli Lilly PD-1 Combination Product, Eli Lilly's development rights for any such Eli Lilly PD-1 Combination Product, Eli Lilly's development rights for any such Eli Lilly PD-1 Combination Product will continue. If we develop sintilimab outside China in concert with a third party, Eli Lilly will be entitled to a percentage of any remuneration we receive from such third party based on the stage of development and commercialization we are in with respect to such third-party collaboration. If we develop sintilimab as a monotherapy outside China on our own, Eli Lilly will be entitled to regulatory and commercial milestone payments and commercial royalties of a percentage of net sales.

As part of the Lilly Ex-China Agreement, we received a US\$20,000,000 upfront payment on June 29, 2015 and can earn royalties of a high-single digit percentage of net sales of Bi-Specific PD-1 Products depending on annual sales volumes.

Under the Lilly Ex-China Agreement, we granted Eli Lilly an exclusive license to our patents and know-how related to sintilimab to develop, manufacture, and commercialize the sintilimab outside China. We also granted Eli Lilly a non-exclusive license to certain of our patents and know-how to develop and manufacture, and an exclusive license to such patents and know-how to commercialize, the Ex-China Bi-Specific PD-1 Products that Eli Lilly has chosen to license from us under the Lilly Ex-China Agreement. In the event that Eli Lilly commercializes an Ex-China Bi-Specific PD-1 Product based on a PD-1 antibody that it has not selected under the Lilly Ex-China Agreement, the milestone payments that it owes to us will be 50% of those listed above, and the royalty payments will be a low-to-mid-single digit percentage of net sales depending on annual volumes.

Each party remains the sole and exclusive owner of its respective intellectual property rights. We will own all inventions and intellectual property developed by us in connection with our activities under the Lilly Ex-China Agreement, while Eli Lilly will own all inventions and intellectual property developed by Eli Lilly in the course of the development, manufacture, or commercialization of the Ex-China Bi-Specific PD-1 Product or otherwise in connection with the Lilly Ex-China Agreement. The parties will jointly own inventions conceived or reduced to practice by the parties jointly and all development and commercialization know-how developed under the agreement. Eli Lilly controls the prosecution and enforcement of the patents related to the Ex-China Bi-Specific PD-1 Products and must consider our advice and suggestions in connection with any prosecution actions and must obtain our approval, which is not to be unreasonably withheld, in connection with any enforcement action.

The term of the Lilly Ex-China Agreement continues on a country-by-country basis until the later of (i) the expiration of the last-to-expire licensed patent in such country, (ii) the expiration of the data exclusivity period that covers the Ex-China Bi-Specific PD-1 Products in such country, and (iii) twelve years after the first commercial sale in such country of the Ex-China Bi-Specific PD-1 Products. In addition to certain customary termination rights such

as the right to terminate for an uncured material breach by the other party or the other party's insolvency, Eli Lilly has the right to terminate the Lilly Ex-China Agreement in its sole discretion by providing 180 days' advance written notice.

Collaboration with Adimab

Beginning in July 2013, and as amended several times including most recently in September 2017, we entered into a collaboration agreement with Adimab, LLC ("Adimab") (the "2013 Adimab Agreement) whereby we agreed to collaborate on programs to co-discover and optimize antibodies directed against various targets. The collaboration began with a program to co-discover and optimize antibodies directed against PD-1 (including sintilimab), for us to develop processes to manufacture such antibodies, and to commercialize such antibodies as pharmaceutical products in China, Hong Kong and Taiwan. We co-discovered sintilimab with Adimab through this collaboration. Over time, we have expanded the scope and number of collaborations to include the discovery, optimization, and development of antibodies targeting PCSK9 (IBI-306) and OX40 (IBI-101), as well as other targets.

Under the 2013 Adimab Agreement, Adimab is primarily responsible for discovery and optimization of individual antibodies delivered to us by Adimab (the "Adimab Products"). Among our pipeline drug candidates, Adimab Products currently include sintilimab, IBI-306, IBI-101, IBI-318 and IBI-319. We are primarily responsible for (i) the development of any Adimab Product, including the conduct of pre-clinical work and clinical trials, (ii) the manufacture of any Adimab Products, including process development, scale-up and formulation, taking place in China, Hong Kong, and Taiwan, and (iii) commercializing the Adimab Products, including associated regulatory activities, everywhere in the world, except for IBI-306 where our commercialization responsibilities only relate to China, Hong Kong and Taiwan. Adimab, likely through a partner, is responsible for commercializing IBI-306 in the rest of the world, including the regulatory activities required to commercialize IBI-306. We have the right of first negotiation to provide worldwide supply of any Adimab Product for development and commercialization. However, in the event we and Adimab are unable to enter into a supply agreement for the clinical or commercial supply of a certain Adimab Product after a three-month negotiation period, Adimab may enter into such agreements with a third party to manufacture such Adimab Product, or elect to manufacture such Adimab Product itself, outside of China, Hong Kong, and Taiwan. If Adimab chooses to manufacture an Adimab Products itself or through a third party, we agree to transfer to Adimab or such third party, at Adimab's expense, all know-how controlled by us necessary and specific to the manufacture of such Adimab Product, except for the related working cell bank.

Under the 2013 Adimab Agreement, we and Adimab established a joint steering committee with equal representation from each party to coordinate and oversee global development, manufacturing and commercialization strategies regarding the Adimab Products. If the parties are unable to resolve a dispute, we have final decision-making authority with respect to the development, manufacture, and commercialization of the Adimab Products in China, Hong Kong, and Taiwan. Adimab has final decision-making authority with respect to development, manufacture, and commercialization of the Adimab Products in the rest of the world.

We and Adimab each own all of our pre-existing intellectual property. Any inventions conceived or reduced to practice while performing activities under the 2013 Adimab Agreement will be jointly owned, regardless of inventorship. We granted Adimab a worldwide, sublicensable, non-exclusive license to our intellectual property for the purpose of discovering Adimab Products. We also granted Adimab a worldwide, royalty-bearing, sublicensable, non-exclusive license under our patents and joint inventions for Adimab to develop, manufacture, and commercialize the Adimab Products. Adimab similarly granted to us a worldwide, royalty-bearing, sublicensable, non-exclusive license under our patents and products.

Under the 2013 Adimab Agreement, Adimab grants us a non-exclusive, worldwide, royalty-bearing, sublicensable license under Adimab's patents related to PD-1 to develop, manufacture, and commercialize PD-1 products. For certain of the PD-1 products (including sintilimab) we have entered into a partnership with Eli Lilly, which is more fully discussed above in "-Collaboration with Eli Lilly". Pursuant to the relationship among Adimab, Eli Lilly and us, we entered into a sublicense agreement so that Eli Lilly will make certain payments directly to Adimab, instead of making such payments indirectly to Adimab through us. Pursuant to our collaboration with Eli Lilly, Adimab received milestone payments of an aggregate of US\$15,000,000 from us and Eli Lilly. These payments include a US\$5,000,000 payment from Eli Lilly to Adimab, a US\$5,000,000 payment from us to Adimab that was made on December 27, 2016 and another US\$5,000,000 payment from us to Adimab that was made on February 1, 2018. Adimab is also entitled to receive from Eli Lilly additional milestone payments based on the development of Bi-Specific PD-1 Products which include IBI-318 and IBI-319, and will be entitled to receive from Eli Lilly a royalty of a low-single digit percentage of net sales in China and a royalty of a mid-single digit percentage of net sales outside of China on annual sales of the PD-1 products covered by the 2013 Adimab Agreement. Adimab will receive a 50% reduction in royalty payments on Bi-Specific PD-1 Products.

Under the 2013 Adimab Agreement, we control the prosecution and enforcement of the licensed patents related to the Adimab Products in China, Hong Kong and Taiwan and Adimab controls the prosecution and enforcement of the licensed patents related to the Adimab Products in all jurisdictions other than China, Hong Kong and Taiwan.

The 2013 Adimab Agreement continues on a country-by-country and product-by-product basis until the later of (i) the expiration of the last-to-expire licensed patent covering an Adimab Product in a particular country and (ii) 12 years after the first commercial sale of the Adimab Product in such country. In addition to the right to terminate in connection with an uncured material breach by the other party, at any time after September 2022, either party may terminate the 2013 Adimab Agreement in its entirety upon six months' prior written notice to the other party if (a) no Adimab Product has entered into clinical trials, (b) no Adimab Product is under development and (c) the absence of development is not the result of a breach by the party seeking to terminate.

Effective January 2016, we entered into an additional collaboration agreement with Adimab (as amended, the "2016 Adimab Agreement") whereby Adimab will discover new antibodies against targets of our choosing, including OX40, (collectively, the "2016 Adimab
Products"). Under the 2016 Adimab Agreement, we granted Adimab a non-exclusive, non-sublicensable license under our patents and know-how so that Adimab could conduct its discovery work.

We retained an option under the 2016 Adimab Agreement to develop and commercialize any 2016 Adimab Products discovered by Adimab in its research. Upon our exercise of the option on a product-by-product basis, Adimab will assign to us all ownership interest in the optioned 2016 Adimab Products and the patents covering such products. Adimab also will grant us a worldwide, royalty-bearing sublicensable license under Adimab's intellectual property to develop, manufacture and sell such optioned 2016 Adimab Products. In exchange for these rights, we made an upfront payment of US\$500,000 to Adimab on March 22, 2016. We also agreed to reimburse Adimab for the time expended by its employees researching the 2016 Adimab Products. Adimab will receive pre-clinical milestone payments totaling up to US\$1,400,000 for each 2016 Adimab Product. Adimab will also receive clinical milestone payments related to OX40 (IBI-101) ranging from US\$1,000,000 to US\$5,000,000 for achievement of different milestones in different countries or regions. For the other 2016 Adimab Products, Adimab will receive the above milestone payments for work done anywhere in the world, including work done in China. Adimab is also eligible to receive a royalty of up to a low single digit percentage of worldwide net sales with respect to each 2016 Adimab Product.

For the OX40 product (IBI-101), for which we have already exercised our option, we agreed to make an upfront payment of US\$750,000 to Adimab on October 31, 2017, and we also agreed to make milestone payments totaling up to US\$9,500,000. Adimab is also eligible to receive a royalty of up to low-single digit percentage for sales of OX40 products.

Under the 2016 Adimab Agreement, we and Adimab each own all of our pre-existing intellectual property. Any inventions conceived or reduced to practice while performing activities under this agreement, other than inventions concerning Adimab's discovery technology, will be owned based on inventorship. Inventions made and owned by Adimab are subject to our option rights, through which we can gain ownership of or a license to such inventions.

Under the 2016 Adimab Agreement, with certain limited exceptions, we must not research, develop or commercialize any antibody related to the 2016 Adimab Products or any modified or derivative form of such antibody or any product related to the foregoing except as permitted by the 2016 Adimab Agreement.

We control the prosecution of all patents covering the 2016 Adimab Products. If we exercise our option under the 2016 Adimab Agreement, we must use commercially reasonable efforts to prosecute at least one optioned 2016 Adimab Products in the United States, Japan and Europe. Both before and after the option is exercised, Adimab will have the right to review and comment on prosecution of any patents covering the 2016 Adimab Products. If we do not exercise the option, all such patents that have been filed must be promptly abandoned without being published.

The 2016 Adimab Agreement continues (i) until the conclusion of the last-to-expire research program in the event that we do not exercise our option or (ii) in the event that we exercise our option, on a country-by-country and product-by-product basis until the later of (a) the expiration of the last-to-expire licensed patent in such country and (b) 12 years after the first commercial sale of the 2016 Adimab Product in such country. Either party may terminate the 2016 Adimab Agreement upon an uncured material breach by the other party.

Collaboration with Hanmi

In March 2017, we entered into a collaboration agreement with Beijing Hanmi Pharmaceutical Co., LTD to develop and commercialize IBI-315, an anti-HER2/PD-1 bi-specific antibody. Beijing Hanmi Pharmaceutical Co., LTD is a subsidiary of Hanmi Pharmaceutical Co., Ltd.

Under the collaboration agreement, the parties agreed to jointly participate in the development of IBI-315. Hanmi will take the lead in initial product development and creation, and subsequent product development outside of China. We will take the lead in product development in China as well as developing the worldwide manufacturing processes. In developing and commercializing IBI-315, the parties will share the development and commercialization expenses and profits.

In the development and commercialization of IBI-315, each party maintains ownership of its own background intellectual property rights, as well as improvements made to that intellectual property by either party under the collaboration agreement. Intellectual property developed by either party under the collaboration agreement that is not an improvement of only one party's intellectual property is jointly and equally owned by both parties. Each party provides the other a co-exclusive (with the other party) fully-paid, royalty free license under such party's intellectual property and joint intellectual property to the extent necessary to perform under the collaboration agreement in the development of IBI-315.

Neither party is obligated to pay any upfront payment, milestone payment or royalty fee under the collaboration agreement, and the Company did not make or receive any payment pursuant to the collaboration agreement during the Track Record Period.

Exclusive License from Protevo

In June 2012, we entered into an agreement ("the Protevo Agreement") with Taiwanbased AP Biosciences, Inc., formerly known as ProtevoBio, Inc. ("Protevo"), whereby Protevo granted us an exclusive, worldwide license under certain of Protevo's patents, patent applications and know-how to develop, manufacture and commercialize biopharmaceutical products incorporating a bi-specific anti-complement/VEGF protein, ACVP1, and its variants (an "ACVP1 Product"). Under the Protevo Agreement, we have the right to sublicense the license granted by Protevo, but we must provide Protevo with advance notice of our intent to enter into a sublicense agreement and the opportunity to discuss and comment on such proposed sublicense agreement. We must use commercially reasonable efforts to develop,

obtain regulatory approval for, manufacture and otherwise commercialize the ACVP1 Product in China. The ACVP1 Product we are currently developing is IBI-302. Upon obtaining regulatory approval and successfully launching the ACVP1 Product in China, we must use commercially reasonable efforts to obtain regulatory approval in the countries that grant regulatory approval to market the ACVP1 Product solely based on its regulatory approval in China or find a sublicensee to develop or commercialize the ACVP1 Product in those other countries. We have not breached the covenant to use commercial reasonable efforts with respect to IBI-302 and there has not been any material impediment to the development of IBI-302.

In exchange for these rights, we paid an upfront payment of US\$250,000 to Protevo. We also paid Protevo milestone payments of US\$250,000 for confirmation of ACVP1 activity *in vitro* and *in vivo*, and US\$500,000 for an IND filing of an ACVP1 Product in China and may owe the following milestone payments totaling up to US\$3,500,000 for an ACVP1 Product in China going forward. These milestone payments are US\$500,000 for initiation of a Phase II clinical trial in China, US\$1,000,000 for initiation of a Phase III clinical trial in China, US\$1,000,000 for initiation of a Phase III clinical trial in China, and US\$2,000,000 for commercial launch of an ACVP1 Product. We also agreed to pay Protevo a royalty of low-single digit percentage of net sales made in China or any of the aforementioned other countries. With respect to sales in the rest of the world, we agreed to pay Protevo 30% of any sublicensing revenue we receive, offsetting such sublicensing for ex-China development costs. In addition, we also agreed to pay Protevo 30% of sublicense royalties we receive, subject to a requirement that the patent application either issues with a valid claim covering the product or has such a claim pending within seven years of the patent's 2011 priority date.

OUR PLATFORM

We have created a fully-integrated platform for the discovery, development, manufacture and commercialization of antibody drug candidates in the fields of oncology, ophthalmology, and autoimmune and metabolic diseases. The full integration of our platform enables smooth collaboration between different functional groups at key points in the lifecycle of a drug candidate with the aim of increasing the speed of development and likelihood of success while at the same time reducing the cost of development. In addition, our platform has been stress tested through the development of sintilimab and the biosimilar drugs in our pipeline by requiring each functional group to perfect their process, approach and collaboration skills.

Within the short period of time since our inception, we have successfully built up all the necessary capabilities of a fully-integrated biologics platform company. These capabilities are housed in four main functional platforms: drug discovery and pre-clinical development, CMC and manufacturing, clinical development, and commercialization. These individual functional platforms have been optimized and great attention has been given to building cross-function integration at key points in the lifecycle of a drug candidate. According to Frost & Sullivan, the research and development expenses likely to be incurred for a potential innovative biologic candidate in China in general range from RMB100 million to RMB150 million during the discovery and pre-clinical development stage, and from RMB250 million to RMB350 million during the clinical development stage. In addition, an efficient operating system for these individual functional platforms has been built, laying a solid foundation for bringing our strong pipeline of innovative drugs from inception through manufacturing and commercialization.

Our fully-integrated platform is capable of addressing the common challenges in engineered antibodies in relation to devising safety measures against immunogenicity, manufacturing for product stability, scaling-up for purity and yield.

- Immunogenicity: Our platform discovers and develops antibodies that are fully . human for the purpose of minimizing immunogenicity. At the discovery stage, the Company, either independently or in collaboration with its partners, designs antibody molecules using human DNA sequences to mitigate immunogenicity risks and also examines amino acid sequences against historical protein databases to eliminate known immunogenicity risks. In addition, the Company designs antibodies such that they have an array of desired properties, such as high target binding affinity, desired Fc functions and high product quality, which in turn can lead to clinical effectiveness at relatively low dosages and frequencies of drug administration that further reduces immunogenicity risks. In the case of the anti-PD-1 product, sintilimab, the Company understands the underlying mechanism of action from the beginning at an early discovery stage, and examines its designed properties throughout the development process. For instance, the Company monitors immunogenicity closely during clinical studies to ensure product safety as well as efficacy. Results from the Company's clinical trials with sintilimab for relapsed/refractory classical Hodgkin's lymphoma have validated the Company's designs for sintilimab, with 1.1% immunogenicity observed.
- Manufacturing for product stability: As each antibody drug candidate goes through the integrated platform from discovery to development and to manufacture, the Company closely monitors the designed critical quality attributes (CQAs) of the antibody that confer on safety and efficacy. The Company utilizes state-of-the-art analytical techniques to ensure the consistency of product quality throughout the manufacturing processes, as any deviation from the Company's design can have ramifications on the required exposure time and frequency on infusion, treatment costs, and patient quality of life.
- Scaling-up for purity and yield: The Company abides by, and in some areas even goes above and beyond, global standards during the manufacturing process. For instance, from toxicology study to clinical manufacturing and then to commercial production, the Company controls the release of incoming raw materials using its quality control system. With scaling-up of manufacturing, the Company takes advantage of the integrated platform to closely monitor, and ensure consistency of, product yield and quality (including purity and impurities), product-related heterogeneity and other general properties. The Company not only uses the controlled raw material release methods to help ensure consistency of product quality, but also employs an array of characterization methods to ensure comparability of product quality including Fc functions. Furthermore, the Company conducts risk analyses and takes the Quality by Design (QbD) approach to apply control strategy in its manufacturing processes including scale-ups.

Drug discovery	Pre-clinical development	Clinical trials		Commercial manufacturing and sales & marketing		
Drug discovery & pre- clinical development						
Hybridoma fectoritige	Cell the engineering and development	Cell banking and cell line characterisation	Assay &	International GMP drug substance		
Fully Internet		Assay & process developmen	e validation	& drug product menufacturing		
These design	group and	Process development group				
(ectroping)		Guality control & assurance group				
Bespecific antitodes. platform		Analytical science group				
Clinical development	Triat design	Trial implementation	analysis	Post-monienting clinical trials		
-		Translational medic	ine			
		Regulatory support	a a			
Commercialisation						
Market study & assessment		Physician education through clinical tests		Medical affairs team		
	External	deflationation		Sales, marketing & market access		

The following chart illustrates the four main functions of our fully-integrated platform.

Drug Discovery and Pre-clinical Development

This aspect of our fully-integrated platform is focused on the discovery and pre-clinical development of new drug candidates. We have discovered 12 drug candidates which are currently in various stages of development, including three discovered solely by ourselves (i.e., IBI-307, IBI-322 and IBI-323) and the other nine discovered in collaboration with our partners (i.e., sintilimab, IBI-306, IBI-101, IBI-188, IBI-110, IBI-939, IBI-318, IBI-319 and IBI-315).

We use various antibody discovery and engineering technologies, either independently or in collaboration with third parties, to generate novel mono-specific or bi-specific antibodies, evaluate their potential efficacy and eventually determine whether the antibodies can be further developed as therapeutics. The four major approaches we use to generate mono-specific antibodies or engineer bi-specific antibodies are summarized below:

- *Hybridoma technology*: We first generate a mouse antibody through immunization of mice with the target antigen. We then convert the mouse antibody into an antibody with characteristics that mimic a human antibody through a process called humanization.
- *Fully humanized mouse*: We licensed mice with a human immune system from third-party developers of human antibody discovery platforms, including Trianni, Inc. and Harbour Antibodies. These mouse strains can be used to discover potential human monoclonal antibody drug candidates. See "– Raw Materials and Suppliers" for more information on the mice strains we use to discover drug candidates.
- *Phage display*: We use a protein target to screen monoclonal antibodies from our own proprietary human synthetic antibody library (also called a phage library). Such process is called phage display.

• *Bi-specific antibody platforms*: We collaborate with third-party developers such as Eli Lilly, Hanmi and Epimab to generate bi-specific antibodies by engineering two different mAbs and assembling them into a single molecule. See "– Collaboration Agreements – Collaboration with Eli Lilly" and "– Collaboration Agreements – Collaboration with Hamni" for more information on our collaborations with Eli Lilly and Hanmi, respectively, in the development of novel bi-specific antibodies.

Our typical drug discovery and development project team brings together relevant specialists from across our Company, as needed, throughout the development of a drug candidate. This includes ongoing involvement of our CMC function to identify, at an early stage, characteristics of a drug candidate that could hamper clinical trials or impede efficient manufacturing of a drug candidate so these issues can be addressed efficiently before the drug candidate progresses to the next stage of development. To ensure effective collaboration, we have project team co-leaders with one leader from each of the groups below.

- *Technology Group*: The technology group handles drug discovery and development steps after the identification of the target for an antibody drug candidate, including genetic engineering, pre-formulation of drug candidates and initial physiologic and chemical characterization. Our technology group has dedicated significant effort to the discovery of bi-specific antibodies that bind to two targets, which is an area at the forefront of immuno-oncology research.
- *Biology Group*: The biology group identifies disease and drug targets and studies the functional aspects of a drug candidate from a chemical and physiologic standpoint, including biochemical and physiologic analysis of antibody and target interactions.

Our drug discovery function is led by a key management team experienced with drug discovery and development and consists of 52 employees as of the Latest Practicable Date, among whom 18 members hold doctorate degrees and 26 members hold master's degrees. Members of the technology group generally have biochemistry, protein engineering and modeling backgrounds. Members of the biology group generally have immunology and in vivo pharmacology backgrounds.

CMC and Manufacturing

This aspect of our fully-integrated platform covers CMC functions including process development and analytical science. Each of these functions is seamlessly coordinated with one another, and this group also supports our manufacturing capability.

Based on the concept of Quality by Design (QbD), we have established a comprehensive, product-oriented platform that facilitates drugability assessment, high expression production cell line development, cell culture, purification, formulation and fill/finish process development and scale-up, analytical development, technology transfer, commercial manufacturing, and quality control. This platform gives us the ability to advance drug candidates to commercialization efficiently and effectively. In addition, we have built an international-standard commercial biopharmaceutical manufacturing facility.

Our CMC capability includes the following functions.

- *Process Development Group*: The process development group focuses on development of full-scale industrial manufacturing processes for clinical and commercial production that are cost-effective and accelerate the speed of drug production. This group has developed highly specialized technology to address the particular challenges inherent in efficiently manufacturing the novel and complex protein-based drug candidates that we develop.
- Analytical Science Group: The analytical science group implements a sciencedriven, clinical and commercial production oriented approach to the development and application of both classic and state-of-the-art analytical techniques and tools throughout the life cycle of each of our drug candidates. This team supports and works closely with all the other functions in our fully-integrated platform, particularly the drug development, process development and quality control functions. This group's work includes:
 - o early-stage assessment of each drug candidate's critical quality attributes to determine its potential for development as a stable and cost-effective new drug, also known as drugability;
 - o comprehensive and thorough research and analysis of protein structure and mechanism of action; and
 - o assessment of product production from development to full-scale manufacture, quality control and drug release strategies for IND and NDA applications.
- *Quality Control and Assurance Group*: The quality control and assurance group oversees the quality of our facilities and our products, as well as the quality systems in research and development, manufacturing and commercialization of drug candidates and potential future commercial products. This group's work includes:
 - o ensuring quality control throughout the manufacturing process, including specification of the drug substance and the drug product, testing of raw materials, and product quality assessments;
 - o establishing a quality assurance system across the entire business, including employee training programs, audits of various business segments and product manufacturing; and
 - o validation of facilities and equipment, which includes laboratory tests to verify that a particular process, method, program, equipment or material works properly.

Our CMC and manufacturing capability is enabled by certain key technologies and processes that are summarized below.

- *Cell Line Engineering and Development*: This is a core process for drug development where, once a biologic drug candidate has been identified, we grow host cells for the purpose of producing therapeutic proteins. A cell line is a population of cells which descend from a single cell and contain the same genetic makeup, thereby producing the same proteins. The productivity of a cell line determines the cost of manufacturing and the quality of a cell line determines the quality of the relevant biologics. We have built a state-of-the-art cell line development platform with proprietary technologies. We conduct cell line engineering and development using third-party cell lines and are developing our own proprietary cell lines. As of the Latest Practicable Date, we had developed more than 20 cell lines for our drug development purposes.
- *Cell Banking and Cell Line Characterization*: After the cell lines are defined and developed, the cell lines are made into a series of cell banks, which consist of an adequate number of vials of cells stored in liquid nitrogen. The process of making cell banks is cell banking. The cell banks are tested and characterized in accordance with regulatory guidance to make sure that they produce the expected biologic drug candidates, are pure with no microbial or mycoplasma contamination, and are not contaminated by viruses.
- Assay and Process Development: This is the process where, upon creation of a cell bank, we develop a manufacturing process that can produce a biologic drug candidate on a large scale and generate consistent results over time. A number of steps are essential in this process. As proteins are typically not stable, we test and develop a buffer solution with stabilization agents, known as a formulation, and combine the proteins with the formulation so as to stabilize the proteins for clinical use. In addition, once a biologic drug candidate is produced, we develop and conduct many assays on the drug candidate to ensure that it is safe, efficacious and consistent from one manufacturing lot to another.
- Assay and Process Validation: Once the manufacturing process and the related assays are developed, we validate them to ensure that the manufacturing and testing of a product will generate consistent results every time. This process is called assay and process validation.

• Drug Substance and Drug Product Manufacturing: After the manufacturing processes and the related assays are validated, the processes and assays are transferred to large scale manufacturing facilities where our drug candidates for clinical trials and for future commercialization are produced. Our manufacturing capabilities include both drug substance and drug product manufacturing, from upstream cell culture, downstream purification, formulation, sterile filling and packaging. Single-use technologies have been used in our drug substance manufacturing. A larger scale stainless steel bioreactor facility is under construction.

The following diagram illustrates the basic process for manufacturing our monoclonal antibodies. Certain aspects of the process vary by the specific monoclonal antibodies being manufactured.





The following figure shows the basic process flow of the formulation and fill/finish procedure.

We operate our manufacturing facilities on our main campus in Suzhou that are designed to comply with both Chinese and international drug manufacturing standards. From our inception, we have focused on constructing and operating manufacturing facilities that are designed to meet rigorous international good manufacturing practice (GMP) standards. We have undergone ordinary course, comprehensive annual audits of our production facility to evaluate compliance with industry GMP and quality compliance standards.

• *Manufacturing Building 1*: Our Manufacturing Building 1 has 21,579.52 m² of floor space and currently houses our first stage production facilities with three 1,000L disposable bioreactors. These facilities produce the drugs that we use for clinical trials. We expect our existing facilities to be able to support our commercial manufacturing needs for our first two products, namely sintilimab and, subject to the speed of the regulatory review process, either IBI-303 or IBI-305, through 2020.

- *Expansion in Manufacturing Building 1*: We have begun construction on our second stage production facilities, which will also be housed in Manufacturing Building 1. When completed, these facilities will be equipped with six 3,000L stainless steel bioreactors, bringing our total production capacity to 21,000L. This expansion will provide us additional capacity to support commercial production as well as clinical trials. These facilities are scheduled to go into operation in the second half of 2019 and we expect them to provide us with sufficient manufacturing capacity to support the growth of our business for at least five years.
- *Manufacturing Building* 2: Our Manufacturing Building 2 has an additional 24,330.12 m² of floor space to accommodate our future growth. We plan to install four 15,000L stainless steel bioreactors in this building as and when needed.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements governing recordkeeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our manufacturing facilities are designed to operate under, and are expected to receive certifications for cGMP requirements. We hold, and our manufacturing facilities operates under, a pharmaceutical manufacturing license issued by the NMPA.

Clinical Development

The clinical development function of our fully-integrated platform manages clinical trials including clinical trial design, implementation, and the collection and analysis of trial data. As of the Latest Practicable Date, we have designed and implemented more than a dozen clinical studies.

Our clinical development function has entered into long-term partnerships with numerous hospitals and principal investigators located in different regions of China that offer us readily available clinical trial facilities and services. We believe the size and geographic diversity of these facilities provide us a significant advantage in implementing large-scale clinical trials and also enable us to conduct multiple clinical trials concurrently.

We use contract research organizations, or CROs, and consultants that manage, conduct and support our clinical trials and pre-clinical studies in China and in the U.S. We selected our CROs weighing various factors, such as their qualifications, academic and professional experience and industry reputation. The CROs provide us with an array of products and services necessary for complex clinical trials. In addition to the scope, depth and quality of their service and product offerings, we place a high value on our CROs' ability to facilitate optimal site selection, timely patient recruitment and efficient conduct of complex clinical trials. Generally, we enter into a master service agreement with a CRO under which we execute a separate work order for each pre-clinical or clinical research project, or we enter into a research and development contract with a CRO for an individual project. We supervise these third-party service providers to ensure that they perform their duties to us in a manner that complies with our protocols and applicable laws and that protects the integrity of the data resulting from our trials and studies. Key terms of an agreement we typically enter into with our CROs are summarized as below:

- *Services*. The CRO provides us with services related to a pre-clinical or clinical research project as specified in the agreement or a work order.
- *Term.* The CRO is required to complete the pre-clinical or clinical research project within the prescribed time limit.
- *Payments*. We are required to make payments to the CRO in accordance with the payment schedule agreed by the parties.
- *Intellectual property rights.* We own all intellectual property rights arising from the pre-clinical or clinical research project.
- *Risk allocation.* Each party should indemnify the other party for losses caused by its fault or gross negligence. If the research fails due to unresolvable technical difficulties or otherwise due to circumstances beyond control, the parties should negotiate how to allocate the losses resulting from such failure.

We believe our strength in recruiting clinical trial participants and our ability to conduct large, high-quality clinical trials enable us to reduce our drug development timelines by generating the requisite data reliably and efficiently. Supported by our CROs and our geographically diverse hospital partners, we are able to recruit specialized populations for otherwise difficult-to-recruit clinical trials. We have the expertise and experience in recruiting for and conducting trials involving a variety of therapeutic areas including oncology, ophthalmology, and autoimmune and metabolic diseases.

The clinical development function also manages the regulatory submission process for our drug candidates, which require filings to be made to and approved by the relevant authorities before clinical trials and commercialization can be initiated. The clinical development function prepare and manage regulatory filings by drafting filing dossiers, addressing regulatory questions and conducting GMP readiness assessments for our drug candidates. We possess extensive knowledge and experience with regard to regulatory filings in China and the United States.

The clinical development function also includes the translational medicine function which produces biomarkers and diagnostics for our clinical trials.

Our clinical development function is comprised of a clinical strategy department and a clinical research and operation department. The clinical strategy department, which consists of 55 members as of the Latest Practicable Date, is led by Mr. Kerry L. Blanchard, M.D., Ph.D., our Chief Science Officer. Dr. Blanchard received a B.S. in chemistry, a Ph.D. in biochemistry and a M.D. from Indiana University. He completed a residency in Internal Medicine and fellowships in Hematology and Medical Oncology at the Brigham and Women's Hospital, the Dana Farber Cancer Center and Harvard Medical School. Dr. Blanchard was previously Senior Vice President in China Medicines Development Unit and External Innovation of Lilly China and has more than 18 years of leading drug discovery and drug development experience. The clinical research and operation department, which consists of 113 members as of the Latest

Practicable Date, is led by Ms. Jessie Chen, our Chief Medical Officer, who has 20 years of in-depth experience in the relevant field. Ms. Chen graduated from the Capital University of Medical Sciences with a bachelor's degree in clinical medicines. She was previously head of the Clinical Trial Management and Portfolio Project Management departments at Pfizer where she accumulated extensive experience in clinical operations, standard operating procedures (SOPs), training, process implementation, clinical data services and portfolio project management.

Commercialization

This aspect of our platform encompasses marketing, sales, medical affairs and market access. We intend to commercialize sintilimab and our other drug candidates in China, if approved, with a direct sales force. We are currently building and expect to have a 250-member commercialization team by the time we receive marketing approval for sintilimab in China. We plan to double that size to a 500-member commercialization team in anticipation of the increased market demand for sintilimab and prior to the commercial launch of our first biosimilar drug candidate in China.

• *Marketing and sales.* We are expanding our sales and marketing team to cover a majority of the provinces and municipalities in China. As of the Last Practicable Date, our marketing leadership team is in place with the head of marketing and three marketing directors on board. Our sales leadership team is also in place with two sales heads and eight regional sales directors on board. We are increasing the size of our sales and marketing force rapidly in preparation for the commercial sales of our first wave of approved drug candidates, and we aim to have all the marketing staff and first line sales managers on board by the end of third quarter of 2018 and build a sizeable sales and marketing team by the end of 2018.

Our sales and marketing force will market our future approved drug candidates to physicians and hospital administrators using a physician-targeted marketing model, focused on promoting the differentiating clinical aspects of our products. Such marketing efforts usually commence several months before the expected approval for the commercialization of a drug candidate.

Our sales representatives will focus on effective market coverage and penetration to meet the anticipated demand for our future approved drug candidates in their respective regions and for their approved indications. We are currently building our sales force that is dedicated to the commercialization of our late-stage core products for their respective first approved indications. We will continue to expand our dedicated sales force as we develop and commence commercialization of more approved products and for additional indications.

• *Medical affairs*. We have also quickly established our medical affairs team comprised of medical managers and medical science liaisons, or MSLs, who are primarily responsible for post-launch clinical data generation and medical communication. Our medical affairs and marketing personnel focus on raising our

brand awareness and recognition by organizing academic seminars and conferences, sponsoring investigator-led clinical trials, providing academic consulting services and developing collaborative clinical solutions.

• *Market access*. Our market access team is responsible for channel and key account management, insurance and reimbursement and patient assistance. We have established strong relationships with physicians, hospital administrators and leading experts in the field of oncology.

Our chief commercial officer, Mr. Min Liu, leads our sales, marketing and market access operations. Mr. Liu was previously a member of the Roche Global Oncology Franchise Leadership Team and vice president and head of one of Roche's two oncology business units in China. The unit he led was in charge of the marketing and sales efforts for products in the fields of lung cancer, gastrointestinal cancer and hematology. In his role as our chief commercial officer, Mr. Liu is supported by key commercial leadership members who have significant commercial experience in the pharmaceutical industry. We provide in-house education and training to our sales force to improve their sales skills and efficiency and to ensure they provide our current and prospective clients with comprehensive information about our product candidates and future products.

To further strengthen our competitive position, we will leverage our co-promotion and co-branding arrangement with Eli Lilly for sintilimab and IBI-301 in China, tapping into Eli Lilly's in-depth knowledge of the China market. We also expect to benefit from Eli Lilly's own commercialization team in China and its institutional relationships in China.

We are supporting numerous investigator-led clinical trials to generate local clinical data and accumulate relevant clinical experience that will support the clinical use of our future approved products. We are building the infrastructure that will allow us to employ centralized information technology to integrate market information from various sources into a unified system to increase the efficiency and effectiveness of our market data collection and analysis.

CUSTOMER

During the Track Record Period, we derived all of our revenues from the license granted to and research and development services provided to a China-based biopharmaceutical company. For the year ended December 31, 2016, we had no revenue. During the year ended December 31, 2017, we entered into agreements with such company for licensing of patented technology and provision of manufacturing and validation services to them with respect to an early-stage drug candidate that we discontinued to develop as a pipeline product candidate, and generated revenues from such activities. This drug candidate we licensed to the customer was an anti-VEGF fusion protein and was developed to treat age-related macular degeneration (AMD) and tumor. We decided to discontinue the development of this drug candidate at a very early preclinical stage when we came to realize the commercial viability of this drug candidate is relatively low as compared to our other pipeline drug candidate, such as IBI-302. At the Latest Practicable Date, this drug candidate remained at preclinical stage.

As of the Latest Practicable Date, none of our Directors or any Shareholder, who, to the knowledge of our Directors, owns more than 5% of our issued share capital immediately following completion of the Global Offering (but without taking into account the exercise of the Over-allotment Option) nor any of their respective associates had any interest in our customer.

RAW MATERIALS AND SUPPLIERS

We develop cell lines either independently or in collaboration with third parties when we begin discovery and development on a new drug candidate. We maintain a master cell bank with separate copies in two locations and we produce working cell banks from the master cell bank.

We licensed transgenic mice from third-party developers of human antibody discovery platforms, including Trianni, Inc. and Harbour Antibodies. These mouse strains have been humanized and therefore express human proteins, and can be used to discover potential human mAb drug candidates against human inflammatory disease, cancer and other targets.

We procure equipment for the development and manufacture of our drug candidates from industry-leading, highly reputable manufacturers and suppliers around the world.

We purchase cell culture media from several reputable third-party suppliers on a regular basis. We test the cell culture media when received to ensure consistent quality. For certain drug candidates, we have developed and used our own proprietary cell culture media with an optimized formulation.

We use contract research organizations, or CROs, and consultants that manage, conduct and support our clinical trials and pre-clinical studies in China and in the U.S. For further details, see "– Our Platform – Clinical Development."

For the two years ended December 31, 2016 and 2017, our purchases from our five largest suppliers in the aggregate accounted for 32.8%, and 39.2% of our total purchases (including value added tax), respectively, and purchases from our largest supplier alone accounted for 11.8%, and 13.1% of our total purchases (including value added tax), respectively. Purchases include raw materials, third-party contracting services for research and development purposes, machines and equipment and administrative services. All of our five largest suppliers during the Track Record Period are independent third parties. None of our Directors, their respective associates or any shareholder who, to the knowledge of our Directors, owned more than 5% of our issued share capital as of the Latest Practicable Date, has any interest in any of our five largest suppliers during the Track Record Period.

We have established relationships with preferred suppliers of raw materials for our manufacturing activities who we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist and we have developed alternative sourcing strategies for these raw materials. These strategies will be

implemented by the end of 2018 and we will establish necessary relationships with these alternative sources based on supply continuity risk assessment. We currently order approximately 70% of our raw materials and services from suppliers with whom we have signed long-term supply contracts, and we order the rest of our raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements.

AWARDS AND RECOGNITIONS

Our leader, Dr. De-Chao Michael Yu, is a biopharmaceutical expert in China who has invented the world's first oncolytic virus-based immunotherapeutic product, Oncorine, and also co-invented and led the development of the first domestic innovative fully human antibody-like therapeutic approved for marketing in China, Conbercept. 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 recognized 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".

Dr. Yu currently serves as the Chairman of the Board of the Chinese Antibody Society, a Deputy Director of the National Technical Committee on Biochemistry Products and Testing Technology of the Standardization Administration of China, a Deputy Director of Drug Research and Development Special Committee of China Pharmaceutical Innovation and Research Development Association, a Deputy Director of the Committee of Cancer Immunology and Cancer Biotherapy of the Chinese Society for Immunology, a Managing Director of the Chinese Association for Medicinal Biotechnology, a Standing Committee Member of the Special Committee of Gene Therapy Society of the Chinese Association of Medicinal Biotechnology, a member of the Special Committee for Precision Medicine of the China Medicinal Biotech Association and a member of the Special Committee for Cancer Biotherapy of the China Anti-cancer Association.

Our Company has received numerous Chinese national, provincial and local level research grants for our innovative drug development efforts, including two grants for the development of our sintilimab and IBI-301 drug candidates which were approved in 2014 by the Office of Key New Drug Innovation of the National Health and Family Planning Commission of the People's Republic of China. A summary of the key research grants that our Company has received is set forth in the table below.

					Approved
Pipeline Candidate	Grant Type	Grant Institution	Project Name	Date of Grant	Grant Amount
IBI-301	2014 National	Office of Key New	Clinical trial of	June 12, 2014	RMB5.28 million
	Major Scientific	Drug Innovation	recombinant		
	and Technological	of the National	human-mouse		
	Special Project	Health and	chimeric		
	for "Significant	Family Planning	anti-CD20		
	New Drugs	Commission of	monoclonal		
	Development"	the People's	antibody (重組人-		
	(2014年國家重大	Republic of China	鼠嵌合抗CD20單		
	新藥創製專項)	(國家衛生計生委	克隆抗體臨床研		
		重大新藥創製科技	究)		
		重大專項實施管理			
		辦公室)			
sintilimab (IBI-308)	2014 National	Office of Key New	Research and	June 12, 2014	RMB3.49 million
	Major Scientific	Drug Innovation	development of a		
	and Technological	of the National	fully human		
	Special Project	Health and	anti-PD-1		
	for "Significant	Family Planning	monoclonal		
	New Drugs	Commission of	antibody (抗PD-1		
	Development"	the People's	全人源單克隆抗體		
	(2014年國家重大	Republic of China	研製)		
	新藥創製專項)	(國家衛生計生委			
		重大新藥創製科技			
		重大專項實施管理			
		辦公室)			
IBI-310/IBI-101	2017 National Key	Development Center	Research and	October 18,	RMB3.51 million
	Research and	for Medical	development of	2017	
	Development Plan	Science and	genetically		
	– Key Special	Technology,	modified		
	Project on	National Health	therapeutic		
	Precision	and Family	antibodies and		
	Medicine	Planning	standardization of		
	Research (2017年	Commission of	clinical treatment		
	國家重點研發計	the People's	(修師型抗體治療		
	劃- 精準醫學研究	Republic of China	樂物 研發與 治療標		
	重點專項)	(國豕衛生計生委)	平化)		
		■ ■			
		研究中心)			

Our research and development capability was recognized as one of the "Top Ten Breakthroughs in the China Biopharmaceutical Industry" (中國醫藥與生物技術十大進展) by China Medicinal Biotechnology Association (中國醫藥生物技術協會) in 2015. In June 2016, our Company was selected to attend the National "12th Five-Year" science and technology innovation achievement exhibition, where our achievements were recognized by national leaders. In recognition of our achievements in innovation-driven drug development, our Company was invited to join and speak at the sixth U.S.-China Innovation Dialogue that took place at the State Department in Washington D.C. in June 2015. We were selected into the List of China's Unicorn Companies for 2017 (2017中國獨角獸企業榜單) by Torch High Technology Industry Development Center, Ministry of Science and Technology (科學技術部火 炬高技術產業中心). Our achievements have been highlighted in the People's Daily and The Wall Street Journal and on China Central Television.

COMPETITION

Our industry is highly competitive and subject to rapid and significant change. While we believe that our fully-integrated platform, our robust pipeline of drug candidates in clinical and pre-clinical trials and our experienced leadership team provide us with competitive advantages, we face potential competition from many different sources working to develop therapies targeting the same indications against which we develop our drug candidates. These include major pharmaceutical companies, such as Merck, Bristol-Myers Squibb, Roche, Jiangsu Hengrui, Qilu Pharmaceutical and Hisun Pharmaceutical, specialty pharmaceutical and biotechnology companies, such as BeiGene, Junshi and Henlius, and academic institutions, government agencies and research institutions. Any drug candidates that we successfully develop and commercialize will compete both with existing drugs and with any new drugs that may become available in the future.

INSURANCE

We maintain insurance policies that we consider to be in line with market practice and adequate for our business. Our principal insurance policies cover property loss due to accidents or natural disasters, product damages during shipment, and adverse events in clinical trials. We do not maintain product liability insurance or key-man insurance.

EMPLOYEES

The following table sets forth a breakdown of our employees by function as of the Latest Practicable Date:

Function	Number	% of Total	
Research and Development	327	42.1	
Manufacturing	206	26.5	
Selling, General and Administrative	244	31.4	
Total	777	100.0	

As of the Latest Practicable Date, we had 678 employees in Suzhou and 99 employees in Shanghai.

Employment Agreements with Key Management and Research Staff

We enter into standard confidentiality and employment agreements with our key management and research staff. The contracts with our key personnel typically include a standard non-compete agreement that prohibits the employee from competing with us, directly or indirectly, during his or her employment and for at least two years after the termination of his or her employment. The contracts also typically include undertakings regarding assignment of inventions and discoveries made during the course of his or her employment. For further details regarding the terms of confidentiality and employment agreements with our key management, please refer to the section headed "Directors and Senior Management" in this prospectus.

Certain of our subsidiaries in China have labor unions and our employees may voluntarily join the relevant labor unions. We believe that we maintain a good working relationship with our employees and we have not experienced any significant labor disputes or any significant difficulty in recruiting staff for our operations.

Training and Development

We provide formal and comprehensive company-level and department-level training to our new employees, which usually takes two days, followed by on-the-job training, which takes about two months. We also provide training and development programs to our employees from time to time to ensure their awareness and compliance with our various policies and procedures. Given our emphasis on operating a fully-integrated platform for our drug development processes, some of the training is conducted jointly by different groups and departments serving different functions but working with or supporting each other in our day-to-day operations.

Employee Benefits

Our employees' remuneration comprises salaries, bonuses, employees provident fund and social security contributions and other welfare payments. In accordance with applicable Chinese laws, we have made contributions to social security insurance funds (including pension plans, medical insurance, work-related injury insurance, unemployment insurance and maternity insurance) and housing funds for our employees. As of the Latest Practicable Date, we had complied with all statutory social security insurance fund and housing fund obligations applicable to us under Chinese laws in all material aspects.

LAND AND PROPERTIES

We built our main campus on 71,104.49 m^2 of land in the Suzhou Industrial Park which we purchased in 2015. This site includes manufacturing, research, administrative and ancillary buildings with a total of 81,779.98 m^2 of floor space. This includes 45,909.64 m^2 of floor space for manufacturing facilities and 35,870.34 m^2 of floor space for laboratories, ancillary buildings and offices, some of which is reserved for future expansion. Our main campus also includes animal laboratories, water treatment facilities, warehouses for storing drugs and chemicals, and a cafeteria and other facilities for employees. Below is a photograph of our main campus in Suzhou.



We still rent 2,425 m² of office space in Suzhou where our Company was based before we built our main campus, and we continue to use this space for research and administrative functions. The relevant rental agreement provides a rental term that expires in November 2018. We also rent 1,893.88 m² of office space in Shanghai for administrative functions. The relevant rental agreement provides a rental term that expires in January 2023. In addition, we rent 980.47 m² of office space in Beijing for administrative functions and the rental term provided by the rental agreement expires in October 2021.

INTELLECTUAL PROPERTY

Intellectual property rights are important to the success of our business. Our future commercial success depends, in part, on our ability to obtain and maintain patent and other intellectual property and proprietary protections for commercially important technologies, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid, enforceable intellectual property rights of third parties.

As of the Latest Practicable Date, we own 19 issued patents and 34 patent applications in China, 1 issued patent and 7 patent applications in the United States, and 11 issued patents and 51 patent applications in the rest of the world relating to certain of our drug candidates and technologies. These patent applications include 16 pending international patent applications under the Patent Cooperation Treaty, or PCT. We have filed seven of these nationally in various jurisdictions, including the European Union, and we plan to file the other 9 nationally in the United States and other jurisdictions, as well as additional priority PCT applications. We are also pursuing additional patent protection for these drug candidates and technologies, as well as for other of our drug candidates and technologies. As of the Latest Practicable Date, in relation to our four core drug candidates in clinical trials, we own three issued Chinese patents and three pending Chinese patent applications, two pending U.S. patent applications, and four pending PCT applications, among others. The patent portfolios for our four core drug candidates and three other clinical stage drug candidates as of the Latest Practicable Date are summarized below:

Sintilimab (IBI-308). We own two pending Chinese patent applications, two pending U.S. patent applications, four pending PCT applications, and corresponding patent applications in other jurisdictions directed to sintilimab, a fully human monoclonal antibody against PD-1, and its use for the treatment of cancer. Any patents that may issue from the currently pending Chinese patent application and U.S. patent application would be expected to expire in August 2036 or January 2037, not including any patent term adjustments. We intend to pursue marketing exclusivity periods that are available under regulatory provisions in certain countries.

IBI-305. We own one pending Chinese patent application directed to IBI-305, our biosimilar product candidate for bevacizumab, and its use for the treatment of cancer. Any patent that may issue from the currently pending Chinese patent application would be expected to expire in December 2034.

IBI-301. We co-own with Hubei University one issued Chinese patent directed to IBI-301, our biosimilar product candidate for rituximab. The expected expiration for the issued Chinese patent is in February 2034.

IBI-303. We own two issued Chinese patents directed to IBI-303, our biosimilar product candidate for adalimumab. The expected expiration for the issued Chinese patents is in November 2033 and December 2034.

IBI-302. We own two issued Chinese patents, two pending U.S. patent applications, two pending PCT applications and corresponding patent applications in other jurisdictions directed to IBI-302, our bi-specific antibody drug candidate for the treatment of wet AMD and solid tumors. In addition, we co-own with AP Biosciences, Inc. one issued U.S. patent, one pending U.S. patent application, one pending Chinese patent application, one pending PCT application and corresponding patent applications in other jurisdictions directed to IBI-302. Any patents that may issue from the currently pending Chinese patent applications and U.S. patent applications would be expected to expire between November 2032 and December 2035, not including any patent term adjustments. We intend to pursue marketing exclusivity periods that are available under regulatory provisions in certain countries.

IBI-306. We own two pending Chinese patent applications and one pending PCT application, directed to IBI-306, our fully human monoclonal antibody drug candidate for the treatment of reduction of hyperlipidemia. The two patents that may be issued from the currently pending Chinese patent applications would be expected to expire in December 2036 and May 2038, respectively, not including any patent term adjustments.

IBI-310. We own three pending Chinese patent applications, directed to IBI-310, our fully human monoclonal antibody drug candidate for the treatment of a variety of cancers in combination with anti-PD-1 monoclonal antibodies, including sintilimab. Any patent that may issue from the currently pending Chinese patent applications would be expected to expire between November 2035 and March 2037, not including any patent term adjustments.

The following table summarizes the details of the granted patents and the filed patent applications owned by the Company or shared with its collaborators on our four core products and three phase 1 innovative drug candidates:

Summary of Chinese and U.S. p	atents and patent	t applications of our	core product			
candidates and phase 1 innovative drug candidates						

Product	Scope of Patent Protection	Iurisdiction	Status	Patent Expiration	Innovent's Market/ Commercial Rights	Marketing Exclusivity Terms	Eligibility for Patent Renewal/ Extension
Sintilimab	Directed to structure and its use	U.S.; China	Pending	August 2036	All rights worldwide, subject to Eli	12 years (U.S.); N/A (China)	N/A
	Directed to formulation and its use	PCT (national phase filings to be made in the U.S. and China)	Pending	July 2037	Lilly's co- promotion right in China, Hong Kong and Macau		N/A
IBI-305	Directed to formulation and its use	China	Pending	December 2034	All rights worldwide	N/A	N/A
IBI-301	Directed to antibody detection method	China	Granted	February 2034	All rights worldwide, subject to Eli Lilly's co- promotion right in China, Hong Kong and Macau	N/A	N/A
IBI-303	Directed to formulation and its use	China	Granted	November 2033	All rights worldwide	N/A	N/A
IBI-306	Directed to structure and its use	PCT (national phase filings to be made in the U.S. and China)	Pending	December 2037	All rights in China, Hong Kong and Macau	12 years (U.S.); N/A (China)	N/A
	Directed to formulation and its use	China	Pending	May 2038			N/A
IBI-310	Directed to formulation and its use	China	Pending	March 2037	All rights worldwide	N/A	N/A
IBI-302	Directed to structure and its use	U.S.; China	Granted (U.S.); Pending (China)	November 2032	All rights worldwide	12 years (U.S.); N/A (China)	The term of the U.S. patent No. 9,988,611 (Application No. US14/362,109) is extended or adjusted under 35 U.S.C. 154(b) by 100 days.
	formulation and its use	U.S.; China	(U.S.); Granted (China)	September 2035 (U.S.); September 2034 (China)			IN/A

Abbreviations: PCT = Patent Cooperation Treaty; N/A = not applicable

As of the Latest Practicable Date, we own 11 issued Chinese utility model patents for our various innovative technologies that are utilized throughout our drug development and manufacturing process, including those related to inoculation, cell culture, chromatography and bioreactors. These utility model patents have a term of 10 years from the date of filing and are expected to expire in and after November 2025.

The term of individual patents may vary based on the countries in which they are obtained. In most countries in which we file patent applications, including China and the United States, the term of an issued patent is generally 20 years from the filing date of the earliest non-provisional patent application on which the patent is based in the applicable country. In the United States, a patent's term may be lengthened in some cases by a patent term adjustment, which extends the term of a patent to account for administrative delays by the United States Patent and Trademark Office, or USPTO, in excess of a patent applicant's own delays during the prosecution process, or may be shortened if a patent is terminally disclaimed over a commonly-owned patent having an earlier expiration date.

In addition, with respect to any issued patents in the United States and Europe, we may be entitled to obtain an extension of the patent's term provided we meet the applicable requirements for obtaining such patent term extensions. For example, in the United States, we may apply for a patent term extension of up to five years as compensation for the patent term lost during clinical trials and the FDA regulatory review process under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The exact duration of the extension depends on the time we spend in clinical studies, as well as getting an NDA approval from the FDA. However, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. In certain other foreign jurisdictions, similar extensions as compensation for regulatory delays are also available.

The actual protection afforded by a patent varies on a claim-by-claim and country-bycountry basis and depends upon many factors, including the type of patent, the scope of its coverage, the availability of any patent term extensions or adjustments, the availability of legal remedies in a particular country and the validity and enforceability of the patent. We cannot provide any assurance that patents will issue with respect to any of our owned or licensed pending patent applications or any such patent applications that may be filed in the future, nor can we provide any assurance that any of our owned or licensed issued patents or any such patents that may be issued in the future will be commercially useful in protecting our product candidates and methods of manufacturing the same.

We may rely, in some circumstances, on trade secret and/or confidential information to protect aspects of our technology. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with consultants, scientific advisers and contractors, and invention assignment agreements with our employees. We have entered into confidentiality agreements and non-competition agreements with our senior management and certain key members of our R&D team and other employees who have access to trade secrets or confidential information about our business. Our standard employment contract, which we used to employ each of our employees, contains an assignment clause, under which we own all the rights to all inventions, technology, know-how and trade secrets derived during the course of such employee's work.

These agreements may not provide sufficient protection of our trade secret and/or confidential information. These agreements may also be breached, resulting in the

misappropriation of our trade secret and/or confidential information, and we may not have an adequate remedy for any such breach. In addition, our trade secret and/or confidential information may become known or be independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to or successfully copy aspects of our products or to obtain or use information that we regard as proprietary without our consent. As a result, we may be unable to sufficiently protect our trade secrets and proprietary information.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. Despite any measures taken to protect our data and intellectual property, unauthorized parties may attempt to or successfully gain access to and use information that we regard as proprietary. See "– Risk Factors – Risks Relating to Our Business – Risk Relating to Our Intellectual Property" for a description of risks related to our intellectual property.

We conduct our business under the brand name of "Innovent" ("信達"). As of the Latest Practicable Date, we had registered 59 trademarks in China and 4 trademarks in Hong Kong and filed 80 trademark applications in China and five trademark applications in other jurisdictions. We are also the registered owner of five domain names and have irrevocable licenses for four domain names.

We enter into collaboration agreements and other relationships with pharmaceutical companies and other industry participants to leverage our intellectual property and gain access to the intellectual property of others. See "– Collaboration Agreements."

As of the Latest Practicable Date, we were not involved in any proceedings in respect of, and we had not received notice of any claims of infringement of, any intellectual property rights that may be threatened or pending, in which we may be a claimant or a respondent.

See Appendix IV – "Statutory and General Information – Further Information about Our Business – Intellectual Property Rights" to this prospectus for further information.

ENVIRONMENTAL MATTERS AND WORKPLACE SAFETY

We strive to operate our facilities in a manner that protects the environment and the health and safety of our employees, patients and communities. We have implemented company-wide environmental, health and safety manuals, policies and standard operating procedures that include management systems and procedures relating to emissions of air, water and other media; waste water generation and treatment; process safety management; handling, use, storage, treatment and disposal of hazardous substances; worker health and safety requirements; third party safety management; emergency planning and response; and product stewardship.

Our environmental, health and safety (EHS) department is responsible for monitoring and enforcing the compliance of our operations with environment, health and safety laws and regulations. This responsibility is executed and shared by separate teams in the EHS department through training; formulation and implementation of strategies, policies, standards and metrics; communication of environmental, health and safety policies and procedures through of a team of coordinators; environmental, health and safety audits; and incident response planning and implementation with a team of volunteer first responders. We also have consultants from Eli Lilly on an as-needed basis to help us on building, maintenance and improvement of our EHS system.

Certain specialized areas of the responsibility are assigned to teams comprised of subject-matter experts with the relevant expertise and experience. For instance, our biosafety subject matter experts are responsible for biosafety training, compliance of our operations with biosafety-related legal requirements, biosafety risk assessment and review of corrective actions and preventative actions (CAPA) that we will take upon the occurrence of any biosafety emergency. We have also retained a subject matter expert from Eli Lilly as a consultant for environment, health and safety matters.

Our manufacturing facilities produce no significant waste products other than water exiting our bioreactors. We treat the waste water exiting our bioreactors at high temperatures in our biological waste disposal facilities and then treat it together with other waste water in our central waste water disposal facilities before discharging it into the city sewer system. The water that we discharge is metered and the meters are connected to the local environmental bureau to permit them to monitor the discharged water remotely.

We have not had any significant workplace accidents in the history of our Company.

LEGAL PROCEEDINGS AND COMPLIANCE

As of the Latest Practicable Date, we were not a party to any actual or threatened material legal or administrative proceedings. We are committed to maintaining the highest standards of compliance with the laws and regulations applicable to our business. However, we may from time to time be subject to various legal or administrative claims and proceedings arising in the ordinary course of business.

PERMITS, LICENSES AND OTHER APPROVALS

As of the Latest Practicable Date, we had obtained all requisite licenses, approvals and permits from relevant authorities that are material to our operations.

Innovent Biologics (Suzhou) Co., Ltd. (信達生物製藥(蘇州)有限公司) holds a pharmaceutical manufacturing license issued by the Jiangsu Provincial Food and Drug Administration, effective through December 31, 2020. It also holds an emission permit for certain specified pollutants issued by the Suzhou Industrial Zone Bureau of Land and Environmental Protection, effective through March 15, 2020.

RISK MANAGEMENT AND INTERNAL CONTROL

Risk Management

We recognize that risk management is critical to the success of our business operation. Key operational risks faced by us include changes in the general market conditions and the regulatory environment of the Chinese and global biologics markets, our ability to develop, manufacture and commercialize our drug candidates, and our ability to compete with other pharmaceutical companies. See "Risk Factors" for a discussion of various risks and uncertainties we face. We also face various market risks. In particular, we are exposed to credit, liquidity, interest rate and currency risks that arise in the normal course of our business. See "Financial Information – Qualitative and Quantitative Disclosure about Market Risk" for a discussion of these market risks.

We have adopted a consolidated set of risk management policies which set out a risk management framework to identify, assess, evaluate and monitor key risks associated with our strategic objectives on an on-going basis. Our audit committee, and ultimately our Directors supervise the implementation of our risk management policies. Risks identified by management will be analyzed on the basis of likelihood and impact, and will be properly followed up and mitigated and rectified by our Group and reported to our Directors.

The following key principles outline our Group's approach to risk management and internal control:

- Our audit committee will oversee and manage the overall risks associated with our business operations, including (i) reviewing and approving our risk management policy to ensure that it is consistent with our corporate objectives; (ii) reviewing and approving our corporate risk tolerance; (iii) monitoring the most significant risks associated with our business operation and our management's handling of such risks; (iv) reviewing our corporate risk in the light of our corporate risk tolerance; and (v) monitoring and ensuring the appropriate application of our risk management framework across our Group.
- Our chief financial officer, Mr. Ronald Hao Xi Ede, will be responsible for (i) formulating and updating our risk management policy and target; (ii) reviewing and approving major risk management issues of our Company; (iii) promulgating risk management measures; (iv) providing guidance on our risk management approach to the relevant departments in our Company; (v) reviewing the relevant departments' reporting on key risks and providing feedbacks; (vi) supervising the implementation of our risk management measures by the relevant departments; (vii) ensuring that the appropriate structure, processes and competences are in place across our Group; and (viii) reporting to our audit committee on our material risks.
- The relevant departments in our Company, including but not limited to the finance department, the legal department and the human resources department, are responsible for implementing our risk management policy and carrying out our

day-to-day risk management practice. In order to formalize risk management across our Group and set a common level of transparency and risk management performance, the relevant departments will (i) gather information about the risks relating to their operation or function; (ii) conduct risk assessments, which include the identification, prioritization, measurement and categorization of all key risks that could potentially affect their objectives; (iii) prepare a risk management report annually for our chief executive officer's review; (iv) continuously monitor the key risks relating to their operation or function; (v) implement appropriate risk responses where necessary; and (vi) develop and maintain an appropriate mechanism to facilitate the application of our risk management framework.

We consider that our Directors and members of our senior management possess the necessary knowledge and experience in providing good corporate governance oversight in connection with risk management and internal control.

Internal Control

Our Board is responsible for establishing our internal control system and reviewing its effectiveness. We have engaged an independent internal control consultant, or the Internal Control Consultant, to perform certain agreed-upon procedures, or the Internal Control Review, in connection with the internal control of our Company and our major operating subsidiaries and to report factual findings on our Group's entity-level controls and internal controls of various processes, including financial reporting and disclosure controls, accounts receivable management, procurement, accounts payable and payment, fixed assets management, human resources and payroll management, cash and treasury management, inventory management, general controls of IT system, taxation management, contract management. The Internal Control Consultant performed the Internal Control Review in April 2018 and a follow-up review in May 2018. As of the Latest Practicable Date, there were no material outstanding issues relating to our Group's internal control.

During the Track Record Period, we regularly reviewed and enhanced our internal control system. Below is a summary of the internal control policies, measures and procedures we have implemented or plan to implement:

- We have adopted various measures and procedures regarding each aspect of our business operation, such as related party transaction, risk management, protection of intellectual property, environmental protection and occupational health and safety. For more information, see "– Intellectual Property" and "– Environmental Matters and Workplace Safety." We provide periodic training about these measures and procedures to our employees as part of our employee training program. Our internal audit department conducts audit field work to monitor the implementation of our internal control policies, reports the weakness identified to our management and audit committee and follows up on the rectification actions.
- Our Directors (who are responsible for monitoring the corporate governance of our Group) with help from our legal advisers, will also periodically review our compliance status with all relevant laws and regulations after the Listing.

- We have established an audit committee which (i) makes recommendations to our Directors on the appointment and removal of external auditors; and (ii) reviews the financial statements and renders advice in respect of financial reporting as well as oversees internal control procedures of our Group.
- We have engaged Guotai Junan Capital Limited as our compliance adviser to provide advice to our Directors and management team until the end of the first fiscal year after the Listing regarding matters relating to the Listing Rules. Our compliance adviser is expected to ensure our use of funding complies with the sections entitled "Future Plans and Use of Proceeds" in this prospectus after the Listing, as well as to provide support and advice regarding requirements of relevant regulatory authorities in a timely fashion.
- We plan to engage a PRC law firm to advise us on and keep us abreast with PRC laws and regulations after the Listing. We will continue to arrange various trainings to be provided by external legal advisers from time to time when necessary and/or any appropriate accredited institution to update our Directors, senior management, and relevant employees on the latest PRC laws and regulations.
- We maintain strict anti-corruption policies among our sales personnel and distributors in our sales and marketing activities and we believe we will therefore be less affected by the increasingly stringent measures taken by the PRC government to correct corruptive practices in the pharmaceutical industry. We also ensure that our sales and marketing personnel comply with applicable promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations, also known as off-label use, and limitations on industry-sponsored scientific and educational activities.