Certain information and statistics set out in this section and elsewhere in this Prospectus relating to the industry in which we operate are derived from the CIC Report[(1)] prepared by CIC, an independent industry consultant which was commissioned by us. The information extracted from the CIC Report should not be considered as a basis for investments in the Offer Shares or as an opinion of CIC as to the value of any securities or the advisability of investing in our Company. We believe that the sources of such information and statistics are appropriate for such information and statistics and have taken reasonable care in extracting and reproducing such information and statistics. We have no reason to believe that such information and statistics are false or misleading or that any fact has been omitted that would render such information and statistics false or misleading in any material respect. Our Directors have further confirmed, after making reasonable enquiries and exercising reasonable care, that there is no adverse change in the market information since the date of publication of the CIC Report or any of the other reports which may qualify, contradict or have an impact on the information in this section. No independent verification has been carried out on such information and statistics by us, the Joint Sponsors, the Joint Global Coordinators, the Joint Bookrunners, the Joint Lead Managers, the Underwriters or any other parties (other than CIC) involved in the Global Offering or their respective directors, officers, employees, advisers, or agents, and no representation is given as to the accuracy or completeness of such information and statistics. Accordingly, you should not place undue reliance on such information and statistics. Unless and except for otherwise specified, the market and industry information and data presented in this Industry Overview section is derived from the CIC Report.

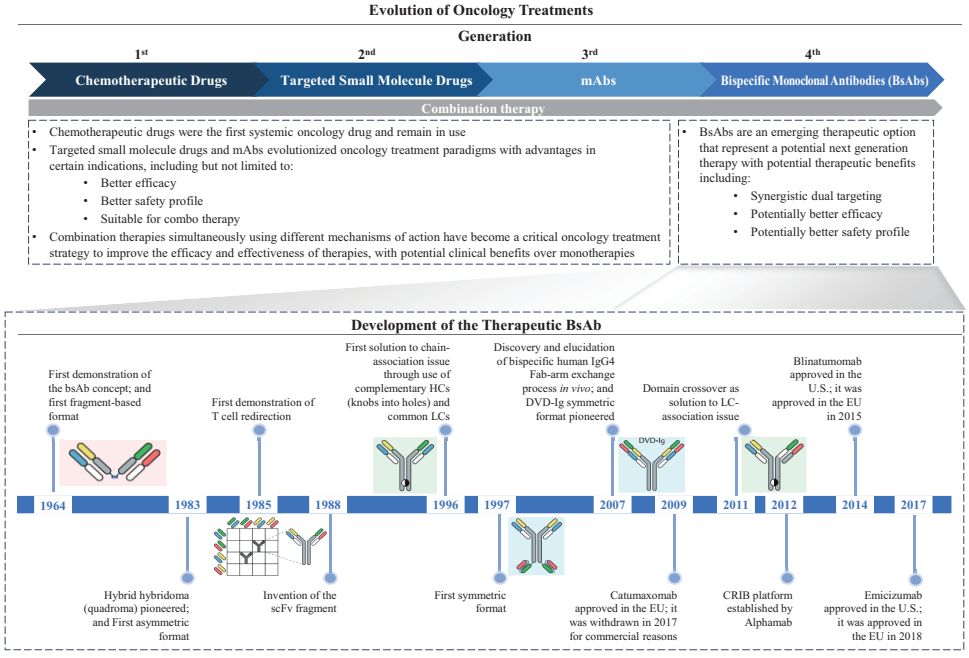
OVERVIEW OF ONCOLOGY DRUG MARKET IN THE PRC AND UNITED STATES

Oncology treatments have undergone significant development over the years, with chemotherapeutic drugs, targeted small molecule drugs and mAbs becoming the major oncology treatments available to date. The typical mechanism of action of chemotherapeutic drugs is to interrupt the cell cycle and slow down or completely stop tumor cells from reproducing. Chemotherapeutic drugs are the first systemic drugs to treat cancer. Although widely used in a broad range of indications, they frequently cause severe side effects. Since the early 2000s, there has been major progress in developing targeted small molecule drugs and mAbs, which have revolutionized oncology treatments, many of which have become global blockbuster drugs. Targeted small molecule drugs generally interfere with specific intracellular

(1) The contract sum to CIC is RMB790,000 for the preparation and use of the CIC Report, and we believe that such fees are consistent with the market rate. CIC is an independent consulting firm founded in Hong Kong. It offers industry research and market strategies and provides growth consulting and corporate training. In compiling and preparing the CIC Report, CIC has adopted the following assumption: (i) the overall social, economic and political environment in the PRC is expected to remain stable during the forecast period; (ii) PRC's economic and industrial development is likely to maintain a steady growth trend over the next decade; (iii) related key industry drivers are likely to continue driving the growth of the global and PRC's biologics and BsAbs market during the forecast period, such as the increasing number of new cancer incidences, increasing number of biologics and BsAbs drugs, supportive government programs and policies, increasing amount of R&D expenditures and improved affordability of drugs; and, (iv) there is no extreme force majeure or industry regulation in which the market may be affected dramatically or fundamentally. CIC conducted both primary and secondary research using a variety of resources. Primary research involved interviewing key industry experts and leading industry participants. Secondary research involved analyzing data from various publicly available data sources, such as the National Bureau of Statistics of the PRC, the International Monetary Fund, World Health Organization, U.S. Food and Drug Administration, Global Health Data Exchange, National Medical Products Administration of China and National Health Commission of the People's Republic of China.

signaling that drives tumor growth and metastasis. The mAbs are the largest category of therapeutic biologics and are used in targeted therapy and immuno-oncology therapy, which have generally shown higher efficacy and lower toxicity in treating cancers than chemotherapy. The mAbs target tumor-selective antigens with a high degree of target specificity, which reduces off-target toxicity and side effects, and have gained increasing acceptance among patients and doctors. Geographically, the United States and the PRC are the two most promising therapeutic biologics markets based on historical and forecast growth. In particular, the PRC, with enhanced patient awareness and broader reimbursement coverage is expected to experience the highest growth compared with other markets, with its therapeutic biologics market size expected to increase at a CAGR of 22.0% from 2018 to 2030.

Different types of oncology drugs can be used in combination treatments to achieve better therapeutic effects. In recent years, combination therapies of two or more mAbs, as well as mAb-based therapy in combination with chemotherapeutic drugs and targeted small molecule drugs, have been increasingly used. In addition, there is emerging research and development on bispecific monoclonal antibody (BsAb) drugs. BsAb is used to describe a large family of molecules designed to recognize two different epitopes or antigens. The original concept of an antibody-based molecule with two different antigen-binding sites was first introduced more than 50 years ago. The subsequent conceptual and technical innovations in generating BsAbs evolved alongside the landmark advances in the fields of antibody engineering and antibody biology. The following diagram illustrates the evolution path of oncology drugs.

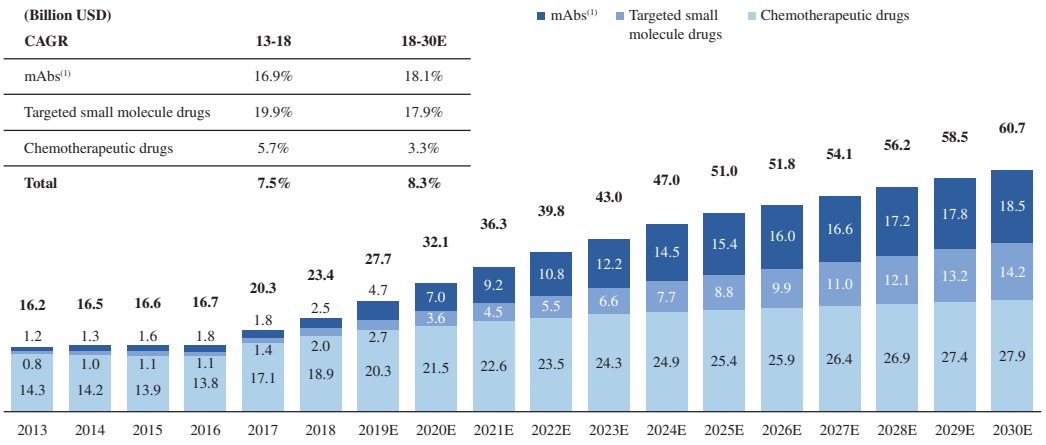


Abbreviations: HC = heavy chain, LC = light chain, DVD-Ig = Dual-variable domain immunoglobulin
Source: CIC Report

BsAbs, with the natural advantage of containing two different antigen-binding sites, are considered as next-generation antibody drugs, especially for oncology. BsAbs are expected to achieve potentially enhanced anti-tumor efficacy through synergistic signaling inhibition effects, acceleration of tumor cell degradation and enhancement of immune responses modulation. BsAbs can also provide improved tumor targeting specificity by recognizing two functionally-complementary tumor-associated antigens.

The following graph sets forth the historical and forecast market size of the oncology drug market in the PRC in terms of sales revenue by therapy for the periods indicated. The PRC oncology drug market grew from US$16.2 billion in 2013 to US$23.4 billion in 2018 in terms of sales revenue, and is expected to reach US$60.7 billion in 2030, representing a CAGR of 8.3% from 2018. mAbs represent the fastest growing therapy type, with a 18.1% CAGR from 2018 to 2030.

2013-2030E Oncology Drugs Market Size in the PRC

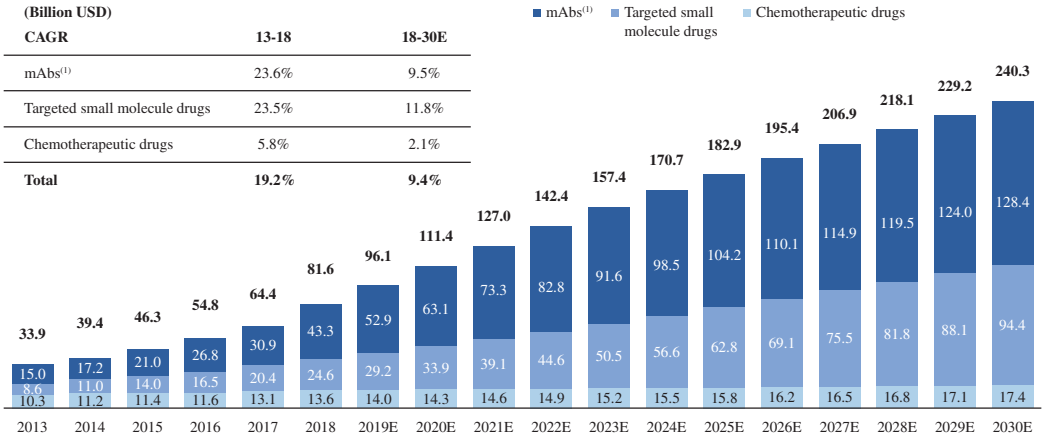


(1) The mAbs include monospecific antibodies and bispecific antibodies and exclude ADCs.

Source: CIC Report

The following graph sets forth the historical and forecast market size of the oncology drug market in the United States in terms of sales revenue by therapy for the periods indicated. In the United States, the oncology drug market grew from US$33.9 billion in 2013 to US$81.6 billion in 2018 in terms of sales revenue, and is expected to reach US$240.3 billion in 2030, representing a CAGR of 9.4% from 2018.

2013-2030E Oncology Drugs Market Size in the U.S.



(1) The mAbs include monospecific antibodies and bispecific antibodies and exclude ADCs.

Source: CIC Report

The mAb market has been a fast-growing segment of the oncology drug market in the PRC and the U.S. The mAb market grew at a CAGR of 16.9% and 23.6% in the PRC and the United States, respectively, from 2013 to 2018. The PRC mAb market is expected to continue its growth trend at a CAGR of 18.1% from 2018 and reach US$18.5 billion in 2030. In the United States, in terms of the sales revenue, the mAb market is expected to continue to be the largest segment of the oncology drug market, and is expected to reach US$128.4 billion in 2030.

The large oncology drug market is directly correlated to patient population. From 2013 to 2018, total cancer incidence in the PRC increased from 3.7 million to 4.4 million, whereas the total cancer incidence in the United States increased slightly from 1.6 million to 1.8 million. Cancer incidence in the PRC and United States is projected to reach 5.8 million and 2.4 million by 2030, respectively. The following tables set forth the cancer incidence by cancer types in the PRC and United States for the periods indicated.

Incidence by Cancer Types in the PRC, 2013-2030E

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Cancer Types	2013	2014	2015	2016	2017	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Lung	732.8	781.0	787.0	823.6	856.6	886.3	916.4	946.8	977.7	1,008.8	1,040.2	1,071.8	1,103.8	1,136.0	1,168.5	1,201.2	1,234.1	1,267.1
Stomach	427.1	410.0	403.0	435.1	459.5	482.5	500.3	514.1	525.0	533.6	542.1	550.5	558.9	567.2	575.4	583.6	591.7	599.8
Colon and rectum	347.9	370.0	388.0	399.2	410.6	422.1	433.8	445.6	457.5	469.6	481.8	494.1	506.6	519.1	531.9	544.7	557.7	570.8
Liver	362.4	365.0	370.0	389.5	406.6	421.5	434.4	447.5	460.6	473.8	487.1	500.4	513.8	527.2	540.7	554.2	567.8	581.3
Breast	278.8	279.0	304.0	308.8	311.5	321.2	330.5	339.3	347.6	355.5	362.9	369.9	376.4	382.4	388.0	393.2	398.0	402.4
Esophagus	276.9	258.0	246.0	272.3	295.5	315.6	332.8	347.4	359.6	370.9	381.3	390.9	399.6	407.5	414.7	421.2	427.0	432.2
Thyroid	143.9	170.0	201.0	202.4	203.7	206.6	209.5	212.3	215.0	217.6	220.2	222.7	225.2	227.6	229.9	232.1	234.2	236.3
Brain, CNS	95.9	101.0	106.0	109.9	112.8	115.7	118.3	120.8	123.1	125.2	127.2	129.0	130.6	132.2	133.5	134.8	135.9	136.9
Cervix	100.7	102.0	111.0	112.3	113.4	114.6	115.7	116.7	117.8	118.8	119.7	120.6	121.5	122.3	123.1	123.9	124.7	125.4
Pancreas	88.4	92.0	95.0	98.5	101.7	105.0	108.4	111.8	115.3	118.8	122.4	126.1	129.8	133.6	137.4	141.4	145.3	149.4
Top 10	**2,854.8**	**2,928.0**	**3,011.0**	**3,151.6**	**3,271.9**	**3,391.1**	**3,500.1**	**3,602.3**	**3,699.2**	**3,792.6**	**3,884.9**	**3,976.0**	**4,066.2**	**4,155.1**	**4,243.1**	**4,330.3**	**4,416.4**	**4,501.6**
Bladder	74.4	78.0	81.4	84.6	87.9	89.7	94.4	97.7	101.1	104.4	107.7	111.1	114.4	117.8	121.1	124.4	127.7	131.0
Gallbladder	49.6	52.0	54.3	56.4	58.6	60.1	63.1	65.4	67.7	70.1	72.5	74.9	77.4	79.9	82.4	84.9	87.5	90.1
Ovary	50.0	51.0	53.1	55.0	55.5	56.7	57.9	59.0	60.0	61.0	61.9	62.8	63.6	64.3	65.0	65.7	66.2	66.8
Soft tissue sarcoma	45.9	46.9	47.9	48.9	49.9	50.9	51.9	52.9	53.9	54.9	55.9	56.9	57.9	58.9	59.9	60.9	61.9	62.9
Nasopharynx	42.1	45.0	46.6	47.4	47.6	48.0	50.3	51.2	52.0	52.9	53.7	54.5	55.3	56.0	56.7	57.4	58.1	58.8
Melanoma	6.7	7.0	7.3	7.6	7.9	7.9	8.3	8.5	8.7	8.9	9.1	9.3	9.4	9.6	9.8	10.0	10.1	10.3
Others	558.5	596.1	627.4	638.9	648.6	664.7	680.8	697.0	713.1	729.1	745.0	760.8	776.4	792.2	807.7	822.9	838.2	853.1
All cancer types	**3,682.0**	**3,804.0**	**3,929.0**	**4,090.4**	**4,227.9**	**4,369.1**	**4,506.8**	**4,634.0**	**4,755.7**	**4,873.9**	**4,990.7**	**5,106.3**	**5,220.6**	**5,333.8**	**5,445.7**	**5,556.5**	**5,666.1**	**5,774.6**

Incidence by Cancer Types in the U.S., 2013-2030E

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Cancer Types	2013	2014	2015	2016	2017	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Breast	238.2	241.9	247.4	247.4	270.9	287.2	298.5	306.3	314.4	322.6	330.9	339.5	348.3	357.2	366.4	375.8	385.4	395.3
Lung	217.6	219.3	221.1	216.9	234.1	245.6	253.4	258.8	263.9	268.6	273.1	277.4	281.4	285.2	288.8	292.3	295.6	298.7
Prostate	186.6	180.3	191.5	193.8	207.2	217.6	225.7	232.0	238.4	245.0	251.6	258.3	265.1	272.1	279.1	286.3	293.6	301.0
Colon and rectum	140.2	142.8	143.4	141.7	153.7	162.1	168.0	172.2	176.4	180.7	185.1	189.5	193.9	198.5	203.1	207.7	212.4	217.2
Melanoma	74.0	78.3	81.9	82.0	83.6	85.3	87.0	88.7	90.5	92.2	93.9	95.7	97.5	99.2	101.0	102.9	104.7	106.6
Bladder	73.1	74.0	74.3	73.2	77.8	80.8	82.9	84.4	85.8	87.3	88.8	90.3	91.8	93.3	94.9	96.4	98.0	99.5
NHL	69.1	70.2	71.0	68.4	73.6	77.1	79.5	81.1	82.7	84.1	85.5	86.8	88.0	89.2	90.3	91.3	92.3	93.3
Kidney	58.6	60.7	62.7	63.5	65.0	66.6	68.2	69.8	71.4	73.1	74.7	76.4	78.1	79.9	81.6	83.4	85.2	87.0
Uterine	51.6	53.7	55.3	57.0	58.8	60.6	62.3	64.1	65.9	67.6	69.4	71.1	72.9	74.6	76.4	78.2	79.9	81.6
Leukemia	50.4	51.2	51.2	48.0	52.7	55.3	56.7	57.6	58.4	59.2	59.9	60.7	61.3	62.0	62.6	63.2	63.8	64.3
Top 10	**1,159.4**	**1,172.4**	**1,199.8**	**1,191.9**	**1,277.4**	**1,338.2**	**1,382.2**	**1,415.0**	**1,447.8**	**1,480.4**	**1,512.9**	**1,545.7**	**1,578.3**	**1,611.2**	**1,644.2**	**1,677.5**	**1,710.9**	**1,744.5**
Liver	30.8	32.7	34.0	33.5	34.5	35.5	36.5	37.4	38.4	39.4	40.3	41.3	42.3	43.2	44.2	45.1	46.1	47.0
Stomach	23.8	24.3	24.2	24.2	25.9	27.1	27.9	28.4	29.0	29.5	30.1	30.7	31.2	31.8	32.4	33.0	33.6	34.2
Ovary	21.6	21.6	21.8	20.4	22.7	23.9	24.5	24.9	25.3	25.6	26.0	26.4	26.8	27.1	27.5	27.9	28.3	28.7
Soft tissue sarcoma	11.8	12.0	12.2	12.4	12.6	12.8	13.0	13.2	13.3	13.5	13.6	13.8	13.9	14.0	14.1	14.2	14.3	14.4
Gallbladder	4.0	4.2	4.1	4.1	4.6	5.0	5.3	5.5	5.7	5.9	6.1	6.2	6.4	6.5	6.7	6.8	6.9	7.0
Nasopharynx	2.1	2.1	2.1	2.2	2.3	2.3	2.3	2.4	2.4	2.4	2.5	2.5	2.5	2.5	2.6	2.6	2.6	2.6
Others	368.1	379.1	386.0	383.6	395.6	405.1	412.8	419.5	426.1	433.0	440.0	446.8	454.2	461.9	469.4	477.5	485.8	494.7
All cancer types	**1,621.6**	**1,648.4**	**1,684.2**	**1,672.3**	**1,775.6**	**1,849.9**	**1,904.5**	**1,946.3**	**1,988.0**	**2,029.7**	**2,071.5**	**2,113.4**	**2,155.6**	**2,198.2**	**2,241.1**	**2,284.6**	**2,328.5**	**2,373.1**

Source: NCCR, NAACCR, CIC Report

According to CIC, the top 10 most prevalent cancer indications by incidence are considered major cancer indications. The aggregate incidence of the ten most prevalent cancer types in the PRC and the United States accounted for 77.6% and 72.3%, respectively, of total cancer incidence, reaching 3.4 million and 1.3 million in 2018, respectively. Lung, colorectal and breast cancers are among the most prevalent cancer types in both countries. Certain subtypes of gastrointestinal cancers, especially gastric cancer, and esophageal cancer, have higher incidence rates in the PRC than in the United States. The number of addressable patients in China in 2018 for late-line unresectable metastatic NPC, locally advanced unresectable or metastatic NSCLC excluding EGFR mutation and ALK translocation, locally advanced or metastatic TNBC, and second-line pancreatic cancer, each being a targeted subset of main indications of KN046, our Core Product, was estimated to be 6,700, 21,700, 22,900 and 52,500, respectively, and is expected to increase at a CAGR of 1.7%, 3.0%, 1.9% and 3.0% from 2018 to 2030, respectively. The oncology drug market size for each specific indication is expected to be correlated to the relevant patient population.

In addition to the large and growing patient pool, the future growth of the oncology drug markets in the PRC and the United States is expected to be primarily driven by (i) the launch of new therapies through continued R&D investment, such as combination therapies and innovative BsAbs for new indications with better efficacy and safety profiles; (ii) expanded usage at different stage of cancer treatments, including neoadjuvant and adjuvant treatments; (iii) extended therapeutic window leading to longer survival of patients; (iv) formulations with improved safety and convenience that enables long-term maintenance usage; (v) potential off-label uses that may accelerate accessibility of drugs to certain diseases not covered by current clinical trial scheme.

In the PRC, there is significant under-penetration in cancer treatment, particularly in immuno-oncology, with a large number of cancer patients needing better treatment. Improved affordability and supportive policies for new drug development and approval are expected to also contribute to faster growth of the oncology drug market in the PRC.

OVERVIEW OF THE IMMUNE CHECKPOINT INHIBITOR MARKET IN THE PRC AND UNITED STATES

Overview of Immune Checkpoint Inhibitor Against PD-(L)1[(2)] and CTLA-4

Immuno-oncology therapy represents a new paradigm of oncology treatment. Immuno-oncology therapy stimulates the patient's own immune system to generate or augment anti-tumor immune responses to fight cancer cells. Major types of immuno-oncology therapy include immune checkpoint inhibitors, cytokines, adoptive T-cell therapy and cancer vaccines. In recent years, immune checkpoint inhibitors have garnered attention as being one of the most promising types of immuno-oncology therapy.

Immune checkpoint inhibitors in the form of monoclonal antibodies (mAbs) against three validated targets, i.e., PD-1, PD-L1 and CTLA-4, are among the major immune-oncology therapies. Currently available clinical data suggests almost all the ten most prevalent cancer types in the PRC and the United States, including the most prevalent ones in both countries (i.e. lung, breast, colorectal, gastric, liver, esophageal cancers) proved to be the most responsive to immune checkpoint inhibitors. To date, the indication coverage of immune checkpoint inhibitors has been continuously expanded in line with increasing clinical trials worldwide.

To date, there are six PD-(L)1 inhibitors and one CTLA-4 inhibitor approved in the global market outside the PRC, and five PD-1 inhibitors approved in the PRC. All of these are monospecific mAbs. Dual targeting of immune checkpoints has become an important cancer treatment strategy, as combination therapies using checkpoint inhibitors as components have demonstrated enhanced efficacy in certain indications compared with single-agent immunotherapies.

In 2018, the global sales of immune checkpoint inhibitors reached US$20.7 billion, indicating a vast market. The immune checkpoint inhibitor market in the United States experienced rapid growth from US$650.2 million in 2013 to US$13.3 billion in 2018 in terms of sales revenue, representing a CAGR of 82.8% and is expected to continue to grow to US$41.4 billion in 2030, representing a CAGR of 10.0% from 2018. The market size of PD-(L)1 inhibitors in the United States was US$12.2 billion in 2018, and is expected to increase to US$36.3 billion in 2030, representing a CAGR of 9.5%. The market size of CTLA-4 inhibitors in the United States was US$1.1 billion in 2018, and is expected to increase to US$5.1 billion in 2030 at a CAGR of 14.0%.

The PRC immune checkpoint inhibitor market, with the first two PD-1 inhibitors approved in 2018, is expected to grow rapidly to US$11.3 billion in 2030 in terms of sales revenue, representing a CAGR of 45.2% from 2018. The market size of PD-(L)1 inhibitors in the PRC was US$0.1 billion in 2018, and is expected to grow to US$10.4 billion in 2030, with a CAGR of 44.2%. Currently, there are no approved CTLA-4 inhibitors in the PRC. The first CTLA-4 inhibitor is estimated to be approved in 2019, considering the average time for drug

(2) Consistent with industry usage of the term, unless otherwise indicated, PD-(L)1 in this section refers to either PD-1 or PD-L1.

candidates to receive BLA approval and that two CTLA-4 inhibitor candidates, namely, BMS's Yervoy and AstraZeneca's tremelimumab, are in phase III clinical trial stage. The market size of CTLA-4 inhibitors in the PRC is expected to be US$0.2 billion in 2019, and is expected to increase to US$0.9 billion in 2030, representing a CAGR of 17.2% from 2019 to 2030.

Overview of Anti-PD-(L)1/CTLA-4 BsAb Market in the PRC and United States

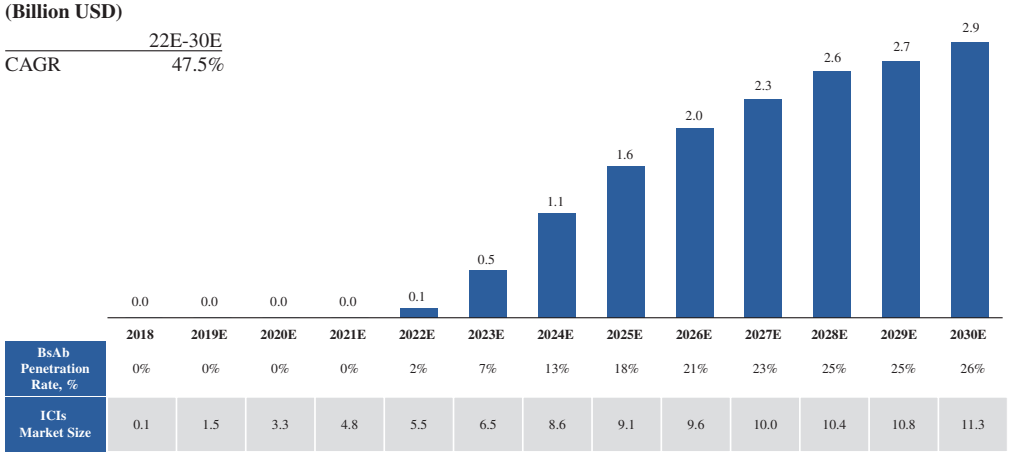
Dual blockade of immune checkpoints with BsAbs are expected to induce potentially superior biological effects previously unattainable with monospecific mAbs. As of April 24, 2019, there were 85 BsAbs in clinical trials, of which 58 candidates use the immune cells engagement mechanism, including immune checkpoints.

Addressable Market Size of Anti-PD-(L)1/CTLA-4 BsAbs in the PRC and United States

The total addressable market size of anti-PD-(L)1/CTLA-4 BsAbs is directly correlated to the addressable patient size with anti-PD-(L)1/CTLA-4 BsAbs. The total addressable patient size of anti-PD-(L)1/CTLA-4 BsAbs in the PRC and the United States refers to the patient population for immune checkpoint inhibitors against PD-(L)1 and/or CTLA-4 with cancer indications that have been approved, or were in clinical trials and could potentially be approved, in each country as of August 31, 2019, which is estimated to be approximately 3.6 million and 1.4 million in 2018, respectively.

The following graph sets forth the estimated market size of anti-PD-(L)1/CTLA-4 BsAbs in the PRC for the periods indicated and the underlying assumptions. The first anti-PD-(L)1/CTLA-4 BsAb is expected to be launched in China in 2022. The market size of anti-PD-(L)1/CTLA-4 BsAbs in the PRC is estimated to be US$0.1 billion in 2022, which is expected to increase to US$2.9 billion in 2030 at a CAGR of 47.5%.

Anti-PD-(L)1/CTLA-4 BsAb Market Size in the PRC

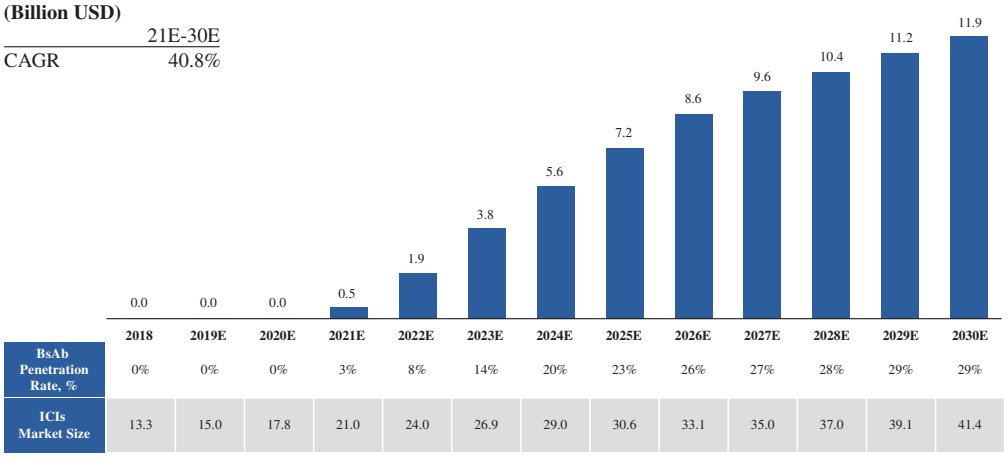


	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
BsAb Penetration Rate, %	0%	0%	0%	0%	2%	7%	13%	18%	21%	23%	25%	25%	26%
ICIs Market Size	0.1	1.5	3.3	4.8	5.5	6.5	8.6	9.1	9.6	10.0	10.4	10.8	11.3

Source: CIC Report

The following graph sets forth the estimated market size of anti-PD-(L)1/CTLA-4 BsAbs in the United States for the periods indicated and the underlying assumptions. The first anti-PD-(L)1/CTLA-4 BsAb is expected to be launched in the United States in 2021. The total market size of anti-PD-(L)1/CTLA-4 BsAbs in the United States is estimated to be US$0.5 billion in 2021, and increased to US$11.9 billion in 2030, representing a CAGR of 40.8%.

Anti-PD-(L)1/CTLA-4 BsAb Market Size in the U.S.



	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
BsAb Penetration Rate, %	0%	0%	0%	3%	8%	14%	20%	23%	26%	27%	28%	29%	29%
ICIs Market Size	13.3	15.0	17.8	21.0	24.0	26.9	29.0	30.6	33.1	35.0	37.0	39.1	41.4

Source: CIC Report

(1) ICIs market size refers to the total market size of immune checkpoint inhibitors, namely PD-1, PD-L1 and CTLA-4 inhibitors. The estimation of ICIs market size considers: (i) the total addressable patients that can be or potentially be treated by immune checkpoint inhibitors against PD-(L)1 and/or CTLA-4 considering currently approved indications in each respective country, as well as potential indications under clinical trials. Off-label prescriptions and any potential indication expansion achieved by anti-PD-(L)1/CTLA-4 BsAbs are not taken into consideration; (ii) the treatment rate that the percentage of total addressable patients is estimated to be treated by the immune checkpoint inhibitors, considering the proportion of respective gene mutation, the progression of the disease, the treatment line of indicated indications and the patient affordability; (iii) the average annual cost per patient, considering currently available pricing information of approved drugs, Patient Assistant Programs (PAPs) and the potential NRDL inclusion in the PRC.

(2) For the anti-PD-(L)1/CTLA-4 BsAbs market size, the forecasted anti-PD-(L)1/CTLA-4 BsAbs penetration rate in ICIs market took reference to (i) the percentage of treated patients of the anti-PD-(L)1/CTLA-4 combination therapy over total immune checkpoint inhibitors treated patients in indications of combo therapy; (ii) the anti-PD-(L)1/CTLA-4 BsAbs are assumed to cover all addressable indications mentioned in assumption 1 in 2030. The average annual cost per patient of anti-PD-(L)1/CTLA-4 BsAbs took reference to the average annual cost of comparable PD-(L)1s.

(3) The estimation of the anti-PD-(L)1/CTLA-4 BsAbs market size is the product of the ICIs market size and the anti-PD-(L)1/CTLA-4 BsAbs penetration rate. The total ICIs market size is assumed to be the largest possible market size that the anti-PD-(L)1/CTLA-4 BsAbs can potentially target, given no indication expansion is assumed.

(4) The launch year of the first anti-PD-(L)1/CTLA-4 BsAb is expected to be 2022 and 2021 in the PRC and the U.S., respectively, considering the current clinical trials information, the past duration of drug development and fast approvals achieved by currently marketed PD-(L)1 inhibitors.

Market Drivers and Trends

The primary market drivers and trends for the anti-PD-(L)1/CTLA-4 BsAb market include:

- *Indication expansion*. Previously untapped indications and new treatment lines for approved indications are being developed, which leads to growing addressable patient population. Anti-PD-(L)1/CTLA-4 BsAbs are expected to cover a broad spectrum of indications of PD-(L)1 or CTLA-4 inhibitors, either for approved indications or indications under development. From 2017 to 2019, 12 new indications obtained approvals for these immune checkpoint inhibitors, including

major treatment lines such as second line treatment for urothelial cancer and second line treatment for cervical cancer. There is also an increasing number of trials for anti-PD-(L)1/CTLA-4 BsAbs in the PRC and the United States covering more indications, with a total of six clinical trials for anti-PD-(L)1/CTLA-4 BsAb candidates targeting new indications in the PRC and United States as of August 31, 2019 including one in phase II stage. Anti-PD-(L)1/CTLA-4 BsAbs are expected to induce biological effects previously unattainable with current-generation immune checkpoint inhibitors, which is expected to lead to a higher likelihood of identifying and developing such antibody drugs for new indications in the foreseeable future.

- *Combination strategies.* Combination therapies of immune checkpoint inhibitors with other oncology drugs, including chemotherapy and targeted small molecule drugs, have become a popular strategy to improve response rates and overall survival benefit for patients. BsAb drugs are expected to also be used as a component in combination therapies. As of August 31, 2019, a majority of the clinical trials for anti-PD-(L)1/CTLA-4 BsAbs were in combination therapies in the PRC, and approximately 33% of clinical trials for anti-PD-(L)1/CTLA-4 BsAbs in the United States were exploring combination therapies, indicating an increasing commercial opportunity for anti-PD-(L)1/CTLA-4 BsAbs.

- *Advancement of precision medicine*. The emerging medical model of precision medicine, supported by the advent of new technologies, is expected to accelerate the development of anti-PD-(L)1/CTLA-4 BsAbs. For example, next-generation sequencing has facilitated identification of biomarkers which may broaden the coverage of cancer patients. Deepened understanding of the mechanism of immune suppression may also help boost the response rate of some patients. In addition, newly developed companion diagnostics have the potential to improve anti-PD-(L)1/CTLA-4 BsAb efficacy, ensure greater safety, shorten product lifecycles, and increase the response rate among patients.

Entry Barriers

There are a number of challenges in developing anti-PD-(L)1/CTLA-4 BsAbs, one of which is reducing the potential toxicity that is significantly intensified under a dual blockade mode, while still maintaining efficacy advantages over monotherapy. Researchers and developers have to select a proper molecule structure that links the proposed mechanisms of action with clinical applications, or develop a better CTLA-4 binding moiety, both of which require extensive engineering experience and a deep understanding of biotechnology. In addition, anti-PD-(L)1/CTLA-4 BsAbs are novel immune checkpoint inhibitors developed in a format that has not been fully validated, which increases the risks of unwanted immunogenicity, short half-life and side effects.

Competitive Landscape

As of the Latest Practicable Date, there has been no approved BsAb simultaneously targeting PD-(L)1 and CTLA-4; however, there are a number of anti-PD-(L)1/CTLA-4 BsAb candidates in clinical development in the PRC and the United States. Currently a majority of approved immune checkpoint inhibitors and candidates are PD-(L)1 inhibitors or CTLA-4 inhibitors. In addition, there is an approved PD-1/CTLA-4 dual blockade therapy that combines a PD-1 inhibitor (Opdivo) and a CTLA-4 inhibitor (Yervoy), and a number of late-stage combination therapies of PD-(L)1 inhibitors and CTLA-4 inhibitors with dual blockade effect in clinical development.

In addition to competing with each other, anti-PD-(L)1/CTLA-4 BsAb candidates are expected to compete with all of the monospecific immune checkpoint inhibitors targeting PD-1, PD-L1 or CTLA-4, including PD-(L)1 inhibitors, and combination therapies of PD-(L)1 and CTLA-4 inhibitors. Compared with monospecific checkpoint inhibitors, studies have

shown the dual blockade of both PD-(L)1 and CTLA-4 checkpoints can induce stronger anti-tumor responses in certain types of cancers than a single blockade of each agent, indicating potentially better efficacy of anti-PD-(L)1/CTLA-4 BsAbs than monospecific inhibitors in certain cancer indications.

PRC

As of August 31, 2019, there were only five approved PD-1 inhibitors in the immune checkpoint inhibitor market in the PRC against PD-(L)1 or CTLA-4. As of the same date, there were 21 PD-(L)1 inhibitor candidates registered with NMPA, 12 of which were at BLA stage or in phase III clinical trials. See "—Overview of PD-(L)1 Inhibitor Market in the PRC and United States—Competitive Landscape—PRC". In addition, there were four CTLA-4 candidates in the PRC as of August 31, 2019, two of which were in phase III clinical trials for NSCLC or SCLC.

As of August 31, 2019, there were three BsAb candidates targeting two different immune checkpoints in the PRC, including two anti-PD-(L)1/CTLA-4 BsAb candidates and one anti-PD-1/PD-L1 BsAb candidate. As of the same date, there were two combination therapy candidates of PD-(L)1 and CTLA-4 inhibitors in phase III clinical trials or later stage in the PRC. The following table sets forth the details of these drug candidates as of August 31, 2019.

Anti-PD-(L)1/CTLA-4 BsAb Candidates in the PRC

Drug candidate name(s)	Company	Immune checkpoint(s)	Indications	Clinical stage	First posted date	Route of entry
KN046	Alphamab	PD-L1/ CTLA-4	NSCLC	Phase II	Jan-2019	Intravenous
				Phase II (with chemo)	Jun-2019	
			ESCC	Phase II	May-2019	
			TNBC	Phase Ib/II (with chemo)	Apr-2019	
			Solid tumors	Phase I	Nov-2018	
AK104	Akeso Biopharma, Inc.	PD-1/CTLA-4	Solid tumors	Phase Ib/II	Dec-2018	Intravenous
			GC/GEJ	Phase Ib/II (with chemo)	Dec-2018	
IBI-318	Innovent	PD-1/PD-L1	Malignant neoplasm	Phase I	Mar-2019	Subcutaneous

Combination Therapy Candidates of PD-(L)1 and CTLA-4 Inhibitors (Phase III or Later Stage) in the PRC

Drug candidate name(s)	Company	Immune checkpoint(s)	Indications	Clinical stage	First posted date	Route of entry
Nivolumab/ Ipilimumab	BMS	PD-1/ CTLA-4	GC/GEJ	Phase III	May-2017	Intravenous
			SCLC	Phase III	Jul-2017	
			Pleural mesothelioma	Phase III	Sep-2017	
			ESCC	Phase III	Feb-2018	
			RCC	Phase III	Mar-2018	
			UC	Phase III	Jun-2018	
			NSCLC	Phase III	Apr-2017	
Durvalumab/ Tremelimumab	AstraZeneca/ MedImmune	PD-L1/ CTLA-4	NSCLC	Phase III	Jan-2017	Intravenous
			SCLC	Phase III	May-2018	
			HCC	Phase III	Jun-2018	

Source: NMPA, CIC Report (As of August 31, 2019)

United States

In the United States, as of August 31, 2019, there were six approved PD-(L)1 inhibitors. There were also a large number of monospecific inhibitor candidates against PD-(L)1 checkpoints for a number of indications in clinical trials. See "—Overview of PD-(L)1 Inhibitor Market in the PRC and United States—Competitive Landscape—United States". In addition, the FDA-approved Yervoy (ipilimumab) was the only approved CTLA-4 inhibitor on the market as first-line monotherapy for unresectable or metastatic melanoma and as a component of combination therapies for other indications. There were also a number of CTLA-4 inhibitor candidates under development in the United States, of which two candidates were in phase III clinical trials for a number of indications such as NSCLC and UC.

As of August 31, 2019, there was one FDA-approved combination therapy of PD-l inhibitor (Opdivo) and CTLA-4 inhibitor (Yervoy). As of the same date, there were three anti-PD-(L)1/CTLA-4 BsAb candidates in clinical trials or later stage, and four combination therapy candidates of PD-(L)1 and CTLA-4 inhibitors in phase III clinical trials or later stage in the United States, respectively. The following table sets forth the details of these drug candidates as of August 31, 2019.

Anti-PD-(L)1/CTLA-4 BsAb Candidates in the U.S.

Drug candidate name(s)	Company	Immune checkpoint(s)	Indications	Clinical stage	First posted date	Route of entry
MEDI5752	AstraZeneca	PD-1/CTLA-4	Solid tumors	Phase I (mono or with chemo)	May-2018	Intravenous
XmAb20717	Xencor, Inc.	PD-1/CTLA-4	Solid tumors	Phase I	May-2018	Intravenous
MGD019	MacroGenics, Inc.	PD-1/CTLA-4	Solid tumors	Phase I	Dec-2018	Intravenous

Approved Combination Therapy of PD-(L)1 and CTLA-4 Inhibitors in the U.S.

Trade name(s) (Generic name(s))	Company	Immune checkpoint(s)	Indications	Treatment line	Date of approval	Patent status	Price per unit	Route of entry
Opdivo (nivolumab)/ Yervoy (ipilimumab)	BMS	PD-1/CTLA-4	Unresectable or metastatic melanoma	2L	Jan-2016	Opdivo and Yervoy both covered by registered patents in the U.S.	US$2,830 for Opdivo (100mg/10ml), US$30,870 for Yervoy (200mg/40ml)	Intravenous
			Intermediate or poor risk advanced RCC	1L	Apr-2018			
			MSI-H or dMMR metastatic CRC	2L	Jul-2018			

Combination Therapy Candidates of PD-(L)1 and CTLA-4 Inhibitors (Phase III or Later Stage) in the U.S.

Drug candidate name(s)	Company	Immune checkpoint(s)	Indications	Clinical stage	First posted date	Route of entry
Nivolumab/ Ipilimumab	BMS	PD-1/CTLA-4	Glioblastoma	Phase III	Jan-2014	Intravenous
			RCC	Phase III	Oct-2014	
			Melanoma	Phase III	Mar-2015	
			NSCLC	Phase III	Aug-2015	
			HNSCC	Phase III	Aug-2016	
			GC/GEJ	Phase III	Oct-2016	
			Pleural mesothelioma	Phase III	Oct-2016	
			UC	Phase III	Mar-2017	
			Esophageal cancer	Phase III	Jun-2017	
			CRC	Phase III	Jul-2019	

Drug candidate name(s)	Company	Immune checkpoint(s)	Indications	Clinical stage	First posted date	Route of entry
Durvalumab/ Tremelimumab	AstraZeneca /MedImmune	PD-L1/ CTLA-4	NSCLC	Phase III	Jan-2015	Intravenous
			HNSCC	Phase III	Sep-2015	
			UC	Phase III	Nov-2015	
			SCLC	Phase III	Mar-2017	
			Solid tumors	Phase III	Apr-2017	
			HCC	Phase III	Oct-2017	
Pembrolizumab/ Ipilimumab	Merck	PD-1/CTLA-4	NSCLC	Phase III	Dec-2017	Intravenous
Cemiplimab/ Ipilimumab	Regeneron Pharmaceuticals, Inc./Sanofi S.A.	PD-1/CTLA-4	NSCLC	Phase III	Mar-2018	Intravenous

Source: FDA, CIC Report (As of August 31, 2019)

For the competitive landscape analysis, see "Business—Our Product Pipeline—Anti-PD-L1/CTLA-4 BsAb Candidate – KN046—Competition".

Overview of PD-(L)1 Inhibitor Market in the PRC and United States

PD-1 and PD-L1 inhibitors act through interfering with the PD-1/PD-L1 pathway, which prevents T-cells from attacking tumor cells within the tumor microenvironment. In the cancer disease state, the use of an inhibitor that blocks the interaction between PD-L1 and the PD-1 receptor can prevent certain tumor cells from evading the immune system. PD-1 and PD-L1 inhibitors are increasingly used for the treatment of many types of cancer, and have been proven to have a better efficacy profile and fewer side effects in a number of cancer indications than the current standard of care.

Market Size of PD-(L)1 Inhibitor Market in the PRC and United States

The first two blockbuster PD-1 inhibitors, Opdivo and Keytruda, were approved by NMPA in June and July 2018, respectively. Currently, there are five PD-1 inhibitors on the PRC market and 20 PD-(L)1 inhibitors at BLA stage or in phase III clinical trials. Considering the growing cancer patient population eligible for PD-(L)1 inhibitor treatment in line with expanding indications as well as the increasing accessibility, affordability and acceptance among patients and physicians of PD-(L)1 inhibitors, the total market size of PD-(L)1 inhibitors in the PRC is projected to grow from US$0.1 billion in 2018 to US$10.4 billion in 2030, representing a CAGR of 44.2%.

The market size of PD-(L)1 inhibitors in the United States has rapidly grown from US$71 million in 2014 to US$12.2 billion in 2018, representing a CAGR 261.5% due to their superior clinical efficacy and safety profiles. Since PD-(L)1 inhibitors are expected to cover more indications in the future, and as a growing number of combination therapies are being approved, the market for PD-(L)1 inhibitors is projected to grow to US$36.3 billion by 2030, with a CAGR of 9.5%.

Market Drivers and Future Trends

The primary market drivers and trends for the PD-(L)1 inhibitor market include:

- *Indication expansion.* The development of PD-(L)1 inhibitors increasingly focuses on indications with no coverage, especially those with sizeable patients or growing incidence rates, such as HCC and BTC in the PRC and esophageal cancer and ovarian cancer in the United States. In addition, there is a trend to use PD-(L)1 as maintenance therapy to avoid recurrent/refractory cancer, which in turn contributes to greater usage for PD-(L)1 inhibitors.

- *Increasing usage for approved indications.* Due to a better efficacy and safety profile, PD-(L)1 inhibitors are increasingly gaining acceptance among patients and physicians, and are emerging as the standard of care for a number of advanced-stage cancers, such as first-line treatment for melanoma and NSCLC, leading to a wider patient coverage for approved indications. In addition, the improved PFS and overall survival benefit for a number of major cancer types, such as urothelial cancer, melanoma and NSCLC, enables a longer treatment period and further increases demand for such drugs.

- *Combination strategy.* Combination therapies with immune checkpoint inhibitors as components are expected to improve the response rate and durability of monotherapies of the inhibitors, leading to potentially better efficacy for approved indications and efficacy in cancer types currently without effective treatments. As of August 31, 2019, there were 88 and 468 clinical trials with a PD-(L)1 inhibitor as a component in a combination therapy in the PRC and United States, respectively. The development of combination therapy increases the market potential for PD-(L)1 inhibitors.

- *Alternative formulations.* Subcutaneous formulation of PD-(L)1 inhibitors is expected to significantly improve patient care by providing (i) access to patients not suitable for intravenous infusions; and (ii) ease of administration leading to less frequent and shorter hospital visits. Subcutaneous administration typically lowers overall medical costs as less frequent and shorter hospital visits associated with subcutaneous administration reduce administrative costs, such as costs for medical personnel. In the case of Herceptin, its subcutaneous formulation saves approximately 30% to 65% in administrative costs to patients compared to intravenous administration, according to CIC. In addition, subcutaneous administration is expected to increase patient acceptance. Currently a number of drug makers are developing the subcutaneous formulation for PD-(L)1 inhibitors, which is expected to take approximately 15% market share of all sales of such inhibitors if the subcutaneous formulation is approved.

- *Improved affordability.* In the PRC, the PD-(L)1 inhibitor market is also driven by improved affordability. Increasing per capita disposable income and per capita healthcare expenditure (including the increasing purchase of private insurance), and the development of the PRC's national reimbursement system are factors that contribute to greater affordability of these relatively costly drugs for patients, thereby fueling market growth.

Entry Barriers

The increasing number of PD-(L)1 inhibitors approved or in the pipeline makes cost control of manufacturing a major focus for researchers and developers, imposing stricter requirements on the yield and efficiency of manufacturing processes. In addition, although subcutaneous administration is highly attractive for PD-(L)1 inhibitors, there are significant challenges in subcutaneous formulation development. This formulation requires a relatively large amount of drug in a very limited injection volume, resulting in a high drug concentration (over 200 mg/ml). However, a high drug concentration faces challenges of increased drug aggregation and viscosity as well as decreased stability.

Competitive Landscape

PRC

As of August 31, 2019, five PD-1 inhibitors were approved in the PRC, namely, BMS's Opdivo, Merck's Keytruda, Junshi's Tuoyi, Innovent's Tyvyt and Hengrui's Ailituo, and there were no approved PD-L1 inhibitors. As of August 31, 2019, there were 21 PD-(L)1 inhibitor candidates registered with the NMPA, of which two were BLA-stage PD-(L)1 inhibitors, and ten were PD-(L)1 inhibitor candidates in phase III clinical trials with a coverage of 17 indications, primarily including NSCLC, UC, ESCC, NPC and HCC. KN035 is the first drug candidate in a phase III clinical trial for BTC in the PRC. The following table sets forth the details of the five approved PD-(L)1 inhibitors in the PRC as of August 31, 2019.

Trade name (Generic name)	Company	Immune checkpoint	Indications	Treatment line	Date of approval	Patent status	Price per unit	Listed on NRDL/PRDL	Route of entry
Opdivo (nivolumab)	BMS	PD-1	EGFR/ALK negative locally advanced or metastatic NSCLC	2L	Jun-2018	Covered by registered patents in the PRC	RMB9,260 (100mg/10ml)	No	Intravenous
Keytruda (pembrolizumab)	Merck	PD-1	Unresectable or metastatic melanoma	2L	Jun-2018	Covered by registered patents in the PRC	RMB17,920 (100mg/4ml)	No	Intravenous
			EGFR/ALK negative metastatic non-squamous NSCLC	1L (with chemo)	Mar-2019				
Tuoyi (toripalimab)	Junshi	PD-1	Unresectable, metastatic malignant melanoma	⩾2L	Dec-2018	Covered by registered patents in the PRC	RMB7,200 (240mg/6ml)	No	Intravenous
Tyvyt (sintilimab)	Innovent	PD-1	Refractory Hodgkin's lymphoma	3L	Dec-2018	Covered by registered patents in the PRC	RMB7,840 (100mg/10ml)	No	Intravenous
Ailituo (camrelizumab)	Hengrui	PD-1	Refractory Hodgkin's lymphoma	3L	May-2019	Covered by registered patents in the PRC	RMB19,800 (200mg)	No	Intravenous

Source: NMPA, CIC Report (As of August 31, 2019)

United States

As of August 31, 2019, there were three approved PD-1 inhibitors, being BMS's Opdivo, Merck's Keytruda and Sanofi S.A. and Regeneron Pharmaceuticals, Inc.'s Libtayo, and three approved PD-L1 inhibitors, namely, Roche's Tecentriq, Merck KGaA and Pfizer's Bavencio and AstraZeneca and MedImmune's Imfinzi. As of the same date, there were eight PD-(L)1 inhibitor candidates in phase III clinical trials with a coverage of 19 indications, primarily including esophageal cancer, ovarian cancer, prostate cancer and multiple myeloma. The following table sets forth the details of the six approved PD-(L)1 inhibitors in the United States as of August 31, 2019.

Trade name (Generic name)	Company	Immune checkpoint	Indications	Treatment line	Date of approval	Patent status	Price per unit	Route of entry
Opdivo (nivolumab)	BMS	PD-1	Unresectable or metastatic melanoma	2L	Dec-2014	Covered by registered patents in the U.S.	US$2,830 (100mg/10ml)	Intravenous (subcutaneous administration under clinical trial)
			Metastatic NSCLC	2L	Oct-2015			
			Advanced renal cell carcinoma	2L	Nov-2015			
			Classical Hodgkin lymphoma	⩾3L	May-2016			
			Recurrent or metastatic squamous cell carcinoma of the head and neck	2L	Nov-2016			
			Locally advanced or metastatic urothelial carcinoma	2L	Feb-2017			
			MSI-H or dMMR metastatic CRC	2L	Aug-2017			
			HCC	2L	Sep-2017			
			Metastatic SCLC	3L	Aug-2018			

Trade name (Generic name)	Company	Immune checkpoint	Indications	Treatment line	Date of approval	Patent status	Price per unit	Route of entry
Keytruda (pembrolizumab)	MSD	PD-1	Unresectable or metastatic melanoma	1L	Sep-2014	Covered by registered patents in the U.S.	US$5,010 (100mg/4ml)	Intravenous
			Metastatic NSCLC	1L (mono or with chemo)	Oct-2015			
			Recurrent or metastatic HNSCC	1L	Aug-2016			
			Refractory cHL	⩾3L	Mar-2017			
			Locally advanced or metastatic urothelial carcinoma	2L	May-2017			
			Unresectable or metastatic, MSI-H or dMMR solid tumors or CRC	⩾3L	May-2017			
			Recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma	⩾3L	Sep-2017			
			Refractory PMBCL	3L	Jun-2018			
			Recurrent or metastatic cervical cancer	1L	Jun-2018			
			HCC	2L	Nov-2018			
			Locally advanced or metastatic Merkel cell carcinoma	1L	Dec-2018			
			Adjuvant treatment melanoma with involvement of lymph node(s)	adjuvant	Feb-2019			
			Advanced RCC	1L (with Axitinib)	Apr-2019			
			Metastatic SCLC	>2L	Jun-2019			
			Recurrent locally advanced or metastatic squamous cell carcinoma (esophageal cancer)	>2L	Jul-2019			
Libtayo (cemiplimab)	Regeneron Pharmaceuticals, Inc./Sanofi S.A.	PD-1	Locally advanced or metastatic CSCC	2L	Sep-2018	Covered by registered patents in the U.S.	US$9,510 (350mg/7ml)	Intravenous
Tecentriq (atezolizumab)	Roche/ Genentech	PD-L1	Locally advanced or metastatic urothelial carcinoma	2L	May-2016	Covered by registered patents in the U.S.	US$9,420 (1,200mg/20ml)	Intravenous
			Metastatic NSCLC	2L	Oct-2016			
			EGFR/ALK negative metastatic non-squamous NSCLC	1L (with Bevacizumab)	Dec-2018			
			Locally advanced or metastatic TNBC	1L (with chemo)	Mar-2019			
			Extensive-stage SCLC	1L (with chemo)	Mar-2019			
Bavencio (avelumab)	Merck KGaA/Pfizer	PD-L1	Metastatic Merkel cell carcinoma	2L	Mar-2017	Covered by registered patents in the U.S.	US$1,680 (200mg/10ml)	Intravenous
			Locally advanced or metastatic urothelial carcinoma	2L	May-2017			
			Advanced RCC	1L (with chemo)	May-2019			
Imfinzi (durvalumab)	AstraZeneca/ MedImmune	PD-L1	Locally advanced or metastatic urothelial carcinoma	2L	May-2017	Covered by registered patents in the U.S.	US$3,780 (500mg/10ml)	Intravenous
			Unresectable, Stage III NSCLC	2L	Feb-2018			

Source: FDA, CIC Report (As of August 31, 2019)

As of the Latest Practicable Date, KN035 had registered clinical trials with the NMPA for BTC (phase III), solid cancers with MSI-H or dMMR (pivotal phase II) and gastric cancer (phase II), and HCC (phase I). For the competitive landscape analysis, see "Business—Our Product Pipeline—Anti-PD-L1 sdAb Candidate – KN035—Competition".

OVERVIEW OF ANTI-HER2 MAB MARKET IN THE PRC AND UNITED STATES

HER2-overexpressing Cancers and Anti-HER2 mAbs

Human epidermal growth factor receptor 2 (HER2) is a validated molecular target for cancer therapy. Over-expression of HER2 proteins has been shown to play a critical role in the progression of malignancies, especially breast cancer, and is also associated with a number of other cancer types, including GC/GEJ, breast cancer, gallbladder cancer, ovarian cancer and colorectal cancer.

The level of overexpression of HER2 in tumors can be classified into HER2 High, HER2 Intermediate and HER2 Low by reference to immunohistochemistry (IHC) or fluorescence *in situ* hybridization (FISH) standards. Cancers with HER2 High expression are expected to be most sensitive to anti-HER2 mAbs. The table below sets forth the incidence of HER2 High expression in various cancer types.

Incidence rate of HER2 High expression of major cancer types

Cancer type	Incidence rate of HER2 High expression
Esophagus	15-39%
Endometrium	11-35%
Stomach	7-34%
Breast	15-30%
Ovary	5-30%
Pancreas	2-29%
Cervix	1-21%
Gallbladder	9-20%
Bladder[(1)]	5-15%
Colon	2-6%
Lung	1-5%
EGFR/ALK negative[(2)]	2-10%
Melanoma	0-5%

Reference: OMar-N. et al. (2015); Rüschoff, J. et al. (2012); Slamon, D.J. et al. (2001); Yan, M. et al. (2014); Yan, M. et al. (2015); Iqbal, N. et al. (2014); Li, K. et al. (2017)

(1) Including urothelial carcinoma.

(2) EGFR/ALK negative lung cancer patients represent 50-70% of the total lung cancer patients.

Source: CIC Report

There are only two approved anti-HER2 monospecific antibodies on the global market, namely trastuzumab and pertuzumab. Both of them are approved in the PRC and the United States. In 2018, the sales revenue of these drugs reached US$5.3 billion in the United States, and the sales revenue of trastuzumab and pertuzumab reached US$0.9 billion in the PRC.

Anti-HER2 BsAb Market in the PRC and United States

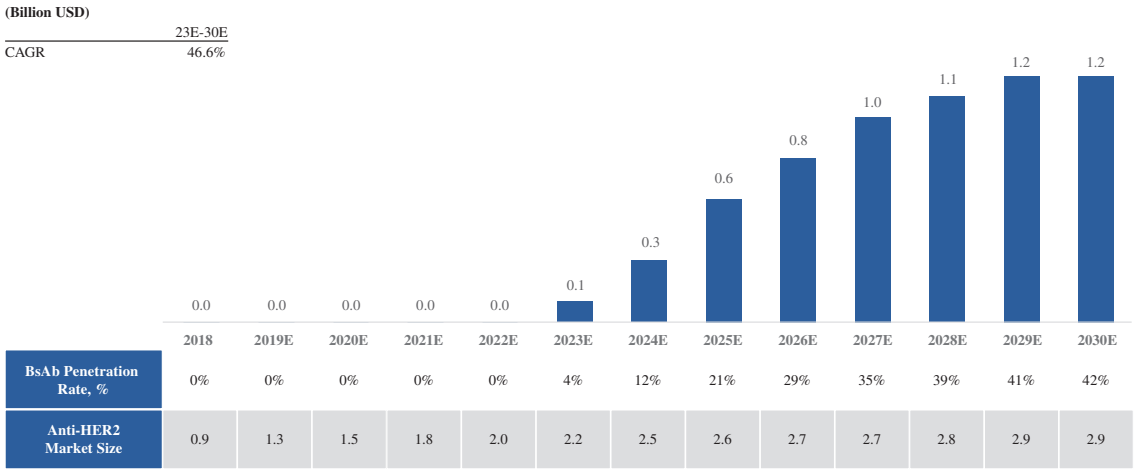
Compared with monospecific antibodies, the ability to bind two different antigens or epitopes simultaneously gives BsAbs potential advantages by blocking different signaling pathways. Major types of anti-HER2 BsAbs in clinical trials include those targeting HER2 and CD3, HER2 and HER3, HER2 and CD137, and two different epitopes of HER2. The bispecific binding mode results in a dual oncogenic signal blockade and overcomes drug resistance through synergistic mechanisms of action, and increases degradation of HER2 proteins on the tumor cell surface, leading to potentially superior anti-tumor efficacy. To date, there are no approved HER2 BsAbs on the market.

Addressable Market Size of Anti-HER2 BsAbs in the PRC and United States

The anti-HER2 BsAbs market is primarily driven by the number of addressable patients with HER2 High cancers. In the PRC, the estimated total addressable patient size of anti-HER2 BsAbs is approximately 0.4 million in 2018. This estimate represents the incidence of HER2 High breast and GC/GEJ, two approved indications for anti-HER2 mAbs in 2018, and the incidence of other potential HER2 High indications that are currently in clinical trials, such as urothelial and bladder cancer and NSCLC. In the United States, the total addressable patient size of anti-HER2 BsAbs is estimated to be approximately 0.2 million in 2018, covering patients with HER2 High breast and GC/GEJ, and other potential indications in clinical trials, such as ovarian cancer, bladder cancer, esophageal cancer, colorectal cancer and NSCLC. Breast cancer and gastric cancer are major indications of HER2-targeted therapies and the incidence rate of HER2 High expression level of breast cancer ranges from 15% to 30%, and such incidence rate of gastric cancer ranges from 7% to 34%, respectively. In general, approximately 81% of HER2-overexpressing breast cancer patients and 57% of HER2-overexpressing gastric cancer patients have low to intermediate HER2 expression level, which presents a large market potential for novel anti-HER2 drug candidates.

The following graph sets forth the estimated market size of anti-HER2 BsAbs in the PRC for the periods indicated and the underlying assumptions. The total market size of the anti-HER2 BsAbs market in the PRC is expected to reach US$0.1 billion in 2023, and is expected to further increase to US$1.2 billion in 2030, representing a CAGR of 46.6% from 2023 to 2030.

Anti-HER2 BsAb Market Size in the PRC

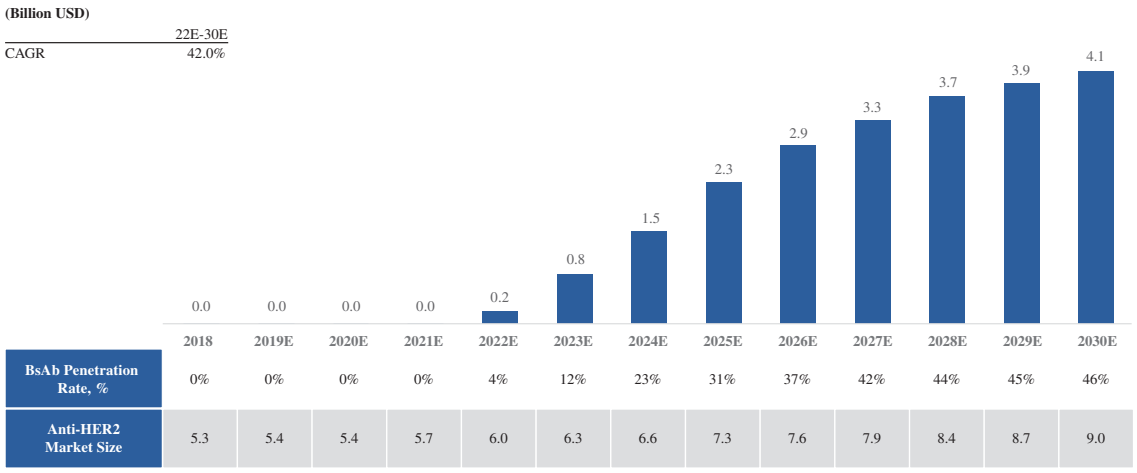


	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
BsAb Penetration Rate, %	0%	0%	0%	0%	0%	4%	12%	21%	29%	35%	39%	41%	42%
Anti-HER2 Market Size	0.9	1.3	1.5	1.8	2.0	2.2	2.5	2.6	2.7	2.7	2.8	2.9	2.9

Source: CIC Report

The following graph sets forth the estimated market size of anti-HER2 BsAbs in the United States for the periods indicated and the underlying assumptions. The total market size of the anti-HER2 BsAbs market in the United States is expected to reach US$0.2 billion in 2022, and is expected to further increase to US$4.1 billion in 2030, representing a CAGR of 42.0% from 2022 to 2030.

Anti-HER2 BsAb Market Size in the U.S.



	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
BsAb Penetration Rate, %	0%	0%	0%	0%	4%	12%	23%	31%	37%	42%	44%	45%	46%
Anti-HER2 Market Size	5.3	5.4	5.4	5.7	6.0	6.3	6.6	7.3	7.6	7.9	8.4	8.7	9.0

Source: CIC Report

(1) Anti-HER2 market size refers to the total market size of anti-HER2 mAbs treatment. The estimation of anti-HER2 market size considers: (i) the total addressable patients that can be or potentially be treated by mAbs against HER2 considering currently approved indications in each respective country, as well as potential indications under clinical trials. Off-label prescriptions and any potential indication expansion achieves by HER2 BsAbs are not taken into consideration; (ii) the treatment rate that the percentage of total addressable patients is estimated to be treated by the anti-HER2 mAbs, considering the proportion of respective gene mutation, the progression of the disease, the treatment line of indicated indications and the patient affordability; (iii) the average annual cost per patient, considering currently available pricing information of approved drugs, Patient Assistant Programs (PAPs) and the potential NRDL inclusion in the PRC.

(2) For HER2 BsAbs market size, the forecasted HER2 BsAbs penetration in anti-HER2 market took reference to (i) the percentage of treated patients of HER2 combo therapy over total HER2 treatment treated patients in indications of combo therapy; (ii) the HER2 BsAbs are assumed to cover all addressable indications mentioned in assumption 1 in 2030. The average annual cost per patient of HER2 BsAbs took reference to the average annual cost of comparable HER2 treatments.

(3) The estimation of HER2 BsAbs market size is the product of the anti-HER2 market size and the HER2 BsAbs penetration rate. The total anti-HER2 market size is assumed to be the largest possible market size that the HER2 BsAbs can potentially target, given no indication expansion is assumed.

(4) The launch year of HER2 BsAbs is expected to be 2023 and 2022 in the PRC and the U.S., respectively, considering the current clinical trials information, the past duration of drug development and clinical results achieved by currently marketed anti-HER2 mAbs.

Market Drivers and Trends

The primary market drivers and trends for the anti-HER2 BsAb market include:

- *Indication expansion outside of breast and gastric cancers.* Current anti-HER2 mAbs are only approved for HER2 High breast and GC/GEJ. However, there are various cancer types with high incidence rates of HER2 High expression, such as endometrial, cervical, urothelial and bladder, ovarian, colorectal and lung cancer, for which there are no approved HER2-targeted therapies, indicating significant unmet needs.

- *Combination therapies.* The observed difficulties in inactivating the significant amount of HER2 proteins on tumor cells with single drugs have driven the development of combinations with HER2-targeted drugs as a component. The combination therapy of trastuzumab, pertuzumab and chemotherapy has shown an improved overall survival benefit in women diagnosed with HER2 High metastatic breast cancer and has become the standard of care in the United States. As HER2-overexpressing cancer biology and resistance mechanisms become increasingly studied, combination therapies of HER2-targeted drugs including BsAbs with other oncology drugs like chemotherapeutic agents, PD-(L)1 inhibitors, endocrine therapy, and new anti-HER2 agents such as pan-HER and HER2 tyrosine kinase inhibitors are being extensively investigated in clinical trials. As of August 31, 2019, approximately 57% of anti-HER2 BsAb clinical trials in the United States deployed combination strategies.

- *Untapped patient population with cancers expressing HER2 at Low and Intermediate levels.* Approximately 66% of breast cancer patients and 24% of gastric cancer patients have HER2 Low to Intermediate expression and are ineligible for currently approved HER2-targeted therapies. Anti-HER2 BsAbs, in particular those targeting two different epitopes of HER2, have the potential to have a comparable or potentially better safety profile and better and longer endurable responses than existing anti-HER2 oncology mAbs. This gives anti-HER2 mAbs the potential to address patients with HER2-overexpressing indications at HER2 Low to Intermediate expression levels.

Entry Barriers

For anti-HER2 BsAbs, one of the major challenges is to select the proper HER2 expression-related signaling pathways that not only lead to a synergistic effect, but can also induce potential additional benefits from enhanced drug distribution or differentiated functionality. Furthermore, since an asymmetrical format has been commonly chosen for current anti-HER2 BsAbs candidates, development of a favorable CMC profile based on a mature asymmetric Fc platform validated for commercial-scale manufacturing, coupled with a robust CMC process suitable for such a platform, could also be a significant challenge. In addition, the development of anti-HER2 BsAbs faces the same science and engineering challenges as other BsAbs, including difficulties in matching the proposed mechanism of action and the intended clinical application, and potential higher risks caused by novel drug properties. See "—Overview of the Immune Checkpoint Inhibitor Market in the PRC and United States—Overview of Anti-PD-(L)1/CTLA-4 BsAb Market in the PRC and United States—Entry Barriers."

Competitive Landscape

PRC

In the PRC, as of August 31, 2019, there were a number of anti-HER2 BsAb candidates in clinical trials. In addition, trastuzumab is approved as a monotherapy or a part of combination therapy for HER2 High breast cancer and GC/GEJ. Trastuzumab with or without chemotherapy is the first-line standard of care for HER2 High metastatic breast cancer in the PRC. Pertuzumab cannot be used alone as it is only approved as a part of a combination therapy with trastuzumab and chemotherapy as an adjuvant or neoadjuvant treatment for HER2 High early breast cancer. As of August 31, 2019, there were 16 anti-HER2 monospecific antibody candidates in clinical trials in China, of which ten were in phase III clinical trials or later stage. Of these late-stage candidates, seven were trastuzumab or pertuzumab's biosimilars. A summary of the competitive landscape of anti-HER2 BsAbs in the PRC is set forth below.

Approved Anti-HER2 Monospecific Antibodies in the PRC

Trade name(s) (Generic name(s))	Company	Target(s)	Indications	Treatment line	Date of approval	Patent status	Price per unit	Listed on NRDL/PRDL	Route of entry
Perjeta (pertuzumab)/ Trastuzumab[(1)]	Roche	HER2/HER2	HER2 High early stage breast cancer	Adjuvant (with chemo)	Dec-2018	Covered by registered patents in the PRC	RMB18,800 (420mg/ 14ml)	No	Intravenous (subcutaneous administration under clinical trial)
			HER2 High early stage breast cancer	Neoadjuvant (with chemo)	Aug-2019				
Herceptin (trastuzumab)	Roche	HER2	HER2 High metastatic breast cancer	2L	Sep-2002	Covered by registered patents in the PRC	RMB7,600 (440mg)	NRDL	Intravenous (subcutaneous administration under clinical trial)
				1L (with chemo)					
			HER2 High breast cancer	2L	Dec-2008				
			HER2 High metastatic GC/GEJ	1L (with chemo)	Oct-2012				

(1) This refers to Perjeta in combination with any drugs with the generic name of trastuzumab.

Anti-HER2 BsAb Candidates in the PRC

Drug candidate name	Company	Targets	Indications	Clinical stage	First posted date	Route of entry
KN026	Alphamab	HER2/HER2	HER2-overexpressing GC/GEJ	Phase II	May-2019	Intravenous
			HER2 High breast cancer, GC/GEJ	Phase I	Aug-2018	
MBS301	Beijing Mabworks Biotech Co., Ltd.	HER2/HER2	HER2 High breast cancer, GC	Phase I	Mar-2019	Intravenous
M802	Wuhan YZY Biopharma Co., Ltd.	HER2/CD3	HER2 High solid tumors	Phase I	Jul-2018	Intravenous

Anti-HER2 Monospecific Antibody Candidates (Phase III or Later Stage) in the PRC[3]

Drug candidate name(s)	Company	Target(s)	Indications	Clinical stage	First posted date	Route of entry
Perjeta (pertuzumab)/ Trastuzumab[1]	Roche	HER2/HER2	HER2 High GC	Phase III	Apr-2014	Intravenous
			HER2 High GC/GEJ	Phase III	Apr-2014	
			HER2 High breast cancer	Phase III	Mar-2015	
Herceptin (trastuzumab)/ Pertuzumab[2]		HER2/HER2	HER2 High breast cancer	Phase III	Feb-2016	Intravenous
Perjeta (pertuzumab)		HER2	HER2 High breast cancer	Phase III	Jan-2015	Intravenous

(1) This refers to Perjeta in combination with any drugs with the generic name of trastuzumab.

(2) The trials refers to Herceptin in combination with any drugs with the generic name of pertuzumab.

(3) This table does not include biosimilar candidates of trastuzumab or pertuzumab.

Source: NMPA, CIC Report (As of August 31, 2019)

United States

In the United States, as of August 31, 2019, there were a number of anti-HER2 BsAb candidates in clinical trials. As of the same date, trastuzumab and pertuzumab were the two most widely prescribed anti-HER2 monospecific antibodies. In addition to the indications approved in the PRC, the combination therapy of trastuzumab, pertuzumab and chemotherapy is also approved as first-line treatment for HER2 High metastatic breast cancer and as a neoadjuvant treatment for HER2 High early breast cancer in the United States. The combination therapy has become the first-line standard of care for HER2 High metastatic breast cancer in the United States. As of August 31, 2019, there were 24 anti-HER2 monospecific antibodies in clinical trials in the United States, of which four were in phase III clinical trials or at BLA stage. Of these late-stage candidates, two were trastuzumab or pertuzumab's biosimilars. A summary of the competitive landscape of anti-HER2 BsAbs in the United States is set forth below.

Approved Anti-HER2 Monospecific Antibodies in the U.S.[2]

Trade name(s) (Generic name(s))	Company	Target(s)	Indications	Treatment line	Date of approval	Patent status	Price per unit	Route of entry
Perjeta (pertuzumab)/ Trastuzumab[1]	Roche	HER2/HER2	HER2 High breast cancer	1L (with chemo)	Jun-2012	Covered by registered patents in the U.S.	US$5,370 (420mg/14ml)	Intravenous (subcutaneous administration under clinical trial)
			HER2 High breast cancer	Neoadjuvant (with chemo)	Sep-2013			
			HER2 High early breast cancer	Adjuvant (with chemo)	Dec-2017			
Herceptin (trastuzumab)	Roche	HER2	HER2 High metastatic breast cancer	1L (with chemo)	Sep-1998	Covered by registered patents in the U.S.	US$4,780 (440mg)	Intravenous and subcutaneous
				≥2L				
			HER2 High breast cancer	Adjuvant (single agent or with chemo)	Nov-2006			
			HER2 High GC/GEJ	1L (with chemo)	Oct-2010			

(1) This refers to Perjeta in combination with any drugs with the generic name of trastuzumab.

(2) This table does not include biosimilar candidates of trastuzumab or pertuzumab.

Anti-HER2 BsAb Candidates in the U.S.

Drug candidate name	Company	Targets	Indications	Clinical stage	First posted date	Route of entry
ZW25	Zymeworks	HER2/HER2	HER2 High GEJ	Phase II	Apr-2019	Intravenous
			HER2 High cancer	Phase I	Sep-2016	
KN026	Alphamab	HER2/HER2	HER2 High breast cancer, GC/GEJ	Phase I	Feb-2019	Intravenous
MCLA-128	Merus	HER2/HR3	Breast cancer	Phase II (with trastuzumab)	Oct-2017	Intravenous
HER2 BATs	Merck	HER2/CD3	Breast cancer	Phase I/II (with pembrolizumab)	Sep-2016	Intravenous
PRS-343	Pieris Pharmaceuticals	HER2/CD137	HER2 High breast cancer, GC, bladder cancer, solid tumors	Phase I (with atezolizumab)	Aug-2018	Intravenous
			HER2 High breast cancer, GC, bladder cancer, solid tumors	Phase I	Nov-2017	
GBR 1302	Glenmark Pharmaceuticals, Ltd	HER2/CD3	Breast cancer	Phase I/II	Jun-2019	Intravenous
			HER2 High solid tumors	Phase I	Jul-2016	
BTRC4017A	Roche	HER2/CD3	Solid tumors	Phase I	Feb-2018	Intravenous

Anti-HER2 Monospecific Antibody Candidates (Phase III or Later Stage) in the U.S.[2]

Drug candidate name(s)	Company	Target(s)	Indications	Clinical stage	First posted date	Route of entry
Perjeta (pertuzumab)/ Trastuzumab[1]	Roche	HER2/HER2	HER2 High breast cancer	Phase III	Dec-2007	Intravenous
			HER2 High GC/GEJ	Phase III	Jan-2013	
MGAH22 (Margetuximab)	MacroGenics, Inc.	HER2	HER2 High breast cancer	Phase III	Jul-2015	Intravenous

(1) This refers to Perjeta in combination with any drugs with the generic name of trastuzumab.

(2) This table does not include biosimilar candidates of trastuzumab or pertuzumab.

Source: FDA, CIC Report (As of August 31, 2019)

For a competitive landscape analysis of the anti-HER2 BsAb candidates and the combination therapies, see "Business—Our Product Pipeline—Anti-HER2 BsAb Candidate – KN026—Competition".

CTLA-4-FC FUSION PROTEIN MARKET IN THE PRC

The treatment of cancer is a complex process that may cause various TEAEs, including unwanted immune responses. Although such adverse immune responses may occur infrequently, they are generally associated with high mortality rates due to the poor physical conditions of many cancer patients treated, and therefore require effective therapies with fast onset. Corticosteroids with progressive tapering are the standard therapies for low-severity adverse immune responses. For severe unwanted immune responses that are not adequately addressed by corticosteroids, other immunosuppressant drugs are recommended. Currently in the PRC, there are a number of different immunosuppressant drug candidates under clinical development. These drug candidates may affect different types of immune cells, and theoretically have the potential of controlling adverse immune responses occurring in oncology treatments. CTLA-4-Fc fusion proteins are a type of immunosuppressant drugs that function in the early stage of T-cell activation and therefore may achieve efficient global downregulation of immune responses. As a result, CTLA-4-Fc fusion proteins have the potential to become a supportive therapy for oncology treatment to mitigate treatment-induced immune disorders, such as (i) irAEs in patients treated with immune checkpoint inhibitor therapy, (ii) severe cytokine release syndrome (CRS) due to massive cytokine release by certain cell therapies (CAR-T and TCR-T) as well as CD3 agonists, and (iii) graft-versus-host diseases during leukemia treatment. CIC estimates that approximately 100,000 patients are suffering from the aforementioned immune disorders in China without effective treatment.

In addition, the CTLA-4-Fc fusion proteins have been clinically-validated for treatment of RA, idiopathic arthritis, psoriatic arthritis and prophylaxis of organ rejection after kidney transplant outside the PRC. In the PRC, RA and prophylaxis of organ rejection after kidney transplant are indications currently being investigated in clinical trials and may present an attractive market of CTLA-4-Fc fusion proteins in the near future.

Overview of RA Drug Market in the PRC

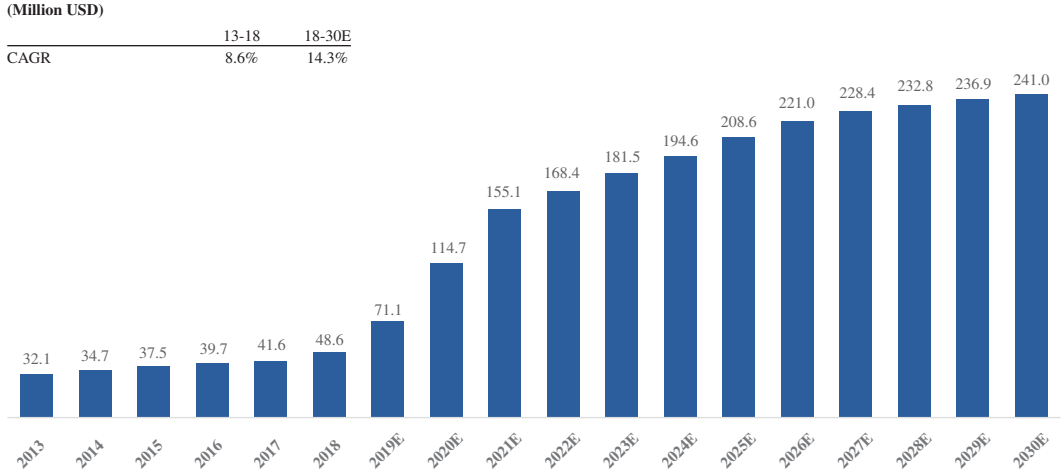
RA is a type of chronic systemic inflammatory auto-immune disease characterized by joint pain, swelling, stiffness, and deformation. The incidence rate of RA is approximately 0.4% of the total PRC population. The RA patient size in the PRC reached 5.3 million in 2018 and is expected to further increase to 5.6 million in 2030. RA substantially influences patients' quality of life and imposes a great treatment burden.

TNF-α Inhibitor Refractory RA Addressable Market in the PRC

Inhibitors of tumor necrosis factor alpha, or TNF-α, are among the most commonly prescribed biologics for RA treatment. TNF-α is considered a major pro-inflammatory cytokine, affecting various aspects of the immune reaction and triggering autoimmune and immune-mediated disorders such as RA. As such, TNF-α inhibitors are developed to suppress the body's natural response to TNF-α. There are a number of TNF-α inhibitors approved in the PRC, which are similar in terms of efficacy but distinct in clinical pharmacokinetic and dynamic properties. They offer a targeted strategy in contrast to the nonspecific immunosuppressive agents traditionally used to treat most inflammatory diseases. The market of TNF-α inhibitors for RA treatment experienced robust growth from US$63 million in 2013 to US$0.1 billion in 2018, representing a CAGR of 8.6% from 2013 to 2018, and is expected to further increase to US$0.5 billion in 2030, representing a CAGR of 14.3% from 2018.

Despite the foregoing, however, certain patients may exhibit inadequate responses, or develop resistance, to TNF-α inhibitors. Approximately 10% to 30% of patients do not respond to TNF-α inhibitors at all and approximately 23% to 46% of patients lose response over time. As a result, approximately 50% of patients receiving TNF-α inhibitors develop TNF-α refractory RA and need alternative treatments. Such patient population was estimated at 3.2 million in the PRC in 2018. The following graph sets forth the addressable market size of the TNF-α inhibitor refractory RA market in the PRC for the periods indicated.

TNF-α Inhibitor Refractory RA Addressable Market in the PRC



(1) The TNF-α inhibitor refractory RA addressable market size is assumed to be a percentage of TNF-α inhibitor market size. The total addressable patient population, the treatment rate and the average annual cost per patient are assumed to be the same as that of the TNF-α inhibitor market. The expected percentage of TNF-α inhibitor market size takes account of the percentage of TNF-α non-response and loss of response.

(2) For the TNF-α inhibitor market, the market estimation considers all RA patients that are eligible for TNF-α inhibition treatment. All currently approved TNF-α inhibitors in the PRC are taken into consideration.

(3) The treatment rate in RA patients is expected to increase due to NRDL inclusions and biosimilar entry, while the average annual cost of TNF-α inhibitors is expected to decrease.

Source: CIC Report

Competitive Landscape

In the PRC, currently, Actemra (IL-6 inhibitor) is the only biologic drug approved for the treatment of patients that have moderate or severe active RA and have exhibited poor responses to the TNF-α inhibitors. There are two CTLA-4-Fc fusion protein candidates under development, i.e., Alphamab's KN019 and BMS's abatacept. In addition, there are a number of other drug candidates currently in clinical development in the PRC that can potentially meet the needs of TNF-α inhibitor refractory RA patients. A summary of the competitive landscape of drugs and drug candidates for TNF-α inhibitor refractory RA patients in the PRC is set out below.

Approved Biologics for TNF-α Inhibitor Refractory RA in the PRC

Trade name (Generic name)	Company	Target	Date of approval	Patent status	Price per unit	Listed on NRDL/PRDL	Route of entry
Actemra (tocilizumab)	Roche	IL-6	Mar-2013	No registered patents in the PRC	RMB830 (80mg/4ml)	PRDL	Intravenous

Biologics Candidates for TNF-α Inhibitor Refractory RA (Phase III or Later Stage) in the PRC

Drug candidate name	Company	Target(s)	Clinical stage	First posted date	Route of entry
Abatacept	Jiangsu Simcere Pharmaceutical Co., Ltd./BMS	B7	BLA	Jul-2018	Subcutaneous
RC18	RemeGen, Ltd.	BLyS/APRIL	Phase III	Nov-2016	Subcutaneous
Tocilizumab	Roche	IL-6	Phase III	Mar-2017	Subcutaneous
SM03	LonnRyonn Pharma Ltd.	CD22	Phase III	Dec-2017	Intravenous
HLX01	Shanghai Henlius Biotech, Inc.	CD20	Phase III	Aug-2018	Intravenous
BAT1806	Bio-Thera Solutions, Ltd	IL-6	Phase III	Feb-2019	Intravenous

Drug candidate name	Company	Target(s)	Clinical stage	First posted date	Route of entry
CMAB806	Jinyu Bio-technology Co., Ltd.	IL-6	Phase III	Apr-2019	Intravenous
rhIL-1Ra	Changchun Institute of Biological Products Co., Ltd.	IL-1	Phase III	Apr-2019	Subcutaneous
LZM008	Livzon Biologics, Ltd.	IL-6	Phase III	May-2019	Intravenous

Source: NMPA, CIC Report (August 31, 2019)

These drugs/drug candidates are differentiated by their targets, with each target representing a specific mechanism of action and having potential advantages in addressing a specific cohort of RA patients. Although there are no head-to-head comparisons for these targets, CTLA-4-Fc fusion proteins are expected to have potentially better efficacy compared with downstream signaling inhibition of IL6, CD20 and CD22. CTLA-4-Fc fusion proteins inhibit T-cell activation at early stages in the pathogenic cascade of RA. See "Business—Our Product Pipeline—CTLA-4 Fusion Protein Candidate – KN019—Competition".

There is no approved CTLA-4-Fc fusion protein in the PRC. Globally, there are two approved CTLA-4-Fc fusion proteins, i.e. BMS's Nulojix (belatacept) and Orencia (abatacept). Orencia is currently approved for RA, idiopathic arthritis and psoriatic arthritis. Nulojix is an improved version of Orencia and currently approved for prophylaxis of organ rejection after kidney transplant. Due to complex glycosylation of the fusion protein structure, it is very difficult to ensure batch-to-batch protein quality consistency in CTLA-4-Fc fusion proteins, which in turn affects their efficacy and safety. KN019 is the only CTLA-4-Fc fusion protein candidate in the PRC with the same amino acid sequence as belatacept and therefore is expected to have better efficacy and safety profile on RA treatment than abatacept. See "Business—Our Product Pipeline—CTLA-4 Fusion Protein Candidate – KN019—Competition".