Global PD-1/PD-L1 Monoclonal Antibody Market Competitive Landscape Postprint

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Abstract

Objective: To analyze the current development status and future trends of PD-1/PD-L1 monoclonal antibodies from a product development perspective. Methods: Data from Clarivate Analytics' Cortellis database were retrieved, and the search results were analyzed using quantitative and comparative analysis methods. Results: Currently, five PD-1/PD-L1 monoclonal antibodies have been launched, four are in pre-registration, and six are in Phase III clinical trials, indicating a rapid growth trend for PD-1/PD-L1 monoclonal antibodies in the future market. Additionally, commercial transactions involving PD-1/PD-L1 monoclonal antibodies are increasing, with over ten transactions having occurred to date, including drug development and commercialization licensing, patent asset sales, and early-stage drug R&D collaborations, among which drug development and commercialization licensing represents the primary transaction model. Conclusion: Although the PD-1/PD-L1 monoclonal antibody market is still in its infancy, with continuous technological development and improvement in the future, it is believed that more PD-1/PD-L1 monoclonal antibodies will be launched, providing new opportunities for the treatment of cancer and other diseases.

Full Text

Preamble

Market Competition Pattern of Global PD-1/PD-L1 Monoclonal Antibodies

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Abstract

Objective: To analyze the development status and future trends of PD-1/PD-L1 monoclonal antibodies from a product development perspective. **Methods:** Data were retrieved from the Cortellis database of Clarivate Analytics (formerly Thomson Reuters IP & Science) as of April 10, 2018. Quantitative and comparative analysis methods were applied to examine drug development and deal-making activities. **Results:** Currently, five PD-1/PD-L1 monoclonal antibodies have been launched, four are in pre-registration, and six are in Phase III clinical trials, indicating rapid market growth ahead. Additionally, commercial transactions involving PD-1/PD-L1 antibodies are increasing, with over ten deals encompassing drug development and commercialization licensing, patent asset sales, and early-stage R&D collaborations—among which licensing for development and commercialization represents the dominant transaction model. **Conclusion:** Although the PD-1/PD-L1 monoclonal antibody market remains in its infancy, continued technological advancement will likely bring more products to market, offering new therapeutic opportunities for cancer and other diseases.

Keywords: PD-1/PD-L1 monoclonal antibody; market competition; clinical R&D

1. Methods

1.1 Data Sources

Data were retrieved from the Cortellis database (formerly Thomson Reuters Pharma) of Clarivate Analytics (formerly Thomson Reuters IP & Science) on April 10, 2018. Drug development and transaction data were searched separately through the "Drugs" and "Deals" advanced search portals. Both searches employed dual constraints by technology and target using the strategy: "monoclonal antibody AND ((Programmed cell death protein 1 modulator, PD-1) OR (Programmed cell death ligand 1 modulator, PD-L1))". "Monoclonal antibody" was searched under the "Technologies" category, while PD-1/PD-L1 targets were searched under "Any action".

1.2 Analysis Methods

The study primarily employed quantitative and comparative analysis. Quantitative analysis examined statistical features, relationships, and changes in numerical data to establish a foundation for comparison. Comparative analysis

identified differences between actual and baseline values to reveal current status and trends.

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2. Results

2.1 Overall R&D Status

As a major focus in cancer immunotherapy, PD-1/PD-L1 inhibitors have attracted significant attention from academia, industry, and investors. Multiple pharmaceutical companies have advanced their PD-1/PD-L1 agents into clinical development for applications in lung cancer, melanoma, colorectal cancer, and other indications. Analysis of the Cortellis database reveals 118 recorded PD-1/PD-L1 monoclonal antibodies globally. Excluding suspended, terminated, and inactive projects, 107 products remain in active development, with 56.1% in discovery/preclinical stages and 37.4% in clinical trials, demonstrating intense R&D activity in this space.

[Figure 1: see original paper] Global R&D Status of PD-1/PD-L1 Monoclonal Antibodies

Note: (1) Pre-registration: Application submitted, awaiting approval; (2) Discovery: Includes discovery/exploration and preclinical pharmacology/toxicology evaluation in animals.

2.2 Development Progress of Key Products

Since *Science* named cancer immunotherapy a "breakthrough" in 2013, remarkable clinical progress has been achieved in treating melanoma, lung cancer, gastric cancer, breast cancer, ovarian cancer, and colorectal cancer. Currently, twelve products are in Phase III trials, registration, or launched stages—all representing near-term market entrants. This includes five launched products (Table 1), three in pre-registration (Table 2), and four in Phase III trials (Table 3).

2.2.1 Launched Products As of April 10, 2018, five PD-1/L1 monoclonal antibodies have received regulatory approval globally (Table 1). These include two anti-PD-1 agents targeting T cells: Merck' s Pembrolizumab (Keytruda) and Bristol-Myers Squibb' s Nivolumab (Opdivo), plus three anti-PD-L1 agents targeting tumor cells: Roche' s Atezolizumab (Tecentriq), Pfizer' s Avelumab (Bavencio), and AstraZeneca' s Durvalumab (Imfinzi). Since the 2014 approvals of Pembrolizumab and Nivolumab for melanoma, these five drugs have collectively gained approval for nearly 20 indications across ten major cancer types, with over 1,000 clinical trials investigating monotherapy or combination regimens. PD-1/L1 drugs have become cornerstone therapies in oncology.

(1) Nivolumab/Opdivo

On July 4, 2014, Nivolumab (Opdivo), developed by Bristol-Myers Squibb and Ono Pharmaceutical, received PMDA approval in Japan for unresectable melanoma (Stage IV), subsequently launching in the US, EU, Canada, Brazil, Mexico, South Korea, Taiwan, and other regions. Research from NYU Perlmutter Cancer Center demonstrated superior adjuvant therapy outcomes with Nivolumab compared to Ipilimumab in post-surgical Stage IIIB, IIIC, or IV melanoma patients [6]. On March 4, 2015, FDA approval for metastatic non-small cell lung cancer (NSCLC) followed, with subsequent approvals in Japan, EU, Australia, Brazil, Canada, Mexico, South Korea, and Taiwan. Ohio State University Comprehensive Cancer Center research showed that while Nivolumab did not extend progression-free survival compared to chemotherapy in advanced NSCLC patients with 5% PD-L1 expression, it provided slightly better overall survival with significantly improved tolerability and safety profile [7]. Nivolumab has also been approved for metastatic renal cell carcinoma, gastric cancer, hepatocellular carcinoma, bladder cancer, colorectal cancer, esophageal cancer, and head and neck cancer.

Notably, on June 15, 2018, Nivolumab' s marketing application was formally approved by China' s National Medical Products Administration (NMPA) for second-line NSCLC treatment, completing priority review in under seven months and becoming the first PD-1/PD-L1 drug approved in China.

(2) Pembrolizumab/Keytruda

On September 4, 2014, Merck' s Pembrolizumab (Keytruda) received FDA accelerated approval for advanced or unresectable melanoma (Stage IV) refractory to prior therapy. As a monoclonal antibody binding to the PD-1 receptor, Pembrolizumab blocks interactions with PD-L1 and PD-L2, reversing PD-1 pathway-mediated inhibition of immune responses including anti-tumor activity. Preclinical mouse models demonstrated tumor growth inhibition through PD-1 blockade. Additional melanoma approvals followed in South Korea (March 2015), Australia (April 2015), EU (July 2015), and Japan (September 2016). Gustave Roussy Institute research showed Pembrolizumab extended progression-free and overall survival while reducing toxicity compared to standard Ipilimumab in advanced melanoma [4]. For metastatic NSCLC, FDA approval was granted on October 2, 2015, with subsequent approvals in Canada (April 2016), EU (August 2016), and Japan (December 2016). In advanced NSCLC patients with 50% PD-L1 expression, Pembrolizumab demonstrated superior progression-free survival, overall survival, and safety compared to platinum-based chemotherapy [5]. The drug has also been approved for head and neck cancer, Hodgkin lymphoma, bladder cancer, colorectal cancer, urothelial cancer, and renal cell carcinoma.

On July 25, 2018, Pembrolizumab received NMPA approval for melanoma, setting a new regulatory record with under six months from CFDA acceptance (February 11, 2018) to approval, becoming the second PD-1/PD-L1 antibody approved in China after Nivolumab.

(3) Durvalumab/Imfinzi

On May 1, 2017, AstraZeneca's Durvalumab (Imfinzi) received FDA accelerated approval for locally advanced or metastatic urothelial carcinoma [8]. This human IgG1 monoclonal antibody blocks PD-L1 interactions with PD-1 and CD80, inhibiting immune responses without antibody-dependent cellular cytotoxicity (ADCC). *In vitro* studies showed increased T-cell activity, and xenograft models demonstrated tumor size reduction through PD-L1 blockade. On February 16, 2018, FDA approval was granted for metastatic NSCLC. The ATLANTIC study demonstrated clinical efficacy and good tolerability in heavily pretreated advanced NSCLC patients, showing durable responses and favorable overall survival regardless of EGFR/ALK mutation status or PD-L1 expression levels [9].

(4) Atezolizumab/Tecentriq

On May 18, 2016, FDA approved Roche' s Atezolizumab (Tecentriq) for locally advanced or metastatic urothelial carcinoma progressing during or after platinum-containing chemotherapy. Atezolizumab blocks PD-L1 interactions with PD-1 and B7-1 receptors, releasing PD-L1/PD-1-mediated immune suppression and activating anti-tumor responses without inducing ADCC. Additional urothelial carcinoma approvals followed in South Korea (January 2017), Canada (April 2017), and EU (September 2017). For metastatic NSCLC, FDA approval was granted on October 19, 2016, with subsequent approvals in Australia, Canada, EU, and Japan. UC Davis Comprehensive Cancer Center research demonstrated superior overall survival compared to docetaxel in previously treated NSCLC patients, with favorable safety profiles irrespective of PD-L1 expression or tumor histology [10].

(5) Avelumab/Bavencio

On March 23, 2017, the PD-L1 immunotherapy Avelumab (Bavencio), co-developed by Merck KGaA and Pfizer, received FDA approval for metastatic Merkel cell carcinoma [11]. Targeting the PD-1/PD-L1 pathway present on immune and certain cancer cells, Avelumab blocks this interaction to enable immune-mediated tumor killing. In May 2017, FDA approved Avelumab for locally advanced or metastatic urothelial carcinoma [12]. The partners are conducting over 30 international clinical trials, including nine Phase III studies across more than 15 tumor types: breast cancer, gastric/gastroesophageal junction adenocarcinoma, head and neck cancer, Merkel cell carcinoma, mesothelioma, melanoma, NSCLC, ovarian cancer, renal cancer, and bladder cancer.

2.2.2 Pre-registration Three PD-1/PD-L1 monoclonal antibodies are currently in pre-registration globally, including two from Chinese companies (Shanghai Junshi and Innovent Biologics) and one from Sanofi/Regeneron (Table 2).

(1) JS-001

On March 9, 2018, Shanghai Junshi Biosciences' anti-PD-1 monoclonal antibody

injection entered NMPA new drug application (NDA) review for melanoma. JS001 is the first domestic anti-PD-1 antibody to receive CFDA clinical trial approval, with ongoing Phase I-III trials for melanoma, nasopharyngeal carcinoma, gastric cancer, lung cancer, esophageal cancer, and urothelial carcinoma at multiple domestic centers. In January 2018, JS001 received FDA approval for clinical trials, marking Junshi' s first global biologics development program. On March 14, 2018, Phase I trials commenced for advanced solid tumors [13].

(2) Cemiplimab/REGN-2810

On September 9, 2017, the Sanofi/Regeneron PD-1 inhibitor Cemiplimab (REGN2810) received FDA Breakthrough Therapy Designation for metastatic cutaneous squamous cell carcinoma (CSCC) and locally advanced, unresectable CSCC in adults. NDA acceptance occurred on December 13, 2017 (US FDA) and April 3, 2018 (EMA). Cemiplimab is in Phase III trials for NSCLC and cervical cancer, and Phase II for basal cell carcinoma.

(3) IBI-308

On December 13, 2017, Innovent Biologics' sintilimab injection (IBI308) NDA was accepted by CDE for Hodgkin lymphoma, becoming the second PD-1/PD-L1 drug submitted for Chinese market approval after Opdivo. Innovent voluntarily withdrew the application in late February 2018 to supplement materials and resubmitted on April 19, 2018. IBI308 blocks PD-1/PD-L1 binding to restore T-cell function for tumor elimination. On April 23, 2018, IBI308 was included in CFDA' s "Priority Review" list (28th batch).

2.2.3 Phase III Clinical Trials Four PD-1/PD-L1 monoclonal antibodies are currently in Phase III trials globally, including two from Chinese companies (Shanghai Hengrui and BeiGene) and two from Novartis and Biocad (Table 3).

(1) SHR-1210

On November 15, 2016, Hengrui Medicine' s PD-1 antibody SHR-1210 entered Phase III trials for hepatocellular carcinoma, with additional Phase III trials initiated on May 10, 2017 for metastatic esophageal cancer and metastatic NSCLC. Since October 2016, the PLA Cancer Center at Nanjing University of Chinese Medicine has conducted clinical studies on SHR-1210 for primary liver cancer (CFDA approval No. 2016L01455), showing promising efficacy with good safety and tolerability, though with a unique adverse event of drug-related cutaneous capillary endothelial proliferation [14].

(2) Spartalizumab/PDR001

On February 27, 2017, Novartis' PD-1 antibody Spartalizumab entered Phase III trials for melanoma, with an additional Phase III trial for endocrine tumors initiated on December 31, 2017. Phase III data are expected in 2019, including Spartalizumab combined with Tafinlar (dabrafenib) and Mekinist (trametinib) for malignant melanoma, and monotherapy for endocrine tumors.

(3) BGB-A317

On November 13, 2017, BeiGene' s independently developed PD-1 antibody BGB-A317 entered Phase III trials for metastatic NSCLC, with an additional Phase III trial for metastatic esophageal cancer initiated on January 31, 2018. BGB-A317 exhibits high affinity and specificity for PD-1, with engineered Fc region optimization to reduce negative interactions with other immune cells. On September 28, 2017, BeiGene presented preliminary Phase I/II dose-validation data at CSCO, showing good tolerability and preliminary anti-tumor activity in Chinese patients with advanced solid tumors.

(4) BCD-100

On August 31, 2017, Russian company Biocad' s PD-1 antibody BCD-100 entered Phase III trials for advanced solid tumors.

Global R&D Status of PD-1/PD-L1 Monoclonal Antibodies (Highest Status: Launched)

Drug Name/Trade Name	Target	Originator Company	Marketing Company	Country/Region	Current Development Status
Pembrolizumab/Keytruda	PD-1 inhibitor	Schering-Plough	Merck & Co	United Arab Emirates, Liechtenstein, Japan, US, EU, Canada, Australia, South Korea, Taiwan, Russia	Stage IV melanoma, metastatic bladder cancer, metastatic NSCLC, metastatic head and neck cancer, Hodgkin lymphoma, metastatic colorectal cancer, metastatic gastric cancer, primary mediastinal large B-cell lymphoma

Nivolumab/Opdivo | PD-1 inhibitor | Ono Pharmaceutical | Bristol-Myers Squibb | Japan, US, EU, Canada, Australia, Brazil, Mexico, South Korea, Taiwan, Russia | Stage IV melanoma, metastatic NSCLC, metastatic renal

cell carcinoma, metastatic bladder cancer, metastatic head and neck cancer, metastatic colorectal cancer, metastatic gastric cancer, mesothelioma |

Durvalumab/Imfinzi | PD-L1 inhibitor | MedImmune | AstraZeneca | US, EU, Japan, Canada, Australia, Brazil, Mexico, South Korea, Taiwan, Russia | Metastatic bladder cancer, metastatic NSCLC, Merkel cell carcinoma |

Atezolizumab/Tecentriq | PD-L1 inhibitor | Genentech | Roche | US, EU, Japan, Canada, Australia, Brazil, Mexico, South Korea, Taiwan, Russia | Metastatic bladder cancer, metastatic NSCLC, hormone-refractory prostate cancer |

Avelumab/Bavencio | PD-L1 inhibitor | Merck KGaA | Merck KGaA & Pfizer | US, EU, Japan, Canada, Australia, Brazil, Mexico, South Korea, Taiwan, Russia | Merkel cell carcinoma, metastatic bladder cancer, metastatic NSCLC |

Global R&D Status of PD-1/PD-L1 Monoclonal Antibodies (Highest Status: Pre-registration)

Drug Name/Trade Name	Target	Originator Company	Marketing Company	Country/Region	Current Development Status
JS-001	PD-1 inhibitor	Shanghai Junshi Biosciences	Shanghai Junshi Biosciences	China	Metastatic esophageal cancer, gastric tumors, nasopharyngeal carcinoma, metastatic head and neck cancer, Stage IV melanoma, advanced solid tumors, metastatic breast cancer, metastatic renal cell carcinoma, neuroendocrine tumors, NSCLC

Drug Name/Trade Name	Target	Originator Company	Marketing Company	Country/Region	Current Development Status
Cemiplimab/REGN-2810	PD-1 inhibitor	Regeneron	Sanofi & Regeneron	US, EU, Russia	Metastatic CSCC, advanced solid tumors, NSCLC, cervical cancer, basal cell carcinoma
IBI-308	PD-1 inhibitor	Innovent Biologics	Innovent Biologics	China	Hodgkin lymphoma, NSCLC, metastatic esophageal cancer, metastatic gastric cancer

Global R&D Status of PD-1/PD-L1 Monoclonal Antibodies (Highest Status: Phase III Clinical Trial)

Drug Name/Trade Name	Target	Originator Company	Marketing Company	Country/Region	Current Development Status
SHR-1210	PD-1 inhibitor	Shanghai Hengrui Medicine	Shanghai Hengrui Medicine	China	Metastatic esophageal cancer, metastatic NSCLC, metastatic gastric cancer, hepatocellular carcinoma, osteosarcoma, metastatic breast cancer, Stage IV melanoma

Drug Name/Trade Name	Target	Originator Company	Marketing Company	Country/Region	Current Development Status
Spartalizumab/PDR001	PD-1 inhibitor	Novartis	Novartis	Switzerland, US, EU	Stage IV melanoma, endocrine tumors, endometrioid carcinoma, metastatic breast cancer, metastatic pancreatic cancer
BGB-A317	PD-1 inhibitor	BeiGene	BeiGene & Celgene	China, US, EU	Metastatic NSCLC, metastatic esophageal cancer, metastatic head and neck cancer, metastatic ovarian cancer, metastatic bladder cancer
BCD-100	PD-1 inhibitor	Biocad	Biocad	Russia	Advanced solid tumors, metastatic lung cancer

2.3 Product Transaction Landscape

PD-1/PD-L1 monoclonal antibody transactions primarily fall into three categories: drug development and commercialization licensing, patent asset sales, and early-stage R&D collaborations. Licensing for development and commercialization accounts for 50% of all transactions (Table 4).

(1) Merck KGaA and Pfizer: $2.85 Billion Avelumab/Bavencio Licensing Deal

On November 17, 2014, Pfizer and Merck KGaA formed a $2.85 billion global strategic alliance to co-develop and commercialize the cancer immunotherapy Avelumab (Bavencio). Pfizer paid $850 million upfront, with Merck KGaA eligible for up to $2 billion in milestones. Since the July 2014 transaction,

Avelumab has advanced to market.

(2) Sanofi and Regeneron: $2.665 Billion Antibody Licensing Deal

On July 1, 2015, Sanofi and Regeneron established a global immuno-oncology collaboration to discover, develop, and commercialize novel antibody therapeutics, including the PD-1 inhibitor Cemiplimab (REGN-2810). The partnership committed up to $1.65 billion in R&D funding, including $100 million for proof-of-concept studies and $650 million for Cemiplimab development. Since July 2015, Cemiplimab has progressed from Phase I to pre-registration.

(3) Innovent and Eli Lilly: $1.456 Billion Tri-Antibody Strategic Alliance

On March 20, 2015, Innovent Biologics and Eli Lilly established a strategic alliance for three innovative biologics, including the anti-PD-1 antibody IBI-308. Innovent out-licensed overseas rights to Lilly for $56 million upfront and up to $1.4 billion in milestones. IBI-308, a domestically developed Class 1 biologic targeting PD-1 for lung, liver, and gastric cancers, advanced from Phase II to pre-registration post-deal.

(4) BeiGene and Celgene: $1.393 Billion Strategic Alliance

On July 5, 2017, Celgene and BeiGene formed a $1.393 billion partnership (covering BGB-A317, azacitidine, and paclitaxel) to develop the PD-1 inhibitor BGB-A317 in solid tumors. BeiGene received $263 million upfront, $150 million equity investment (35% premium), $980 million in milestones, and royalties on future sales, while Celgene gained global rights (excluding Japan) to BGB-A317 for solid tumors. Since July 2017, BGB-A317 has advanced from Phase II to Phase III.

(5) Sorrento and Servier: $1 Billion PD-1 Antibody Licensing Deal

On July 6, 2016, Sorrento Therapeutics and Les Laboratoires Servier signed a licensing agreement for the PD-1 antibody STI-A1110, granting Servier exclusive global rights for development, registration, and commercialization across all indications, including hematologic and solid malignancies. Sorrento received $28.23 million upfront and up to $972 million in milestones. STI-A1110 remains in early development, not yet in clinical trials.

(6) Incyte and MacroGenics: $900 Million PD-1 Antibody Licensing Deal

On October 27, 2017, Incyte and MacroGenics signed a global exclusive collaboration for MacroGenics' PD-1 inhibitor MGA-012. Incyte paid $150 million upfront and $750 million in milestones, with MacroGenics eligible for 15-24% royalties on future sales. MGA-012 remains in Phase I.

(7) WuXi Biologics and Arcus: $816 Million PD-1 Antibody Licensing Deal

On August 17, 2017, WuXi Biologics and Arcus Biosciences signed an agreement licensing exclusive North American, Japanese, and European rights for the PD-1 antibody GLS-010 (developed with Harbin Gloria Pharmaceuticals). Arcus will pay up to $816 million, including $18.5 million upfront and $797.5 million in milestones, plus royalties. GLS-010 remains in Phase I.

(8) BMS and Merck: $625 Million Pembrolizumab/Keytruda Patent Settlement

On January 20, 2017, Bristol-Myers Squibb/Ono Pharmaceutical and Merck settled global patent litigation over Pembrolizumab (Keytruda). Merck paid $625 million upfront, plus 6.5% royalties on Keytruda sales from 2017-2023 and 2.5% from 2024-2026. Keytruda remains on the market.

(9) AstraZeneca and Celgene: $450 Million Durvalumab/Imfinzi Licensing Deal

On April 24, 2015, AstraZeneca and Celgene partnered to develop Durvalumab (Imfinzi) combination therapies for hematologic malignancies, with AstraZeneca receiving $450 million upfront. Durvalumab has since advanced from Phase III to market.

(10) Medivation and CureTech: $335 Million Pidilizumab Exclusive Development Rights

On October 23, 2014, Medivation acquired global exclusive rights to CureTech' s PD-1 antibody Pidilizumab (CT-011) for $335 million, including $5 million upfront and $330 million in milestones. Pidilizumab' s development has since been terminated.

Top 10 PD-1/PD-L1 Monoclonal Antibody Commercial Transactions in 2017 (Examples)

Transaction Type	Companies	Deal Value (USD M)	Upfront Payment (USD M)	Milestones (USD M)	Drug(s)	Status at Deal	Current Status
Drug Development/Commercialization	Merck KGaA & Pfizer	2,850	850	2,000	Avelumab	Early development	Launched
Drug Development/Commercialization	Sanofi & Regeneron	2,665	1,000	1,665	Cemiplimab; REGN1 2810	Phase I	Pre-registration

Transaction Type	Companies	Deal Value (USD M)	Upfront Payment (USD M)	Milestones (USD M)	Drug(s)	Status at Deal	Current Status
Drug Development/Commercialization	Innovent & Eli Lilly	1,456	56	1,400	IBI-308	Phase II	Pre-registration
Drug Development/Commercialization	BeiGene & Celgene	1,393	263	1,130	BGB-A317	Phase II	Phase III
Drug Development/Commercialization	Sorrento & Servier	1,000	28.23	972	STI-A1110	Early development	Early development
Drug Development/Commercialization	Incyte & Macrogenics	900	150	750	MGA-012	Phase I	Phase I
Drug Development/Commercialization	WuXi Biologics & Arcus	816	18.5	797.5	GLS-010	Phase I	Phase I
Patent License	BMS/Ono & Merck	625	625	0	Pembrolizumab	Launched	Launched
Drug Development/Commercialization	AstraZeneca & Celgene	450	450	0	Durvalumab	Phase III	Launched
Exclusive Development Rights	Medivation & CureTech	335	5	330	Pidilizumab	Phase II	Terminated

Note: For transactions involving multiple drugs, "Status at Deal" and "Current Status" refer specifically to the PD-1/PD-L1 antibody component (bolded in table).

3. Summary and Outlook

PD-1/PD-L1 immunotherapy represents a highly promising class of cancer treatments. Research institutions are actively investigating monotherapy and combination approaches across multiple cancer types to maximize clinical value. Since the 2014 launches of Nivolumab and Pembrolizumab, expanding indications have driven rapid sales growth, exceeding $9 billion globally in 2017. Evaluate Pharma projects cumulative sales will reach $30 billion by 2022. Beyond multinational corporations (BMS, Roche, Merck, AstraZeneca), domestic Chinese competition is intensifying among Innovent Biologics, Hengrui Medicine, Junshi Biosciences, and BeiGene, with Hengrui' s SHR1210 already in Phase III trials in China.

Novel target discovery remains a key trend in antibody research, though none have matched PD-1/PD-L1' s impact. As combination therapy becomes standardized, immunotherapy-based regimens represent the future direction, though optimal combinations for survival benefit require further investigation. Comprehensive clinical trials are needed to identify best practices for safe, effective, and rational drug use.

Given the high technological content and value of biologics, multinationals employ comprehensive patent protection covering numerous indications worldwide. While multiple domestic PD-1/PD-L1 antibodies are in clinical development, Chinese market entrants may face patent litigation risks, as evidenced by the global patent dispute between Merck and BMS. Domestic companies should carefully assess patent risks and strategically position themselves by developing antibodies against novel targets or epitopes to secure patent strongholds.

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Note: Figure translations are in progress. See original paper for figures.