Global Monoclonal Antibody Drug R&D Status and Development Trends (Postprint)

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Abstract

Monoclonal antibody drugs, with their unique mechanisms of action and high efficacy, have played an immeasurably important role in the treatment of malignant tumors and autoimmune diseases, becoming a global research and development hotspot. Based on the Cortellis database under Clarivate Analytics, and employing a method that combines quantitative analysis with expert insights, this study presents a comprehensive panorama of the global research, development, and commercialization of monoclonal antibody drugs from multiple dimensions, including overall R&D and commercialization status, major countries/regions, technologies and types, targets and mechanisms of action, market share, and product transactions. The analysis results show that there are 133 monoclonal antibody drugs approved globally, among which humanized monoclonal antibody drugs account for 37.6% of the total number of approved monoclonal antibody drugs. The therapeutic targets are primarily concentrated on HER, TNF, CD20, PD-1/L1, VEGF, and CD3, with drugs acting as HER2 tyrosine kinase receptor inhibitors representing the largest number. The United States leads far ahead in the research, development, and commercialization of monoclonal antibody drugs, while China ranks second in the total number of monoclonal antibody drugs under development and approved; however, the number of approved monoclonal antibody drugs in China is only eight. In 2017, there were 22 monoclonal antibody drugs with sales exceeding US$1 billion. The total number of transactions for monoclonal antibody drugs worldwide reached 1,408, with drug development and commercialization licensing being the primary transaction mode. In the future, the development trend of monoclonal antibody drugs will advance toward novel targets, new indications, and new treatment regimens, which will generate more "blockbuster drugs."

Full Text

Preamble

Current Status and Development Trends of Global Monoclonal Antibody Drugs*

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Abstract

Monoclonal antibody drugs have become a global R&D hotspot, playing an invaluable role in the treatment of malignant tumors and autoimmune diseases through their unique mechanisms of action and high efficacy. Based on data from Clarivate' s Cortellis database, this study employs a combination of quantitative analysis and expert insights to present a comprehensive landscape of global monoclonal antibody drug R&D and commercialization across multiple dimensions, including overall development and commercialization status, key countries/regions, technologies and categories, targets and mechanisms of action, market share, and product transactions. The analysis reveals that among 133 monoclonal antibody drugs currently on the market worldwide, humanized monoclonal antibodies account for 37.6% of the total. The primary targets are concentrated on HER, TNF, CD20, PD-1/L1, VEGF, and CD3, with HER2 tyrosine kinase receptor inhibitors representing the largest category. The United States leads overwhelmingly in monoclonal antibody drug R&D and commercialization, while China ranks second in total number of monoclonal antibodies in development or on the market, though only 8 have been approved for domestic market launch. In 2017, 22 launched monoclonal antibody drugs achieved annual sales exceeding $1 biliion in 2017. Access to 1408 monoclonal antibodies deal records, drug development/commercial license was the primary agreement type. In the future, the development trend of monoclonal antibodies will be focused on new targets, new indications and new therapeutic schemes, and then more "blockbuster drugs" will be produced.

Key words Monoclonal antibodies Clinical R&D Commercial deal 单克隆抗体是由单个 B 淋巴细胞克隆所分泌的抗体，由于 B 淋巴细胞只能产生一种专有的、针对一种抗原决定簇的抗体，所以具有理化性质高度专一、生物活性单一、与抗原结合特异性强等特点 [1]。经过 30 多年的研究和发展，单克隆抗体药物在肿瘤和自身免疫疾病治疗领域取得了巨大进展，同时也是医药领域增长速度最快、最有前景的发展方向。因此，本文将单克隆抗体药物作为研究对象，分析全球单克隆抗体药物的研发和商业化现状、市场发展情况，以期对我国单克隆抗体产业的发展起到支撑作用。

1 研究方法

采用科睿唯安 (Clarivate analytics) 的 Cortellis 数据库作为检索对象，检索时间是 2018 年 10 月 19 日，其中研发和商业化阶段、药物种类、作用靶点、主要国家/地区分布、产品市场份额、药物交易分别从 "Drugs" 和 "Deals" 两个入口进行检索，检索词均采用 "技术 (technologies)"

中“单克隆抗体（monoclonal antibody)”。分析方法采用定量分析、定性调研和专家智慧相结合的方法。分析工具借助于 Cortellis 数据库的分析平台以及 Excel 等数据处理工具。

2.1 研发和商业化阶段总体分布

药物从探索发现到商业化上市需要经历多个阶段，从 Cortellis 的数据来看，除去终止、ChinaXiv 合作期刊撤回、无报道的药物外，全球至今共记录有 2423 个处于研发和商业化阶段的单克隆抗体药物（研发和商业化阶段包含已上市、注册、预注册、临床 3 期、临床 2 期、临床 1 期、临床前、发现和暂停，下同)。其中研发状态处于发现阶段的药物有 1843 个，处于临床阶段（含临床 1 期、临床 2 期、临床 3 期）的药物有 1123 个，处于上市阶段的药物有 133 个。(由于一种单克隆抗体药物在不同国家或针对不同适应症时可能处于不同的研发和商业化阶段，因此，处于每个阶段的药物数量总和大于全部药物数量 2423 个）图 1 [Figure 1: see original paper] 全球单克隆抗体药物处于研发和商业化各阶段的数量分布 Fig.1 Quantity distribution of monoclonal antibodies in R&D and industrialization

2.2 主要国家/地区

单克隆抗体药物作为生物药的新兴细分品种，迎来全球各国的研发和竞争热潮。目前共有上百个国家/地区竞逐单克隆抗体药物市场，其中药物研发和商业化数量排名前十的国家/ 地区（仅统计企业总部所在国家/地区）见图 3 [Figure 3: see original paper]。受益于良好的创新药研发环境，总部位于美国的企业在单克隆抗体药物研发和商业化方面遥遥领先，单克隆抗体药物数量高达 761 个，其中已上市的药物有 64 个；总部位于中国（不含台湾）的企业的单克隆抗体药物数量排名第二，但是已上市的药物仅有 8 个，这说明加快单克隆抗体药物在我国的上市进程是一个亟待解决的问题。

ChinaXiv 合作期刊图 2 [Figure 2: see original paper] 单克隆抗体药物数量 TOP10 的国家/地区 Fig.2 Global TOP10 countries/regions of monoclonal antibodies

2.3 技术和种类

基因工程抗体技术主要包括人源化技术、抗体库技术和转基因小鼠技术等，在这些技术的推动下，单克隆抗体人源化程度不断提高，并不断往小型化、功能化等方向拓展。根据结构可分为：单克隆抗体（鼠源单抗、嵌合单抗、人源化单抗、全人源单抗）和抗体偶联药物、多特异性抗体、抗体融合蛋白、小分子抗体（Fab、ScFv、VHHS）等新型单克隆抗体。其中人源化单克隆抗体药物的上市数量最多，占单克隆抗体药物上市总数的 37.6%；新型单克隆抗体中小分子抗体的上市数量最多，占单克隆抗体药物上市总数的 9.8%。

图 3 各细分种类已上市单克隆抗体药物的数量分布 Fig.3 Quantity distribution of each kind of launched monoclonal antibodies ChinaXiv 合作期刊

2.4 靶点及作用机制

迄今为止，单克隆抗体药物的生物学功能主要体现在抑制肿瘤生存的关键分子、激活针对肿瘤的免疫固有性和适应性、抗体偶联细胞毒药物三个方面 [2]。单克隆抗体药物的靶点主要集中在 HER、TNF、CD20、PD-1/L1、VEGF 以及 CD3，其中靶向 HER2 的单克隆抗体药物数量最多，作用机制是下调 HER2 表达水平并抑制肿瘤生长 [3]。靶向 TNF- 的单克隆抗体药物数量排名

第二，作用机制是中和血液中游离型 TNF- 和免疫细胞表面跨膜型 TNF- 活性，阻断 TNF- 与 I 型 TNF- 受体 p55 及 II 型 TNF- 受体 p75 的亚基结合 [4]。

表 1 药物主要靶向作用数量 TOP10 Table 1 TOP10 target-based actions of monoclonal antibodies 主要靶向作用数量（个）HER2 酪氨酸激酶受体抑制剂 TNF- 配体抑制剂 TNF 结合剂 B 淋巴细胞 CD20 抗原抑制剂程序性细胞死亡蛋白-1 抑制剂 VEGF 配体抑制剂 程序性细胞死亡蛋白-1 配体抑制剂表皮生长因子受体拮抗剂 HER2 酪氨酸激酶受体调节剂 CD3 调节剂

2017 年，全球已上市的单克隆抗体药物中销售额高于 10 亿美元的有 22 个，销售额排

名前十的单克隆抗体药物的介绍如下：(1) Adalimumab (Humira) 阿达木单抗 Adalimumab 最初是由 BASF Knoll 和 Cambridge Antibody Technology (CAT) 合作研发的 TNF- 全人源单克隆抗体，通用名为阿达木单抗 [5]。2001 年，Abbott 收购 BASF Knoll，并将该抗体市场化。Adalimumab 于 2002 年获得美国食品药品管理局（FDA）批准，并于

2003 年获得欧洲药品管理局（EMEA）批准。2013 年，Abbott 因业务发展需要将 AbbVie

独立拆分出来，AbbVie 负责 Adalimumab 后期的生产开发和销售。此前，Abbott 与 Eisai 达成协议，将 Adalimumab 用于治疗类风湿关节炎的日本、韩国及台湾市场授权给 Eisai。截至目前，Adalimumab 在全球已经获批类风湿样关节炎、幼年特发性关节炎、银屑病关节炎、强直性脊柱炎、克罗恩氏病等 15 个适应症。在中国，Adalimumab 已经获批三个适应症：2010 年获批类风湿关节炎适应症，2013 年获批强直性脊柱炎适应症，2017 年获批中重度斑块型 ChinaXiv 合作期刊银屑病适应症。(2) Infliximab (Remicade) 英夫利西单抗 Infliximab 是由 Johnson & Johnson、Merck、Mitsubishi Tanabe Pharma 共同研发的人/鼠 IgG1k 同型链上的嵌合单克隆抗体 [6]，主要用于治疗克罗恩病、溃疡性结肠炎、类风湿样关节炎、强直性脊柱炎、银屑病关节炎、斑块性银屑病等疾病，通用名为英夫利西单抗。

Infliximab 于 1998 年获得 FDA 批准，在美国、欧洲、日本和中国共同销售。注射用 Infliximab 于 2006 年进入中国，并于 2017 年进入国家医保药品目录。(3) Rituximab (Rituxan; MabThera) 利妥昔单抗 Rituximab 是由 Roche 生产的抗 CD20 人鼠嵌合型单克隆抗体，该药是第一个被批准用于肿瘤治疗的单克隆抗体，是肿瘤内科治疗史上一个重要的里程碑，通用名为利妥昔单抗。

1997 年，Rituximab 获得美国 FDA 批准，用于治疗复发难治性滤泡淋巴瘤，随后又获准用

于治疗其他 B 细胞非霍奇金淋巴瘤；1999 年，中国食品药品监督管理局（CFDA）批准 Rituximab 进口，用于治疗滤泡淋巴瘤和弥漫性大 B 细胞淋巴瘤。Rituximab（375mg/m2 标准剂量）联合化疗，显著提高了 B 细胞非霍奇金淋巴瘤的治愈率，它不仅能使患者获得临床缓解，而且能显著延长患者的无进展生存和 5 年总生存率，从而为治愈更多的 B 细胞非霍奇金淋巴瘤提供了可能 [7]。(4) Trastuzumab (Herceptin) 曲妥珠单抗 Trastuzumab 由 Genentech 公司开发，而后除日本与美国以外地区的开发与销售权被转让给 Roche，该药是全球首个获准用于治疗 HER2-阳性的人源化单克隆抗体，也是首个治疗 HER2-阳性早期乳腺癌的靶向药物，通用名为曲妥珠单抗。Trastuzumab 最先于 1998 年在美国上市，临床上联合紫杉醇用于 HER2-过

度表达的乳腺癌的一线治疗 [8]，或单独给药用于上述疾病的二线与三线治疗，2010 年又获批用于 HER2-阳性转移性胃癌的治疗。Trastuzumab 于 2003 年进入中国市场。随着临床研究的深入，Trastuzumab 应用于乳腺癌、卵巢癌、胃癌、肺癌和肾癌等多种肿瘤的治疗，其安全性与有效性在国内外长期的临床实践中得到了广泛验（5）Bevacizumab (Avastin) 贝伐珠单抗 Bevacizumab 是 Roche 旗下 Genentech 开发的全球首个可广泛用于多种肿瘤的抗血管生成药物，通用名为贝伐珠单抗。Bevacizumab 于 2004 年首次获得 FDA 批准用于治疗转移性结直肠癌，目前已拓展到结直肠癌、非小细胞肺癌、胶质母细胞瘤、肾细胞癌、宫颈癌、卵巢癌、输卵管癌、腹膜癌等多个实体瘤适应症。Bevacizumab 于 2005 年在欧洲获批，2010 ChinaXiv 合作期刊年在中国上市用于治疗转移性结直肠癌，2015 年又被 CFDA 批准用于治疗非小细胞肺癌。

与单独给药相比，Bevacizumab 的精确作用方式使其能够与化疗药物有效结合，并提高肿瘤的治疗效果 [9]。(6) Nivoluma (Opdivo) 纳武利尤单抗 Nivolumab 是由 Bristol-Myers Squibb (BMS) 和 Ono Pharmaceutical 联合开发的一种抗 PD-1 完全人源化的 IgG4 型单克隆抗体，该药是 FDA 批准的首个抗 PD-1 靶向药物，用于其他疗法难治性晚期黑素瘤 [10]，通用名为纳武利尤单抗。BMS 的 Nivolumab 于 2014 年获得日本医药品与医疗器械局 (PMDA)、美国 FDA 的批准，2015 年获得欧洲 EMA 批准，并由 Ono Pharmaceutical 和 BMS 在美国、欧洲和日本共同销售。2018 年 6 月，CFDA 批准 Nivolumab 单抗注射液进口注册申请，这是我国批准注册的首个以 PD-1 为靶点的单克隆抗体药物，用于治疗表皮生长因子受体（EGFR）基因突变阴性和间变性淋巴瘤激酶（ALK）阴性、既往接受过含铂方案化疗后疾病进展或不可耐受的局部晚期或转移性非小细胞肺癌（NSCLC）成人患者。

自上市以来，Nivolumab 已相继获批 11 个适应症，分别是：黑色素瘤（一、二线）、非小细胞肺癌（二线）、肾细胞癌、经典霍奇金淋巴瘤、结直肠癌、头颈癌、膀胱癌、肝癌、转移性 Merkel 细胞癌、晚期胃癌、胃癌（日本），随着 Nivolumab 适应症的不断增多，Nivolumab 市场份额随之不断攀升。(7) Ustekinumab (Stelara) 优特克单抗 Ustekinumab 是 Johnson & Johnson 研发的一种高亲和力、全人源化 IgG1k 单克隆抗体，其靶点为 IL-12/IL-23 的 p40 亚基 [11]。Ustekinumab 于 2008 年在加拿大上市，随后于 2009 年获得美国 FDA 批准上市，2011 年获得日本 PMDA 批准上市，该药批准的适应症为中度至重度斑块状银屑病、活跃的银屑病性关节炎和克罗恩氏病。Ustekinumab 由 Johnson & Johnson 在欧洲、美国和日本市场销售。(8) Denosumab (Pralia) 地诺单抗 Denosumab 是由 Amgen 研发的首个靶向核因子 kB 受体活化因子（RANK）配体的全人源单克隆抗体，通用名为地诺单抗。2007 年，Daiichi Sankyo 从 Amgen 获得 Denosumab 在日本的开发及销售权利，并于 2012 年 4 月以商品名 RANMARK（皮下注射，120mg）在日本市场推出，用于治疗多发性骨髓瘤所致的骨骼并发症以及由实体瘤所致的骨转移。

Denosumab 于 2013 年通过快递通道获得 FDA 批准，用于骨质疏松 (绝经后骨质疏松)、延缓骨转移癌患者骨相关并发症 (病理性骨折、脊髓压迫等) 的发生、恶性肿瘤患者高钙血症、ChinaXiv 合作期刊芳香化酶和雄激素缺乏所诱导的骨质丢失以及骨巨细胞瘤患者的临床治疗 [12]。截止目前，Denosumab 已经在全球 80 多个国家上市。(9) Pembrolizumab (Keytruda) 帕博利珠单抗 Pembrolizumab 是由 Merck 研发的一种与 PD-1 受体结合的人源化单克隆抗体，可以阻断 PD-1 与 PD-L1 和 PD-L2 的结合，通用名为帕博利珠单抗。Pembrolizumab 是美国 FDA 批准的首个不依据肿瘤来源，而依据生物标记物进行区分的抗肿瘤疗法，可谓广谱抗癌药 [13]。Pembrolizumab 于 2014 年获得美国 FDA 批准，2015 年获得欧洲 EMA 批准，2016 年获得日本 PMDA 批准，并由 Merck 在美国、欧洲和日本市场销售。2018 年 7 月，Pembrolizumab 的中国获得 CFDA 批准，成为继 BMS 的 Nivoluma 之后第 2 个正式在中国上市的 PD-1/PD-L1 单抗类药物，适用于晚期恶性黑色素瘤。

自上市以来，Pembrolizumab 相继获批以下适应症：黑色素瘤（一、二线）、非小细胞肺癌（一、二线）、经典霍奇金淋巴瘤、头颈癌、晚期胃癌。值得一提的是，2016 年 10 月，Pembrolizumab 获批非小细胞肺癌一线治疗适应症，而 Nivolumab 则在此重要适应症上惨遭失败，以至于在 2017 年第四季度，销售额遥遥领先的 Nivolumab 面临被 Pembrolizumab 赶超的尴尬境地。随着 Pembrolizumab 适应症的不断增多，特别是一线非小细胞肺癌治疗适应症，Pembrolizumab 的市场份额将快速扩大。（10）Ranibizumab (Lucentis) 雷珠单抗 Ranibizumab 是由 Roche 旗下 Genentech 和 Novartis 合作开发的第二代人源化抗血管内皮生长因子（VEGF）重组鼠单克隆抗体片段，由 Bevacizumab 的部分抗体片段衍生加工而成。Roche 拥有该药在美国的商业化权利，Novartis 则拥有该药在美国以外国家和地区的独家权利。Ranibizumab 于 2006 年获得 FDA 批准，用于年龄相关性黄斑变性（AMD）的临床治疗 [14]。随后，Ranibizumab 分别于 2010 年、2012 年及 2015 年被批准用于视网膜静脉阻塞（RVO）导致的黄斑水肿、糖尿病性黄斑水肿（DME）及糖尿病视网膜病变（DR）的治疗。

2012 年，Ranibizumab 被 CFDA 批准上市，用于湿性年龄相关性黄斑变性（wAMD）的治

ChinaXiv 合作期刊表 2 2017 年销售额 10 亿美元以上的单克隆抗体药物汇总 Table 2 The monoclonal antibodies of annual sales over $1 billion. Globally, 1,408 monoclonal antibody drug transactions have been recorded, with drug development and commercialization licensing representing the primary transaction type. Future trends will focus on novel targets, new indications, and innovative treatment regimens, promising the emergence of more "blockbuster drugs."

Keywords: monoclonal antibody; clinical development; commercialization transaction

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2.6 Current Status of Product Transactions

To date, a total of 1,408 monoclonal antibody drug transactions have been recorded. The three main transaction types are drug development and commercialization licensing (29% of all transactions), drug funding (15%), and early-stage drug R&D collaboration (14%). The top ten monoclonal antibody drug commercialization deals by value in 2017 are detailed in .

The following cases illustrate key transaction patterns from that year:

(1) Vir-Visterra $1 Billion Early-Stage R&D Collaboration
On October 18, 2017, Vir and Visterra entered into a $1 billion agreement to jointly advance and commercialize infectious disease programs including VIS-FLX, VIS-RSV, and VIS-FNG based on Visterra' s Hierotope platform. The collaboration combines Visterra' s antibody design and production capabilities with Vir' s infectious disease expertise, covering VIS-FLX, VIS-RSV, VIS-FNG, and two additional R&D programs.

(2) Incyte-MacroGenics $900 Million PD-1 Monoclonal Antibody Licensing Deal

On October 24, 2017, Incyte and MacroGenics announced a global partnership for the PD-1 monoclonal antibody MGA012. Under the agreement, Incyte gained exclusive worldwide rights to develop and commercialize MGA012 for all indications, while MacroGenics retained development pipeline ownership. Incyte paid $150 million upfront, with MacroGenics eligible for 15-24% sales royalties upon approval and commercialization.

(3) ImmuNext-Sanofi $500 Million CD40L Drug Development and Commercialization Agreement

On January 9, 2017, ImmuNext partnered with Sanofi to develop innovative protein therapeutics for autoimmune disorders. The anti-CD40L monoclonal antibody candidate INX-201, in preclinical development for lupus and multiple sclerosis, offers therapeutic potential across multiple autoimmune diseases. ImmuNext could receive up to $500 million in milestone payments plus double-digit sales royalties.

(4) Merck-Domain $257 Million Adenosine Receptor Research Collaboration

On January 23, 2017, Merck collaborated with Domain, providing $257 million in milestone payments and royalties to support Domain' s GPCR technology platform for adenosine receptor drug development. Merck gains worldwide rights to resulting assets, with next-generation adenosine receptor antagonists representing a key addition to its immuno-oncology pipeline.

(5) Celularity-TNK Therapeutics $200 Million CAR Patent Exclusive License

On June 12, 2017, Celularity signed an exclusive patent license agreement with TNK Therapeutics (a Sorrento Therapeutics subsidiary) covering CAR constructs for anti-CD38, anti-CD20, anti-CD123, anti-CD16, and anti-CD19 CAR-T cell therapies. Celularity paid $100 million upfront (50% of the $200 million total) to access anti-CD38 CAR structures and placental/umbilical cord blood-derived or adult cells.

(6) AbCellera Biologics-Pfizer $90 Million Therapeutic Antibody Research Collaboration

On January 5, 2017, AbCellera Biologics partnered with Pfizer to develop novel therapeutic antibodies. AbCellera applied its proprietary monoclonal antibody screening platform to identify functional modulating antibodies against undisclosed membrane protein targets, receiving $90 million in commercial milestone payments and research support.

(7) HanAll Biopharma-Harbour BioMed $81 Million HL161 and HL036 Licensing Agreement

On September 12, 2017, HanAll Biopharma (Daewoong Pharmaceutical Group) and China' s Harbour BioMed signed a strategic partnership for Greater China rights to innovative biologics. Harbour BioMed gained exclusive rights to develop, manufacture, and sell the anti-FcRn fully human monoclonal antibody HL161 (for myasthenia gravis, neuromyelitis optica, ITP, pemphigus) and the

novel anti-TNF eye drop HL036 (for inflammatory ocular diseases including diabetic retinopathy, wet AMD, dry eye, non-infectious uveitis). HanAll receives up to $81 million in milestones plus tiered sales royalties, retaining rights outside Greater China.

(8) US Government $30.5 Million Funding for Emergent BioSolutions' Viral Hemorrhagic Fever Antibody
On February 13, 2017, Emergent BioSolutions received funding from the US Biomedical Advanced Research and Development Authority (BARDA) for monoclonal antibody development against viral hemorrhagic fever. The 36-month base period is valued at $7.4 million, with total potential funding reaching $30.5 million if all options are exercised. Emergent will utilize its Center for Innovation in Advanced Development and Manufacturing (CIADM) facilities.

(9) Kiniksa Pharmaceuticals-Primatope Therapeutics $21.3 Million KPL-404 Licensing Agreement
On September 30, 2017, Kiniksa Pharmaceuticals licensed KPL-404, a monoclonal antibody inhibitor of CD40/CD40L interaction in preclinical development for autoimmune diseases.

(10) Bill & Melinda Gates Foundation $20.5 Million Funding for Achaogen' s Gram-Negative Bacteria Antibody
On May 4, 2017, Achaogen received funding from the Bill & Melinda Gates Foundation to develop a monoclonal antibody against Gram-negative bacteria (including neonatal sepsis) for developing countries. The agreement includes $10.5 million in funding plus a $10 million equity investment.

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3 Summary and Outlook

Since FDA approval of the first therapeutic monoclonal antibody drug in 1986, monoclonal antibody drugs have matured across all dimensions—from target discovery to technological improvement, clinical research to commercialization strategies—establishing themselves as mainstream innovators in the pharmaceutical field.

The global monoclonal antibody drug market has reached approximately $100 billion, maintaining over 10% annual growth in the past decade—significantly higher than the 5-6% industry average. The United States represents the world' s largest monoclonal antibody drug R&D hub. PD-1/L1 drugs and antibody Fc fusion proteins demonstrate broad market prospects, while multi-specific antibodies and antibody-drug conjugates are entering new developmental phases.

Future monoclonal antibody R&D will concentrate on three directions: novel targets, new indications, and innovative treatment regimens:

(1) Novel Target Discovery
The identification of PD-1/PD-L1 rapidly expanded the oncology monoclonal

antibody market. With advances in post-genomics and metabolomics, increasingly diverse monoclonal antibody targets will be discovered and investigated, continuously expanding the drug category.

(2) New Indication Expansion
Single indications address limited patient populations. As basic research deepens and clinical trials achieve breakthroughs, monoclonal antibody drugs will penetrate therapeutic areas beyond malignant tumors and autoimmune diseases, enhancing competitiveness and market potential.

(3) Innovative Treatment Regimens
Clinical evidence demonstrates that combination therapies often achieve significantly superior efficacy compared to monotherapies. Developing novel treatment regimens can substantially improve drug utilization frequency and applicability scope.

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