Antibodies to watch in 2024

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Agenda

- Definitions, data sources, objectives, limitations of the data
- Annual number of antibody therapeutics entering clinical study, 2000–2022
- Trends in approvals of antibody therapeutics
- Clinical phase transitions and approval success rates
- First approvals of antibody therapeutics granted in 2023 and those in review
- Trends in late-stage development of antibody therapeutics
  - “Antibodies to Watch” for possible transition to regulatory review

Definitions,
Data sources,
Objectives,
Limitations of the data

Definitions, inclusion/exclusion criteria

- **Antibody therapeutic**: Recombinant protein-based molecule with at least one antigen binding site derived from an antibody-gene that is evaluated as a therapeutic; excludes polyclonal antibodies from a natural source, antibody-encoding DNA, Fc only / Fc fusion proteins, and diagnostics
- **Commercial sponsor**: Public or private for-profit entity; excludes non-profit and government entities
- **Innovative**: Unique in composition of matter; excludes biosimilars
- **Clinical status**: Most advanced clinical study; excludes early-stage studies for molecules in Phase 2/3 or 3 studies or in reg.review, approved
- **First**: First instance of an event; excludes second, third, etc.

Sources of data

- Public disclosures from primary sources, including but not limited to:
  - Company press releases, presentations, meeting abstracts, quarterly and annual reports, etc.
  - Clinical trials registries, such as clinicaltrials.gov
  - Regulatory agency documents from FDA, EMA, Health Canada, NMPA, etc.
  - WHO INN lists
- We cannot rely on secondary sources such as commercial databases because:
  - Our inclusion / exclusion criteria is specialized
  - Lags in data updates, esp. terminations, in databases
  - Introduction of errors that occur during data processing

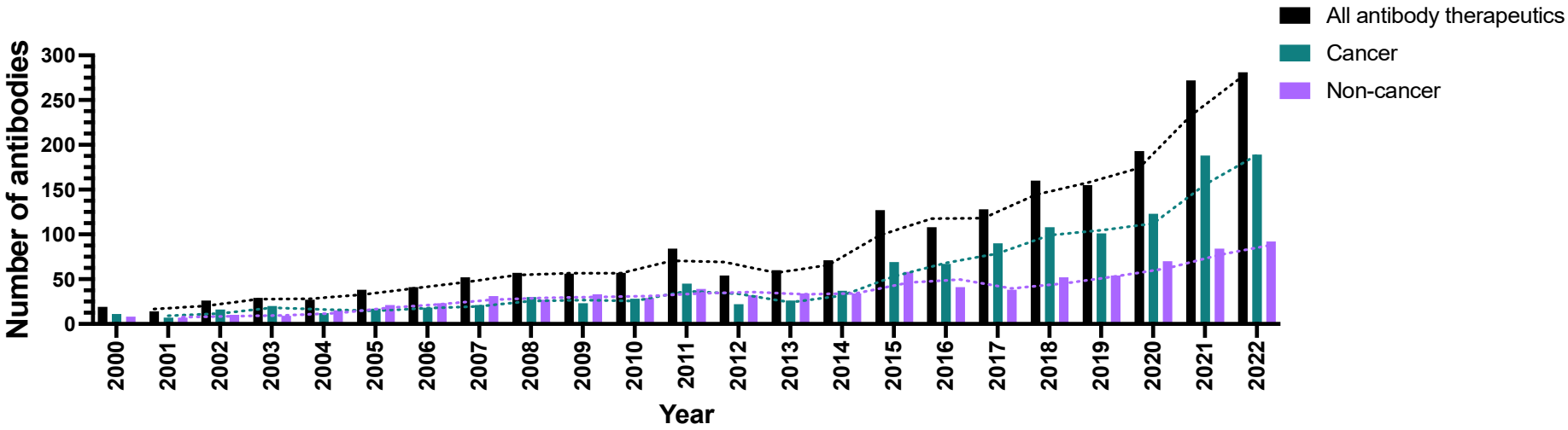
Objectives

- To determine trends in antibody therapeutic development over time
  - Overall, as well as focus on particular therapeutic areas, formats, or targets
- To determine clinical success rates for antibody therapeutics development, as conducted by the biopharmaceutical industry
  - Clinical phase transition rates
  - Overall marketing approval rates
- To assess innovation in the biopharmaceutical industry

Limitations of the data

- Lag times between event (e.g., IND filing), public disclosure (cryptic or otherwise), and our identification of event
- Particularly for early-stage molecules,
  - Composition category may not be known (e.g., not identified or identified as biologic); if identified as antibody, details are often missing (e.g., sequence source, format)
  - Phase 1 studies may be done in healthy volunteers; TA may change
  - Clinical study initiation date may be difficult to determine; termination date may be impossible to determine
- Information for status can be inconclusive
  - Clinicaltrials.gov records not updated
  - Company pipelines not updated
- Clinical phases are often blended
  - Early-stage: Phase 1, Phase 1/2, Phase 2
  - Late-stage: Pivotal Phase 2, Phase 2/3, Phase 3

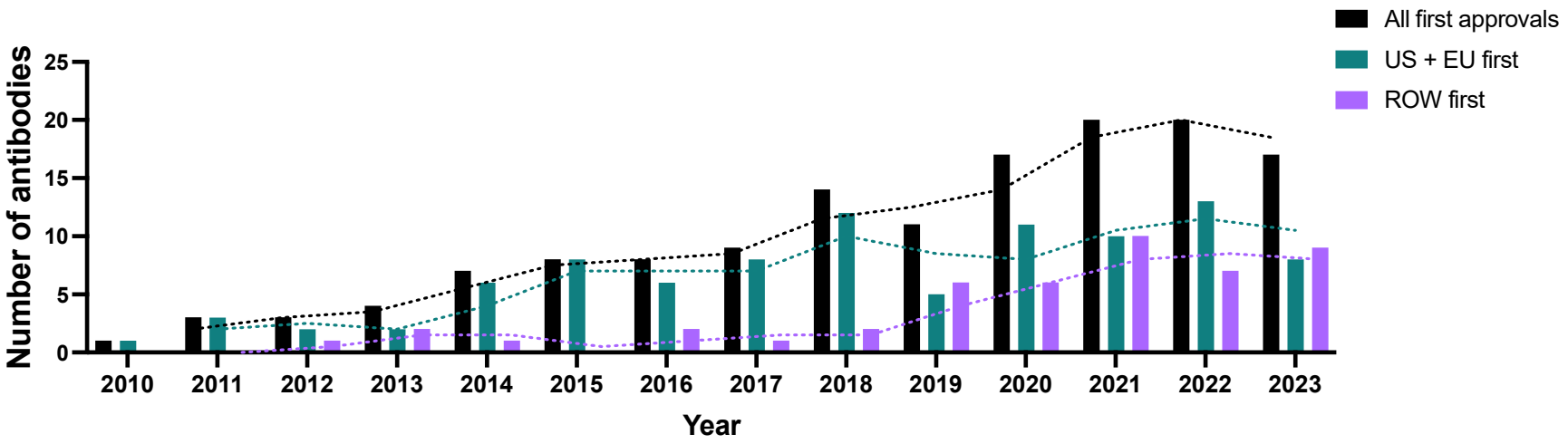
Annual number of antibody therapeutics entering clinical study, 2000–2022



Black bars, all antibody therapeutics. Green bars, antibody therapeutics for non-cancer indications only. Purple bars, antibody therapeutics for cancer only.
Dotted lines, 2-y moving averages. Totals include only antibody therapeutics sponsored by commercial firms; those sponsored solely by government, academic or nonprofit organizations were excluded. Biosimilar antibodies and fc fusion proteins were also excluded.

Trends in approvals of antibody therapeutics

Annual first approvals for antibody therapeutics during 2010–2023



Black bars: Annual total number. Green bars: Annual total US or EU first approvals. Violet bars: Annual total first approval in any country or region other than the US or EU.
Dotted lines represent the 2-y moving averages for the respective set of bars.
Top two ROW countries contributing to totals in 2010–22: China and Japan.

Abbreviations: EU, European Union; ROW, rest of world; US, United States of America.

Clinical phase transition and approval success rates for antibody therapeutics

Objective: Quantify success

- Key questions:
  - What percentage of commercially sponsored antibody therapeutics that enter clinical study are ultimately granted at least one marketing approval?
  - Has this percentage changed over time?

References:

1. Gosse ME, DiMasi JA, Nelson TF. Recombinant protein and therapeutic monoclonal antibody drug development in the United States from 1980 to 1994. Clin Pharmacol Ther. 1996 Dec;60(6):608-18.
2. Reichert JM. Monoclonal antibodies in the clinic. Nat Biotechnol. 2001 Sep;19(9):819-22
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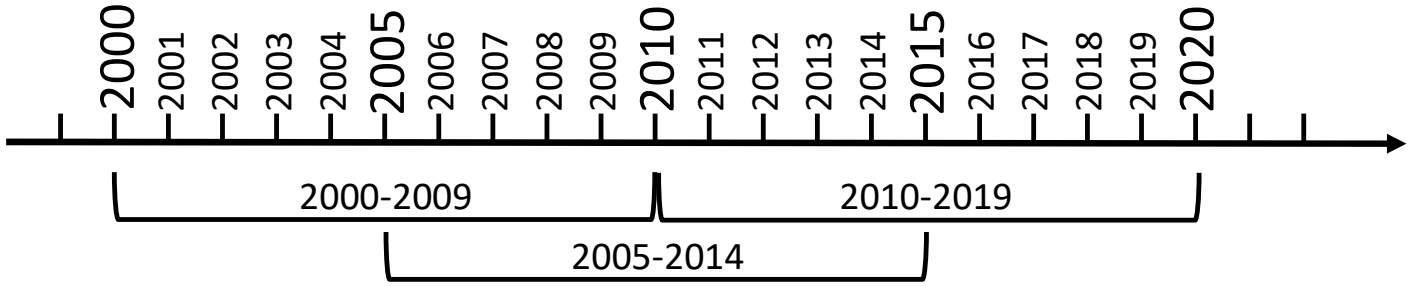
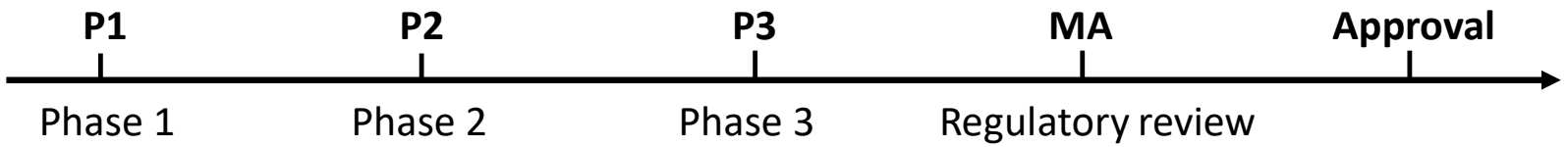
5. Nelson AL, Dhimolea E, Reichert JM. Development trends for human monoclonal antibody therapeutics. Nat Rev Drug Discov. 2010 Oct;9(10):767-74. doi: 10.1038/nrd3229.
6. Kaplon H, Reichert JM. Antibodies to watch in 2019. MAbs. 2019 Feb/Mar;11(2):219-238. doi: 10.1080/19420862.2018.1556465.
7. Crescioli S, et al. Antibodies to watch in 2024. MAbs. 2024 Jan. doi: 10.1080/19420862.2023.2297450

Phase transition and approval success rates

(antibody therapeutics which entered clinical studies in 2000-2019)

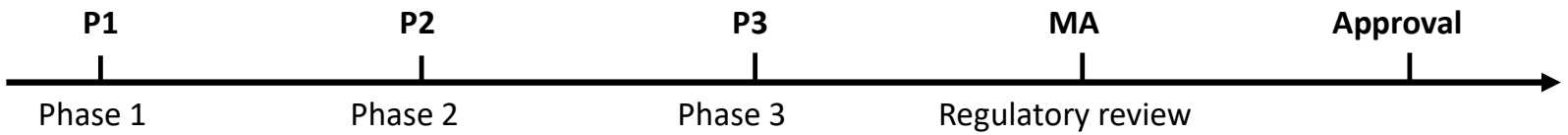


Phase transition and approval success rates



1. Phase 1;
2. Phase 2 (including Phase 1/2);
3. Phase 3 (including pivotal Phase 2 and Phase 2/3);
4. Regulatory review in US/EU or global;
5. Approved in US/EU or global;
6. All development terminated at Phase 1;
7. All development terminated at Phase 2 (including Phase 1/2);
8. All development terminated at Phase 3 (including pivotal Phase 2 and Phase 2/3);
9. All development terminated in regulatory review in US/EU or global

Phase transition and approval success rates



Phase transition success rate:

$$\frac{\text{\# mAbs transitioned to the next Phase}}{\text{\# mAbs entered in Phase} - \text{\# mAbs active in Phase}} = \frac{\text{\# mAbs transitioned to the next Phase}}{\text{\# mAbs transitioned to the next Phase} + \text{\# mAbs terminated at that Phase}}$$

P1 to Approval success rate:

$$\text{P1 to P2 phase transition success rate} \times \text{P2 to P3 phase transition success rate} \times \text{P3 to MA phase transition success rate} \times \text{MA to Approval phase transition success rate}$$

Percent completion of a cohort:

$$\frac{\text{\# mAbs with known fate}}{\text{\#mAbs in the cohort}} = \frac{\text{\# mAbs approved} + \text{\# mAbs terminated}}{\text{\# mAbs in the cohort}}$$

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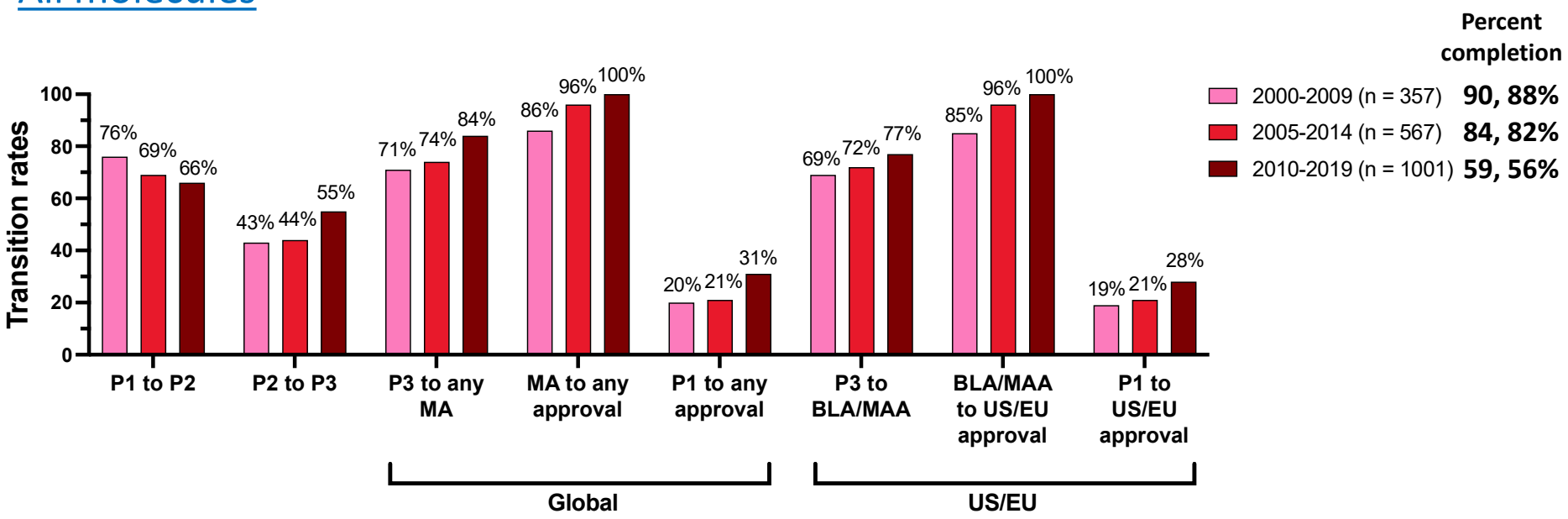
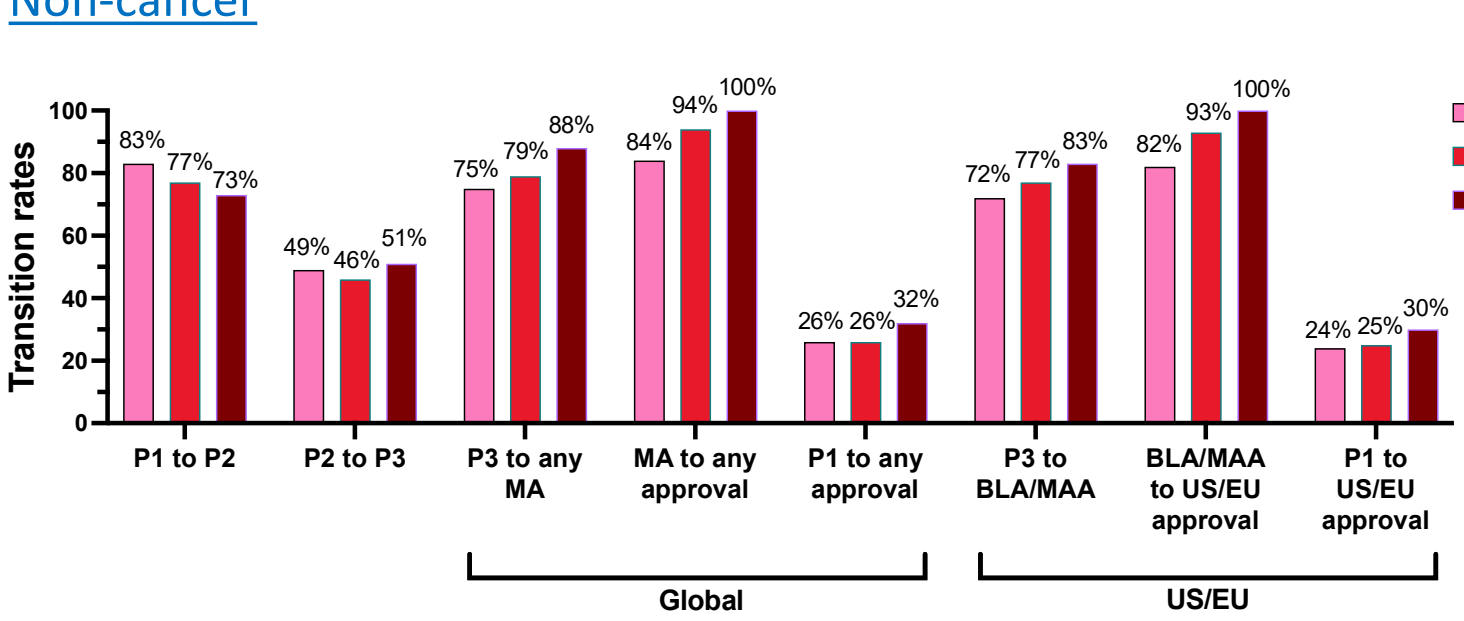
Phase transition and approval success rates

All molecules



Phase transition and approval success rates

Non-cancer



Percent completion

- 2000-2009 (n = 181) **88, 85%**
- 2005-2014 (n = 301) **81, 78%**
- 2010-2019 (n = 408) **59, 57%**

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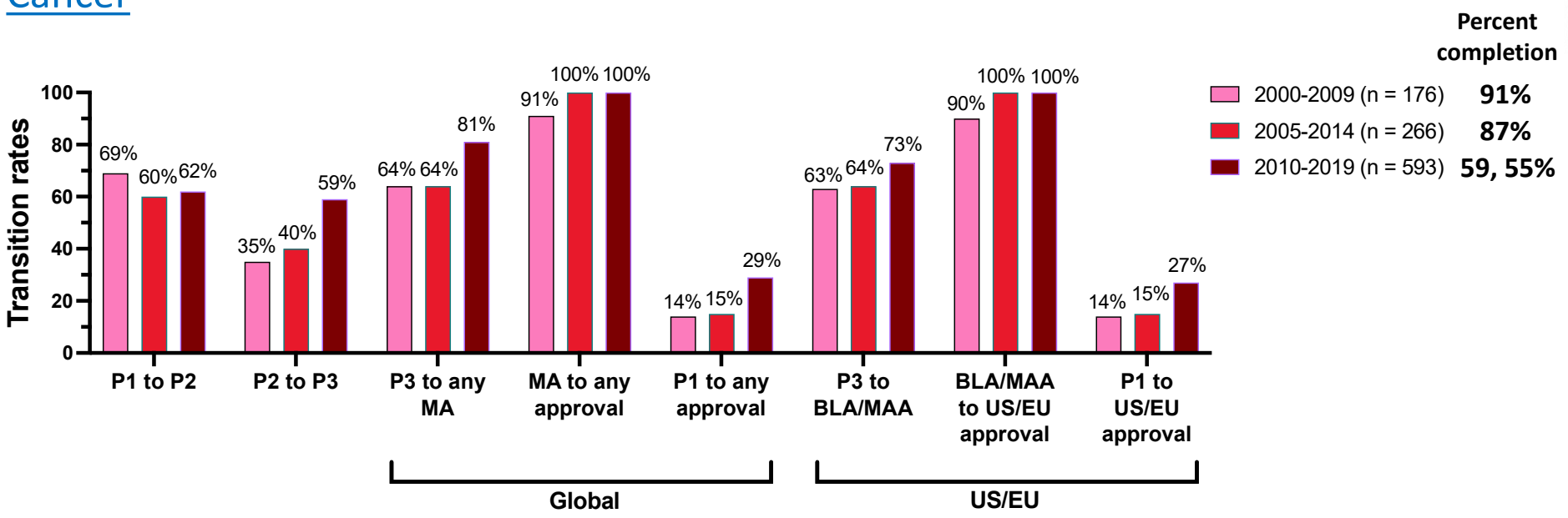
Phase transition and approval success rates

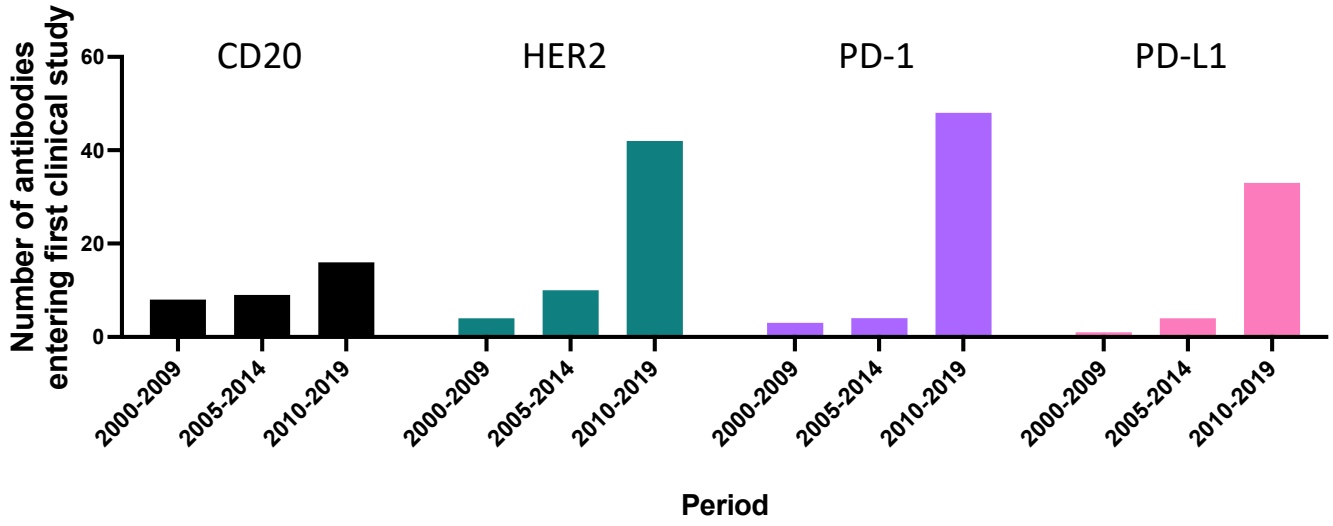
Cancer



Phase transition and approval success rates

The increase in P1 to Approval success rate in the 2010-2019 cohort seems to be due to the increase in the P1 to Approval success rate for the antibodies for cancer within the cohort.

Increase in number of antibodies against well-validated targets in the cancer cohort



Phase transition and approval success rates

Comparison with our previous analysis

2000-2009 cohort	Percent completion	P1 to Approval in US/EU success rate
Antibodies to watch in 2019	76%	21%
Antibodies to watch in 2024	88%	19%

2005-2014 cohort	Percent completion	P1 to Approval in US/EU success rate
Antibodies to watch in 2019	58%	22%
Antibodies to watch in 2024	82%	21%

Phase transition and approval success rates

Comparison with Biotechnology Innovation Organization (BIO) reports

	Period	Success rate	Type of data	
BIO study (2021)	2006–2015	11.6%	Data for all phase transitions for all diseases for which each molecule was evaluated in clinical studies during the designated period	Success was defined as an approval only in US.
BIO study (2016)	2011–2020	12.1%		
Our study	2000-2019	19-28% (global) 20-31% (US/EU)	Data for the most advanced phase of development achieved by the molecule	Success is defined as an approval in any country or specifically in US or EU.

The BIO method
- includes more terminations compared to our method;
- excludes non-US approvals.

→ Approval success rates for monoclonal antibodies substantially lower than ours

1. Thomas D, Chancellor D, Micklus A, LaFever S, Hay M, Chaudhuri S, Bowden R, Low AW. Clinical development success rates and contributing factors 2011–2020. Biotechnology Innovation Organization Report; 2021 Feb. [accessed 2023 Sept 12].
2. Thomas D, Burns J, Audette J, Carroll A, Dow-Hygelund C, Hay M Clinical development success rates 2006-2015. Biotechnology Innovation Organization Report; 2016. [accessed 2023 Sept].

First approvals in 2023

First approvals: Non-cancer indication

INN (brand name)	Target; format	Indication first approved	Country/region of approval in 2023
Lecanemab (Leqembi)	Amyloid beta protofibrils; Humanized IgG1κ	Early Alzheimer disease	US, Japan
Rozanolixizumab (RYSTIGGO)	FcRn; Humanized IgG4κ	Generalized myasthenia gravis	US, Japan
Pozelimab (VEOPOZ)	Complement C5; Human IgG4κ	CHAPLE disease	US
Mirikizumab (Omvoh)	IL-23p19; Humanized IgG4κ	Ulcerative colitis	US, EU, Japan, Australia, UK, Canada, Israel
Concizumab (Alhemo)	Tissue factor pathway inhibitor; Humanized IgG4κ	Hemophilia A or B with inhibitors	Canada, Australia, Switzerland
Lebrikizumab (EBGLYSS)	IL-13; Humanized IgG4κ	Atopic dermatitis	EU
Tafolecimab (SINTBILO)	PCSK9; Human IgG2κ	Primary hypercholesterolemia and mixed dyslipidemia	China
Divozilimab (Ivlizi)	CD20; Humanized IgG1κ	Multiple sclerosis	Russia

First approvals: Cancer indication

INN (brand name)	Target; format	Indication first approved	Country/region of approval in 2023
Talquetamab (Talvey)	GPCR5D, CD3; Humanized IgG4κ bispecific	Multiple myeloma	US, EU, UK, Switzerland
Elranatamab (Elrexfio)	BCMA, CD3; Humanized IgG2κ bispecific	Multiple myeloma	US, EU, Switzerland, Brazil
Epcoritamab (EPKINLY)	CD20, CD3; Humanized IgG1κ/λ bispecific	Diffuse large B-cell lymphoma	US, Japan, UK, Canada
Glofitamab (COLUMVI)	CD20, CD3e; IgG1κ/λ bispecific	Diffuse large B-cell lymphoma	US, EU, Australia, Canada, UK, China
Retifanlimab (Zynyz)	PD-1; Humanized IgG4κ	Merkel cell carcinoma	US
Narlumosbart (Jinlitai)	RANKL; Human IgG4κ	Giant cell tumor of bone	China
Zuberitamab (Enrexib)	CD20; Chimeric IgG1κ	Diffuse large B-cell lymphoma	China
Adebrelimab (Arelili)	PD-L1; Humanized IgG4κ	Extensive-stage small cell lung cancer	China
Socazolimab	PD-L1; Human IgG1λ	Cervical cancer	China

Antibodies in regulatory review
(excludes all approved products)

Non-cancer indication:

Regulatory review in US and/or EU only

INN or drug code	Target; format	Indication under review	Country/region of review
Narsoplimab	MASP-2; Human IgG4λ	Hematopoietic stem cell transplant-associated thrombotic microangiopathy	US (BLA resubmission expected in 2024)
Axatilimab	CSF-1R; Humanized IgG4κ	Graft vs. host disease	US
Marstacimab	Tissue factor pathway inhibitor; Human IgG1λ	Hemophilia	US (PDUFA date in Q4 2024), EU
Vilobelimab	Complement C5a; Chimeric IgG4κ	SARS-CoV-2 induced septic acute respiratory distress syndrome	EU
Garadacimab	Factor XIIa; Human IgG4λ	Hereditary angioedema	EU

Non-cancer indication:

Regulatory review in US, EU and RoW

INN or drug code	Target; format	Indication under review	Country/region of review
Donanemab	Amyloid beta; Humanized IgG1κ	Early Alzheimer disease	US (accelerated approval, CRL; traditional approval, decision expected Q1 2024), EU, Japan
Crovalimab	Complement C5; Humanized IgG1κ	Paroxysmal nocturnal hemoglobinuria	US, EU, Japan, China

Non-cancer indication:

Regulatory review in RoW only

INN or drug code	Target; format	Indication under review	Country/region of review
Suciraslimab	CD22; Chimeric IgG1κ	Rheumatoid arthritis	China
Batoclimab	FcRn; Human IgG1λ	Generalized myasthenia gravis	China
Ebdarokimab	IL-12/23p40; Humanized IgG1κ	Psoriasis	China
Xeligekimab	IL-17A; Human IgG4κ	Psoriasis	China
Vunakizumab	IL-17A; Humanized IgG1κ	Psoriasis	China
Ebronucimab	PCSK9; Human IgG1λ	Primary hypercholesterolemia and mixed hyperlipidemia, heterozygous familial hypercholesterolemia	China
Recaticimab	PCSK9; Humanized IgG1κ	Hypercholesterolemia	China
Ongericimab	PCSK9; Humanized IgG4κ	Hypercholesterolemia	China
CM310	IL-4 Rα; Humanized	Atopic dermatitis	China

Cancer indication:

Regulatory review in US and/or EU only

INN or drug code	Target; format	Indication under review	Country/region of review
Trastuzumab duocarmazine	HER2; Humanized IgG1κ ADC	HER2+ breast cancer	US (CRL issued in May 2023)
Patritumab deruxtecan	HER3; Human IgG1κ, ADC	Non Small cell lung cancer	US (PDUFA date June 26, 2024)
Odronextamab	CD20, CD3; Human IgG4κ bispecific	Diffuse large B-cell lymphoma	US, EU
Tarlatamab	DLL3, CD3; scFv-scFv-scFc Bispecific	Small cell lung cancer	US (PDUFA date June 12, 2024)
Zanidatamab	HER2, HER2 bispecific biparatopic; scFv-Fc x Fab-Fc (Fc IgG1)	Biliary tract cancers (BTC)	US
Cosibelimab	PD-L1; Human IgG1λ	Squamous cell carcinoma	US (CRL)

Cancer indication:

Regulatory review in US, EU and RoW

INN or drug code	Target; format	Indication under review	Country/region of review
Zolbetuximab	Claudin 18.2; Chimeric IgG1κ	HER2-negative gastric or gastroesophageal junction adenocarcinoma	US (CRL), EU, Japan, China

Cancer indication:

Regulatory review in the RoW only

INN or drug code	Target; format	Indication under review	Country/region of review
Trastuzumab botidotin	HER2; Humanized IgG1κ ADC	HER2+ breast cancer	China
Enlonstobart	PD-1; Human IgG4κ	Cervical cancer	China
Iparomlimab	PD-1; Humanized/chimeric IgG4κ	Cancer	China
Iparomlimab, Tuvonralimab	PD-1, CTLA-4; mixture	Cancer	China
Ivonescimab	PD-1, VEGF-A; IgG1κ-[scFv]2 bispecific	Lung cancer	China
Benmelstobart	PD-L1; Humanized IgG1κ	Small cell lung cancer	China
Tagitanlimab	PD-L1; Humanized IgG1κ	Nasopharyngeal cancer, solid tumor indications	China
Sacituzumab tirumotecan	TROP-2; Humanized ADC	Triple negative breast cancer	China

“Antibodies to Watch” for possible transition to regulatory review in 2024

Non-cancer indication:

INN or drug code	Target(s); format	Indication of relevant late-stage study	Most advanced clinical phase
AZD3152	SARS-CoV-2	Prophylaxis of COVID-19	Phase 3
Bentracimab	Ticagrelor; Human IgG1l Fab	Reversal of the antiplatelet effects of ticagrelor	Phase 3
Rademikibart	IL-4 Rα; Human IgG4κ	Atopic dermatitis	Pivotal Phase 2
Depemokimab	IL-5; Humanized IgG1κ	Eosinophilic asthma, chronic rhinosinusitis with nasal polyps	Phase 3
Imsidolimab	IL-36 R; Humanized IgG4κ	Generalized pustular psoriasis	Phase 3
Anselamimab	Amyloid; Chimeric IgG1κ	Amyloid light chain amyloidosis	Phase 3
Latozinemab	Sortilin; Human IgG1κ	Frontotemporal dementia	Phase 3
Apitegromab	Myostatin; Human IgG4λ	Spinal muscular atrophy	Phase 3

Cancer indication:

Hematological malignancies

INN or drug code	Target(s); format	Indication of relevant late-stage study	Most advanced clinical phase
Linvoseltamab	BCMA, CD3; Human IgG4κ, Bispecific	Multiple myeloma	Phase 3
Felzartamab	CD38; Human IgG1λ	Multiple myeloma	Phase 3
Apamistamab-Iodine (131I)	CD45; Murine IgG1κ, Radiolabeled	Ablation of bone marrow prior to transplantation in AML patients	Phase 3
Sabatolimab	TIM-3; Humanized IgG4κ	Myelodysplastic syndrome	Phase 3

Cancer indication: Solid tumors

INN or drug code	Target(s); format	Indication of relevant late-stage study	Most advanced clinical phase
~~Tusamitamab ravtansine~~	~~CEACAM5; Humanized IgG1κ, ADC~~	~~NSCLC~~	~~Phase 3 (discontinued)~~
Tiragolumab	TIGIT; Human IgG1κ	NSCLC	Phase 3
Datopotamab deruxtecan	TROP-2; Humanized IgG1κ, ADC	HR+/HER2- breast cancer	Phase 3
MRG002	HER2; Humanized IgG1, ADC	HER2+ breast cancer	Phase 3
Botensilimab	CTLA-4; Human IgG1κ	Colorectal cancer	Pivotal Phase 2
Bifikafusp alfa, Onfekafusp alfa	Fibronectin extra-domain B; Human scFv-based immunocytokine (IL-2, TNF), mixture	Melanoma	Phase 3
Zenocutuzumab	HER2, HER3; Humanized IgG1κ Bispecific	NRG1+ pancreatic ductal adenocarcinoma	Pivotal Phase 2
Erfonrilimab	PD-L1, CTLA-4; Humanized/chimeric IgG1, Bispecific	Pancreatic ductal adenocarcinoma	Phase 3

Key messages

- Antibody therapeutics are entering clinical study and being granted marketing approvals world-wide, in increasing numbers recently.
- Therapeutic antibodies that entered first clinical studies in the 2000-2019 period have approval success rates in the range of 14–32%, with higher rates associated with antibodies for non-cancer indications and recent development.
  - Phase transition and approval success rates increased globally and in US+EU, for antibodies that entered clinical studies after 2010 compared to those that entered in 2000-2009.
- Antibody therapeutic development efforts by the biopharmaceutical industry are robust and increasingly successful.
- 17 antibody therapeutics were granted a first approval in 2023, and 31 are currently in regulatory review in at least one country or region.
- Based on recent company disclosures, 19 investigational antibody therapeutics are forecast to enter regulatory review by the end of 2024.
- “Antibodies to Watch in 2024”published in *mAbs* Jan 5, 2024.

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- The Antibody Society and their corporate sponsors

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- The Antibody Society is a non-profit trade association
- Business intelligence focused on the commercial antibody therapeutic sector
  - Antibody News distributed via LinkedIn and email to members
    - Business deals, acquisitions, financing news
    - Regulatory agency designations, e.g., orphan drug, FT, PRIME
    - Antibodies entering first-in-human or more advanced clinical studies
    - Marketing application submissions and approvals in the US, EU and ROW
    - Withdrawals and terminations
  - Annual Antibodies to Watch article published in *mAbs*
  - Up-to-date data on late-stage pipeline, antibodies in regulatory review and approved can be downloaded from antibodysociety.org
  - Complete clinical pipeline data provided to corporate sponsors

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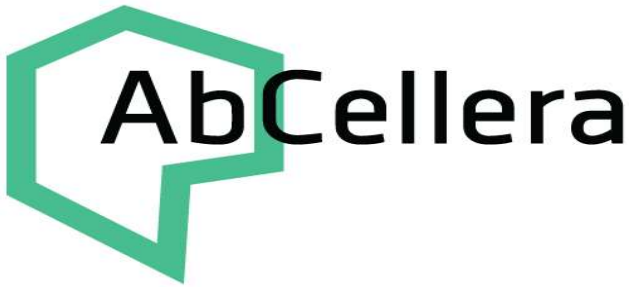


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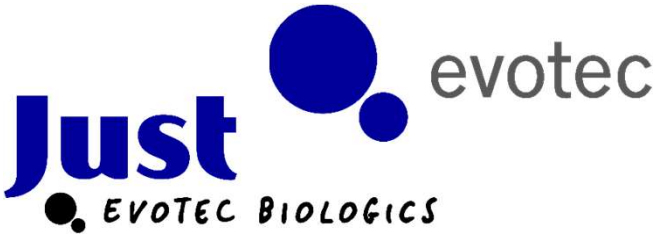
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