Antibodies to Watch in 2023

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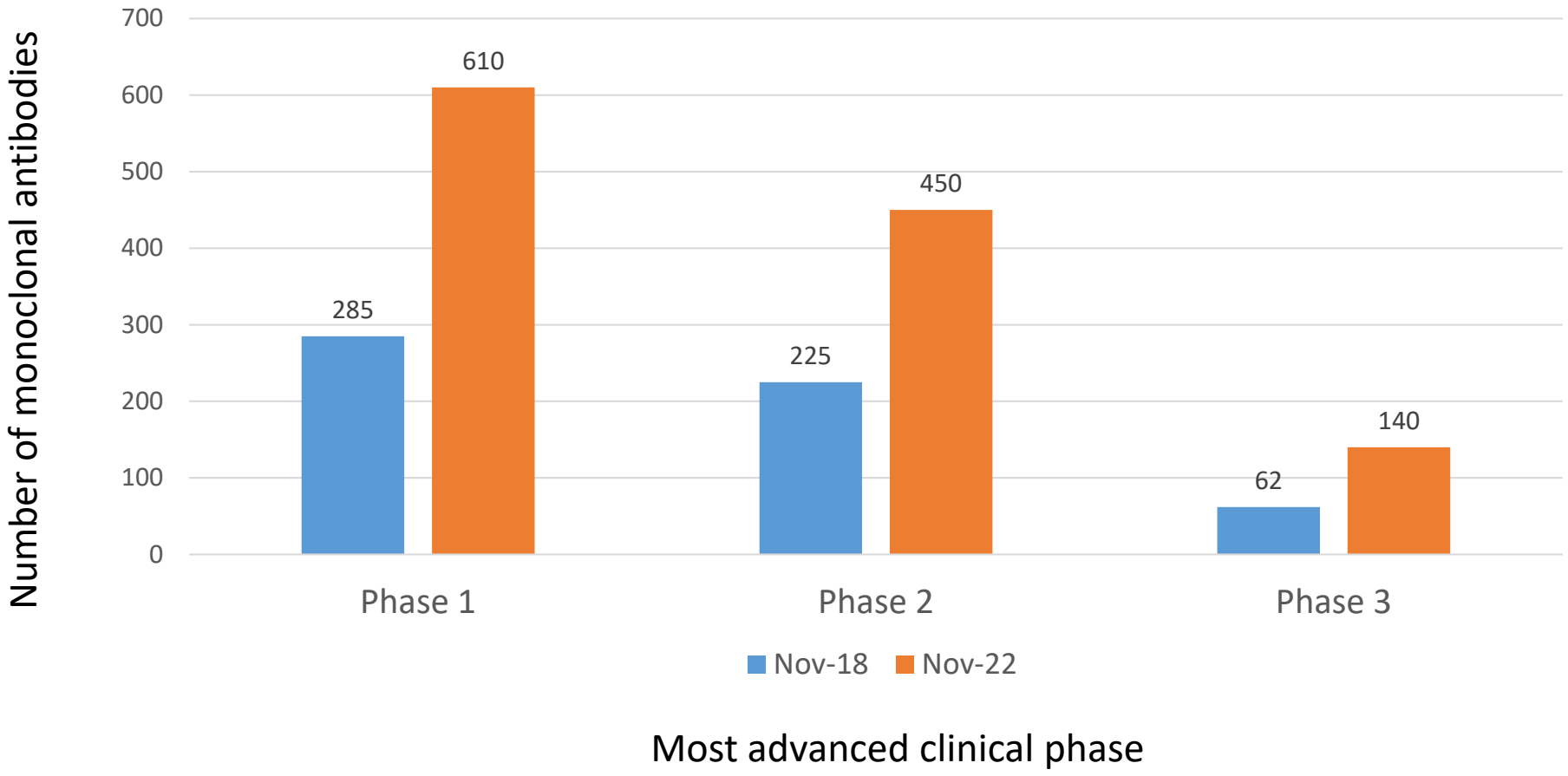
Agenda

- Increase in commercial antibody therapeutics clinical pipeline
- Trends in approvals of antibody therapeutics in US or EU (expression system)
  - First approvals of antibody therapeutics in US or EU in 2022 or 2023
  - Antibody therapeutics now in regulatory review in US or EU
- First approvals of antibody therapeutics granted in 2022 and those in review in the ROW
- Trends in late-stage development of antibody therapeutics
  - “Antibodies to Watch” for possible transition to regulatory review
- Trends in the development of bispecifics

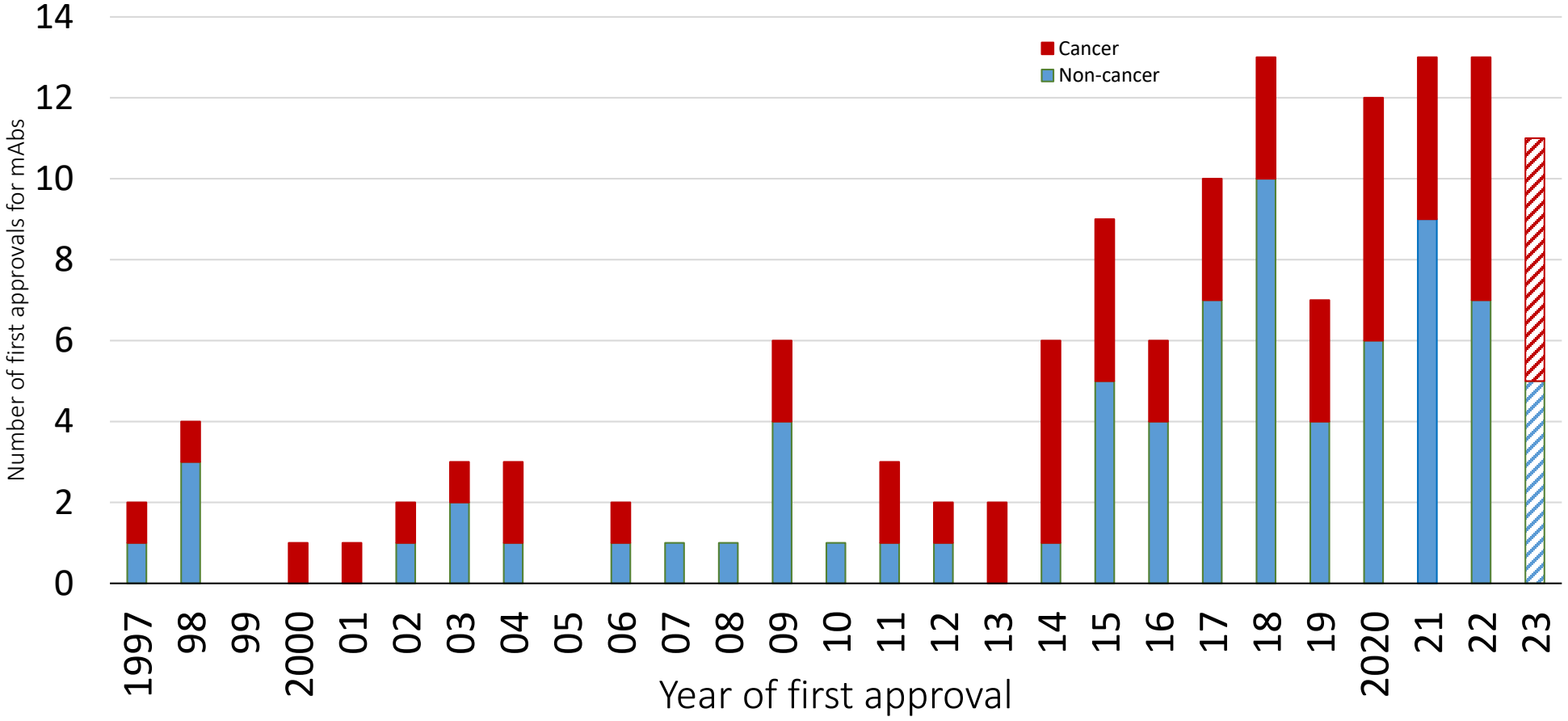
Antibody therapeutics in the clinic: 2018 vs 2022*



*Includes commercial development only; molecules in Phase 1/2 and 2/3 studies incorporated as Phase 2 and Phase 3, respectively.
Figure based on data available as of Nov 1, 2022; 2018 data from "Antibodies to Watch in 2019", mAbs, 11 (2019). doi.org/10.1080/19420862.2018.1556465
Percentage increase 2018 vs 2022 = 110%.

First approvals in the EU/US

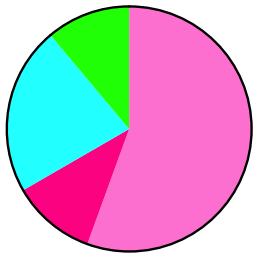
Annual first approvals in the US or EU



2023 projection based on data as of Jan 5, 2023.
Tables of approved mAbs and antibodies in review available at www.antibodysociety.org/antibody-therapeutics-product-data/;
Online table includes non-US/EU approvals.

Expression system of antibodies first approved in the US or EU

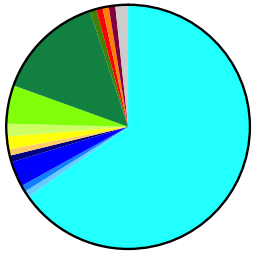
Antibody fragments



- E. coli bacteria
- E. coli BL21(DE3) bacteria
- Chinese hamster ovary (CHO) cells
- Murine myeloma cells (Sp2/0)

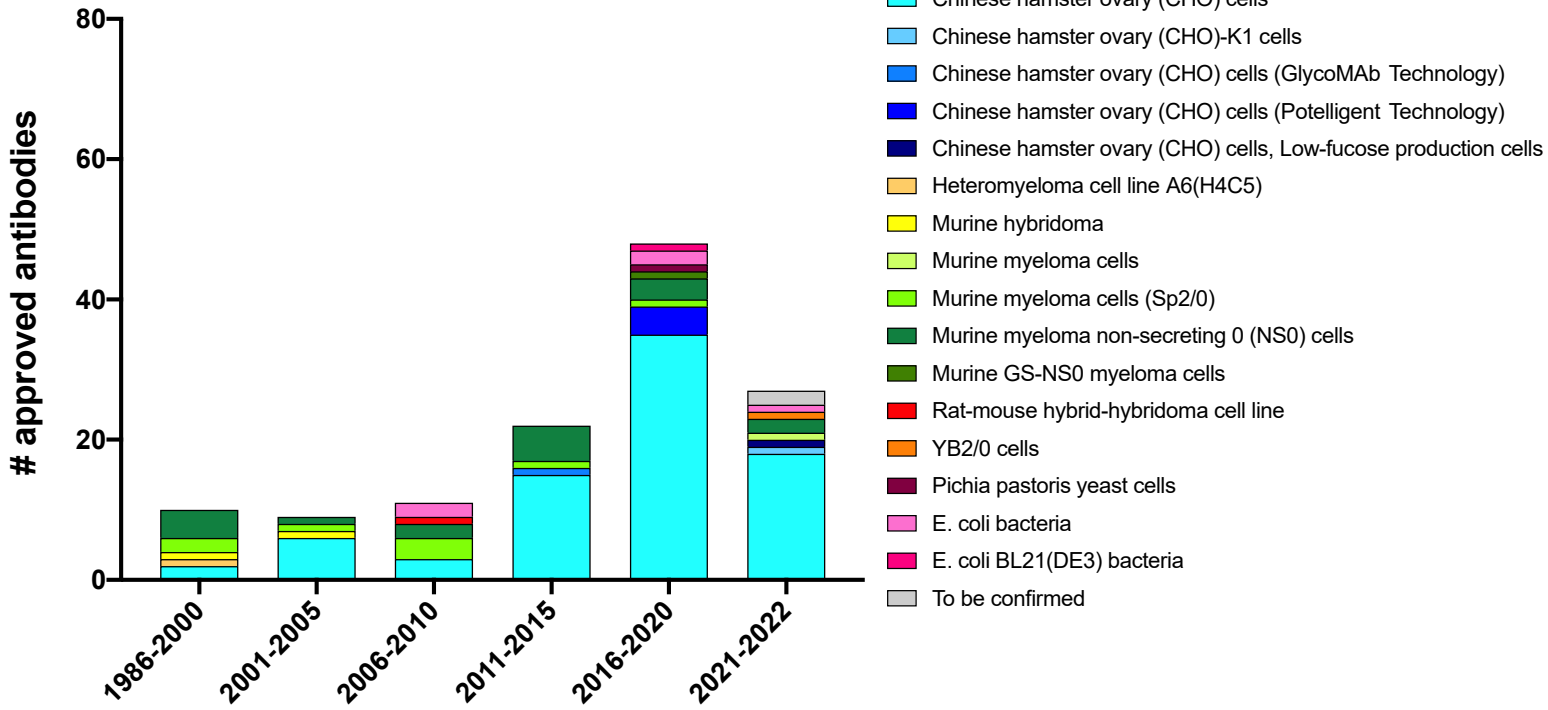
Total=9

Full length antibodies



Total=118

- Chinese hamster ovary (CHO) cells
- Chinese hamster ovary (CHO)-K1 cells
- Chinese hamster ovary (CHO) cells (GlycoMAb Technology)
- Chinese hamster ovary (CHO) cells (Potelligent Technology)
- Chinese hamster ovary (CHO) cells, Low-fucose production cells
- Heteromyeloma cell line A6(H4C5)
- Murine hybridoma
- Murine myeloma cells
- Murine myeloma cells (Sp2/0)
- Murine myeloma non-secreting 0 (NS0) cells
- Murine GS-NS0 myeloma cells
- Rat-mouse hybrid-hybridoma cell line
- YB2/0 cells
- Pichia pastoris yeast cells
- To be confirmed



First EU/US approvals in 2022: Non-cancer

INN; Brand name	Target; Format	Indication first approved	Date of first EU approval	Date of first US approval	Expression system
Faricimab (Vabysmo)	VEGF-A, Ang-2; Human/humanized IgG1 κ/λ **bispecific**	Diabetic macular edema, wet AMD	15/9/2022	28/1/2022	Chinese hamster ovary (CHO) cells
Sutimlimab (Enjaymo)	C1s; Humanized IgG4κ	Cold agglutinin disease	15/11/2022	4/2/2022	Chinese hamster ovary (CHO) cells
Tixagevimab / cilgavimab (Evusheld)	**SARS-CoV-2**; Human IgG1κ	COVID-19	25/3/2022	NA (EUA)	Chinese hamster ovary (CHO) cells
Spesolimab (SPEVIGO)	IL-36 receptor; Humanized IgG1κ	Generalized pustular psoriasis	9/12/2022	1/9/2022	Chinese hamster ovary (CHO) cells
Nirsevimab (Beyfortus)	RSV; Human IgG1κ	**Prevention of RSV infection**	31/10/2022	In review	Chinese hamster ovary (CHO) cells
Teplizumab (TZIELD)	CD3; Humanized IgG1κ	**Delay of onset of Stage 3 Type 1 diabetes**	NA	17/11/2022	Chinese hamster ovary (CHO) cells
Ublituximab (BRIUMVI)	CD20; Chimeric IgG1κ	Multiple sclerosis	In review	28/12/2022	**YB2/0 cells**

Complete list of US- and EU-approved mAbs (1986 to present) and antibodies in review available at: www.antibodysociety.org/antibody-therapeutics-product-data/

First EU/US approvals in 2022: Cancer

INN; Brand name	Target; Format	Indication first approved	Date of first EU approval	Date of first US approval	Expression system
Tebentafusp (Kimmtrak)	**gp100**, CD3; **Bispecific immunoconjugate**	Metastatic uveal melanoma	1/4/2022	25/1/2022	E. coli bacteria
Mosunetuzumab (Lunsumio)	CD20, CD3; Humanized IgG1κ **bispecific**	Follicular lymphoma	3/6/2022	22/12/2022	Chinese hamster ovary (CHO) cells
Teclistamab (TECVAYLI)	BCMA, CD3; Humanized/human IgG4λ **bispecific**	Multiple myeloma	23/8/2022	25/10/2022	Chinese hamster ovary (CHO) cells
Relatlimab (Opdualag)	**LAG-3**; Human IgG4κ	Melanoma	15/9/2022	18/3/2022	Chinese hamster ovary (CHO) cells
Tremelimumab (Imjudo; combo with durvalumab)	CTLA-4; Human IgG2κ	Hepatocellular carcinoma	Positive opinion as of Dec 15, 2022	21/10/2022	Murine myeloma non-secreting 0 (NS0) cells
Mirvetuximab soravtansine (ELAHERE™)	**FRα**; Humanized IgG1κ **ADC**	Ovarian cancer	NA	14/11/2022	Chinese hamster ovary (CHO) cells

Complete list of US- and EU-approved mAbs (1986 to present) and antibodies in review available at: www.antibodysociety.org/antibody-therapeutics-product-data/

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First EU/US approvals in 2023: Non-cancer

INN; Brand name	Target; Format	Indication first approved	Date of first EU approval	Date of first US approval	Expression system
Lecanemab (LEQEMBI)	Amyloid beta protofibrils; Humanized IgG1κ	Alzheimer's disease	In review	6/1/2023	Chinese hamster ovary (CHO) cells

First EU/US approvals in 2023: Cancer

INN; Brand name	Target; Format	Indication first approved	Date of first EU approval	Date of first US approval	Expression system
Retifanlimab (Zynyz)	PD-1; Humanized IgG4κ	Merkel Cell Carcinoma (MCC)		22/3/2023	Chinese hamster ovary (CHO) cells

Complete list of US- and EU-approved mAbs (1986 to present) and antibodies in review available at:
www.antibodysociety.org/antibody-therapeutics-product-data/

US or EU first regulatory review
(excludes all approved products)

EU+US review or EU only

INN	Target; Format	Indication under review	Status in EU	Status in US
Elranatamab	BCMA, CD3; Humanized IgG2 **bispecific**	Multiple myeloma	In review	In review
Toripalimab	PD-1; Humanized IgG4κ	Nasopharyngeal, esophageal squamous cell carcinomas	In review	In review (**decision delayed travel issue**)
Trastuzumab duocarmazine	HER2; Humanized IgG1κ **ADC**	HER2+ unresectable locally advanced or metastatic BC	In review	In review (**PDUFA date 12/5/23**)
Epcoritamab	CD20, CD3; Humanized IgG1κ/λ **bispecific**	Large B-cell lymphoma	In review	In review (**PDUFA date 21/5/2023**)
Glofitamab	CD20, CD3e; IgG1λ/κ **bispecific**	Diffuse large B-cell lymphoma	In review	In review (**PDUFA date 1/7/2023**)
Talquetamab	**GPRC5D, CD3**; Humanized IgG4κ/λ **bispecific**	Multiple myeloma	In review	In review
Lebrikizumab	IL-13; Humanized IgG4κ	Atopic dermatitis	In review	NA
Mirikizumab	IL-23p19; Humanized IgG4κ	Ulcerative colitis	In review	In review
Rozanolixizumab	FcRn	Generalized myasthenia gravis	In review	In review
Tislelizumab	PD-1; Humanized IgG4κ	Esophageal squamous cell carcinoma	In review	In review (2nd cycle)
Sugemalimab	PD-L1; Human IgG4λ	Metastatic non-small cell lung cancer (NSCLC)	In review	NA
Serplulimab (HANSIZHUANG)	PD-1; Humanized IgG4κ	Extensive-stage small cell lung cancer (ES-SCLC)	In review	NA

Note: Products previously approved in either region and biosimilars are excluded

US review only

INN	Target; Format	Indication under review	Status in EU	Status in US
Pozelimab	Complement 5; Human IgG4	**CHAPLE disease**	NA	In review (**PDUFA date 20/8/2023**)
Concizumab	Tissue factor pathway inhibitor; Humanized IgG4	Hemophilia	NA	In review
Cosibelimab	PD-L1; Human IgG1λ	Squamous cell carcinoma	NA	In review
Donanemab	Amyloid β; Humanized IgG1κ	**Early Alzheimer's disease**	NA	In review (2nd cycle)
Sintilimab	PD-1; Human IgG4κ	Non-small cell lung cancer	NA	In review (2nd cycle)
Narsoplimab	**MASP-2**; Human IgG4λ	SC transplant-associated thrombotic microangiopathy	NA	In review (CRL appealed)
Omburtamab-I131	B7-H3; Murine IgG1 radiolabeled	CNS/leptomeningeal metastasis from neuroblastoma	Neg. opinion	In review (2nd cycle; asset deprioritized)

Note: Products previously approved in either region and biosimilars are excluded

Approvals / regulatory review in the rest of the world in 2022

First RoW approvals in 2022

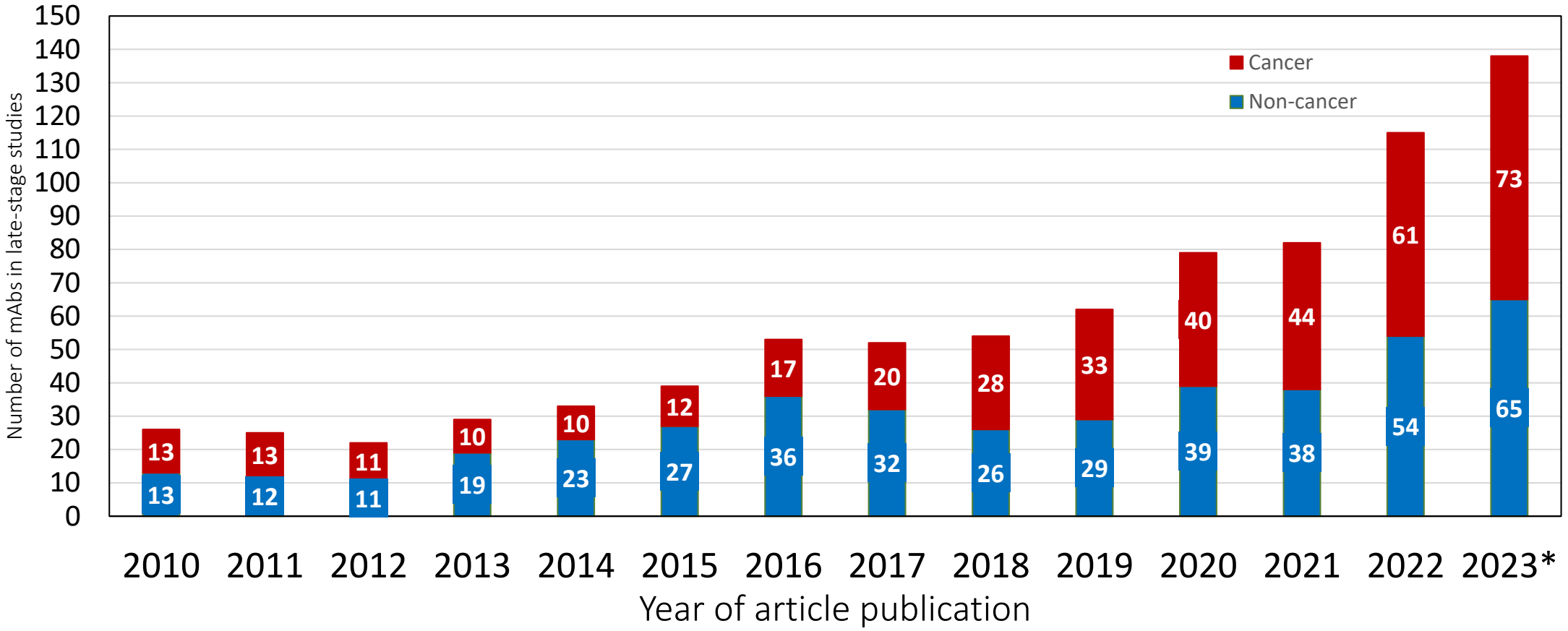
INN, Brand name	Target; Format	Indication first approved	Status
Ormutivimab	Rabies virus; Human IgG1λ	Rabies infection	Approved in China
Serplulimab (HANSIZHUANG)	PD-1; Humanized IgG4κ	MSI-high/dMMR solid tumors	Approved in China
Cadonilimab (开坦尼®)	PD-1, CTLA-4; Humanized IgG1κ **bispecific**	Cervical cancer	Approved in China
Pucotenlimab (Puyouheng)	PD-1; Humanized IgG4κ	MSI-high/dMMR solid tumors	Approved in China
Ripertamab (Anpingxi®)	CD20; Chimeric IgG1κ	Diffuse large B-cell lymphoma	Approved in China
Nemolizumab (Mitchga®)	IL-31R; Humanized IgG2κ	Atopic dermatitis	Approved in Japan
Ozoralizumab (Nanozora®)	TNF, albumin; Humanized **bispecific nanobody**	Rheumatoid arthritis	Approved in Japan

RoW: Regulatory review

INN, Brand name	Target; Format	Indication first approved or in review	Status
Geptanolimab (Aibining 艾比寧®)	PD-1; Humanized IgG4κ	Peripheral T-cell lymphoma	Regulatory review in **China**
Socazolimab	PD-L1; Human IgG1λ2	Cervical cancer	Regulatory review in **China**
Adebrelimab	PD-L1; Humanized IgG4κ	Small cell lung cancer	Regulatory review in **China**
Tagitanlimab	PD-L1; Humanized IgG1κ	Solid tumor indications	Regulatory review in **China**
Crovalimab	Complement C5; Humanized IgG1κ	Paroxysmal nocturnal hemoglobinuria	Regulatory review in **China**
Narlumosbart	RANKL; Human IgG4κ	Unresectable or surgically difficult giant cell tumor of bone	Regulatory review in **China**
Tafolecimab	PCSK9; Human IgG2κ	Primary hypercholesterolemia and mixed dyslipidemia	Regulatory review in **China**
Concizumab	Tissue factor pathway inhibitor; Humanized IgG4κ	Hemophilia A or B with inhibitors	Regulatory review in **Japan**
Enlonstobart	PD-1; Human IgG4κ	recurrent or metastatic cervical cancer	Regulatory review in **China**

Trends in late-stage development of antibody therapeutics

Antibodies in late-stage studies over time



*2023 estimate as of Oct 1, 2022. Data incl. late-stage studies listed as not yet recruiting on clinicaltrials.gov, excludes antibodies for COVID. Data from 'Antibodies to watch' articles published in *mAbs*. Table of antibodies in late-stage studies available at https://www.antibodysociety.org/antibodies-in-late-stage-clinical-studies

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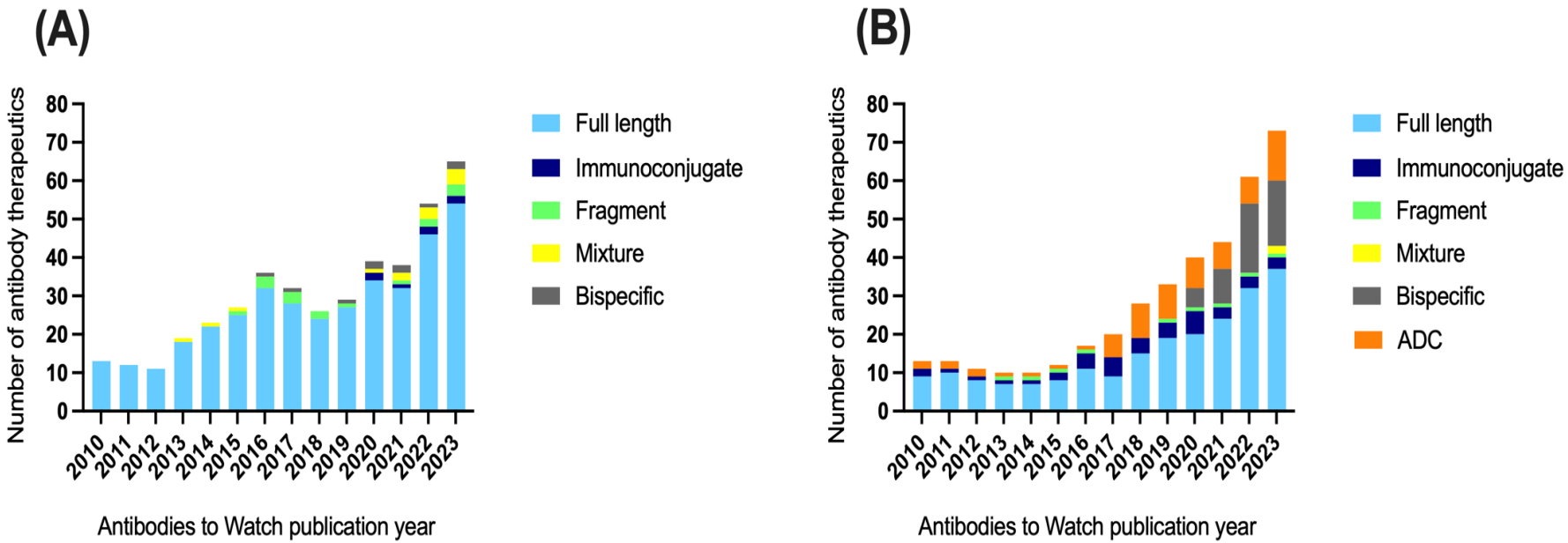
Late-stage pipeline formats over time



“Antibodies to Watch” for possible transition to regulatory review in 2023

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Regulatory submission anticipated in 2023: Non-cancer

INN	Target; Format	Indication of relevant late-stage study*	Status
Garadacimab	Factor XIIa; Human IgG4λ	Hereditary angioedema	Phase 3 (BLA, 2023)
Suciraslimab	CD22; chimeric IgG1κ	Rheumatoid arthritis	Phase 3 (NDA, 2023)
Tarcocimab tedromer	VEGF; Humanized IgG1κ **antibody-biopolymer conjugate**	Retinal vein occlusion	Phase 3 (BLA, 2023)
Axatilimab	Colony stimulating factor 1 receptor; Humanized IgG4κ	Graft vs. host disease	Phase 3 (BLA, 2023)

*Indication for which a regulatory submission is anticipated. Table includes information publicly available as of December 1, 2022.

Regulatory submission anticipated in 2023: Cancer (1)

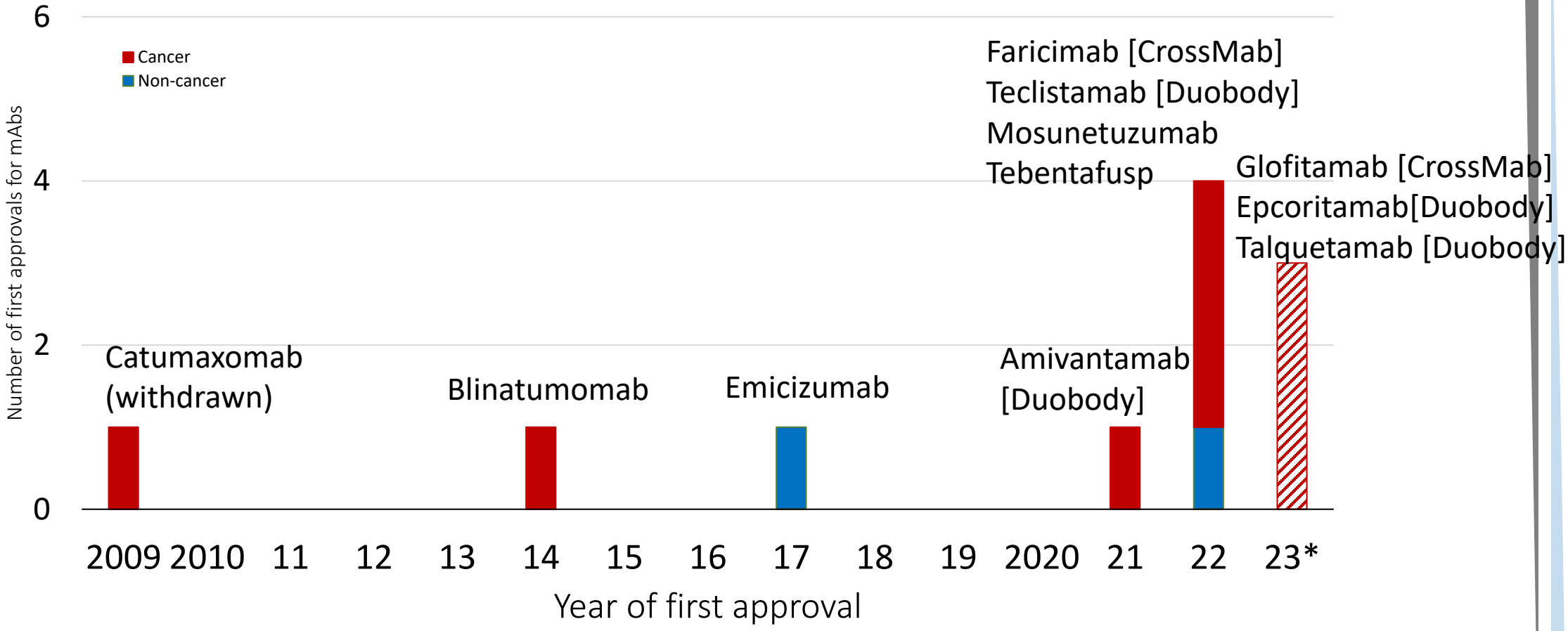
INN	Target; Format	Indication of relevant late-stage study*	Status
Felzartamab	CD38; Human IgG1κ	Multiple myeloma	Phase 3 (BLA, 2023)
Nofazinlimab	PD-1; humanized IgG4κ	Hepatocellular carcinoma	Phase 3 (NDA, 2023)
Camrelizumab	PD-1; Humanized IgG4κ	Hepatocellular carcinoma	Phase 3 (NDA, 2023)
Sugemalimab	PD-L1; Human IgG4λ	Relapsed or refractory extranodal natural killer/T-cell lymphoma	Phase 3 (BLA, 2023)
Tiragolumab	**TIGIT**; Human IgG1κ	Non-small cell lung cancer, esophageal cancer	Phase 3 (2023)
Zolbetuximab	**Claudin-18.2**; Chimeric IgG1κ	Gastric and gastro-esophageal junction adenocarcinoma	Phase 3 (BLA, 2023)

Regulatory submission anticipated in 2023: Cancer (2)

INN	Target; Format	Indication of relevant late-stage study*	Status
Apamistamab-Iodine-131	CD45; Murine IgG1κ, **radiolabeled**	Acute myeloid leukemia	Phase 3 (BLA, H1 2023)
Datopotamab deruxtecan	TROP-2; Humanized IgG1κ **ADC**	Non-small cell lung cancer	Phase 3 (H1 2023)
Tusamitamab ravtansine	**CEACAM5**; Humanized IgG1κ **ADC**	Non-small cell lung cancer	Phase 3 (2023)
Upifitamab rilsodotin	**NaPi2b,** Humanized IgG1κ **ADC**	Ovarian cancer	Phase 3 (BLA, 2023)
Erfonrilimab	PD-L1, CTLA-4; Humanized/chimeric IgG1 **bispecific VH-VH-h-CH2-CH3 dimer**	Non-small cell lung cancer	Phase 3 (NDA)
Odronextamab	CD20, CD3; Human IgG4κ **bispecific**	Non-Hodgkin's lymphoma	Pivotal Phase 2 (BLA, H2 2023)
Linvoseltamab	BCMA, CD3; Human IgG4κ **bispecific**	Multiple myeloma	Pivotal Phase 2 (BLA, 2023)
Zanidatamab	HER2, HER2; Humanized IgG1 **bispecific**	Biliary tract cancer	Pivotal Phase 2 (2023)

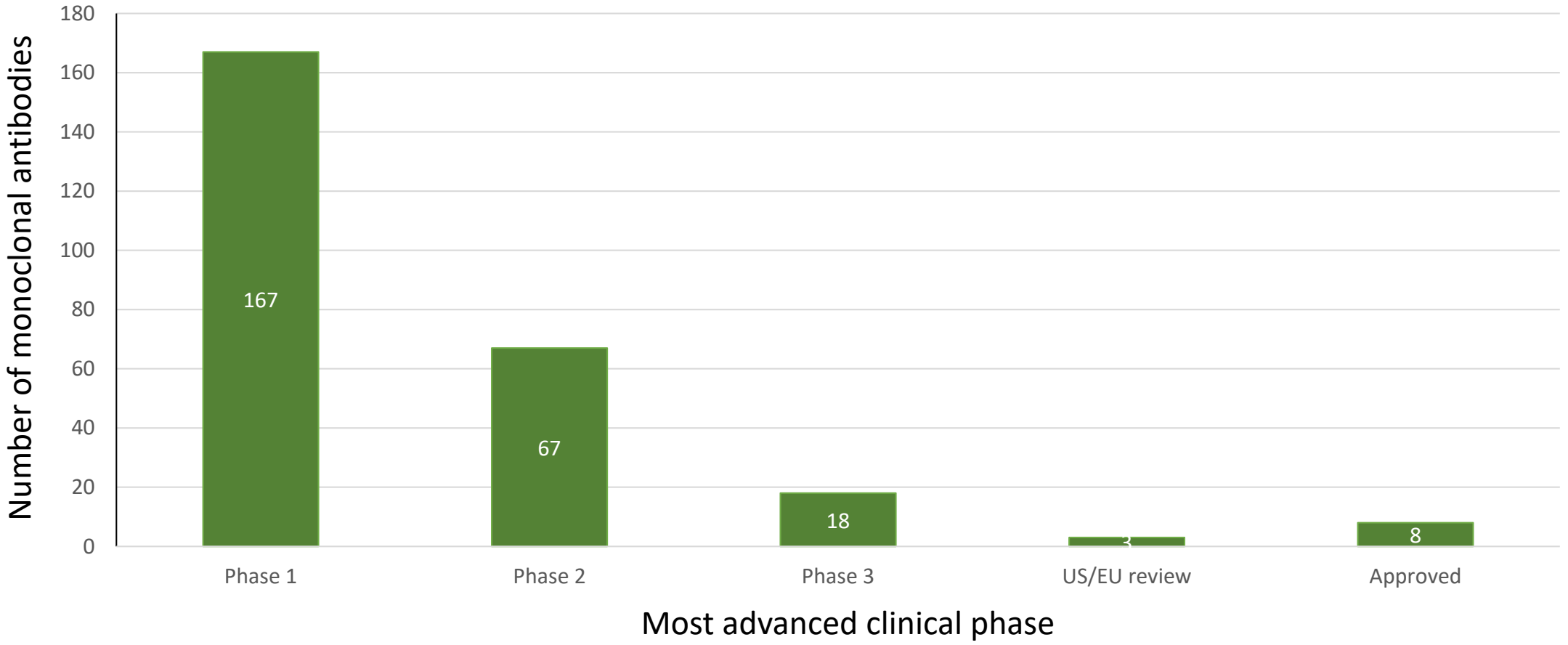
Trends in bispecific antibody development

Annual first approvals for bispecifics (US or EU)



*Projection based on publicly available information. Tables of approved mAbs and antibodies in review available at www.antibodysociety.org/antibody-therapeutics-product-data/; online table includes non-US/EU approvals.

Antibody bispecifics clinical pipeline*



*Includes commercial development only; molecules in Phase 1/2 and 2/3 studies incorporated as Phase 2 and Phase 3, respectively.
Figure based on data available as of Nov 1, 2022.

Key messages

- 2022 approvals of antibody therapeutics in the US or EU matched historical record of 13
- Rate of entry into US or EU regulatory review has increased, but approvals have not kept pace, and the number of BLA second cycles is up, leading to record numbers in review (15 to >20)
- Late-stage pipeline growth continues to exceed expectations
- Lots of activity expected in the bispecific space in the near future
- “Antibodies to Watch in 2023”published in *mAbs* Dec 6, 2022

Acknowledgements

- ‘Antibodies to Watch in 2023’ co-authors
  - Dr. Janice M. Reichert, The Antibody Society (Antibodies to Watch in 2010-2023)
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  - Dr. Alicia Chenoweth, King’s College London (Antibodies to Watch in 2022-2023)
  - Dr. Jyothsna Visweswaraiah, Seismic Therapeutic (Antibodies to Watch in 2023)
- The Antibody Society and their sponsors

Join The Antibody Society to keep up to date!

- 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
  - 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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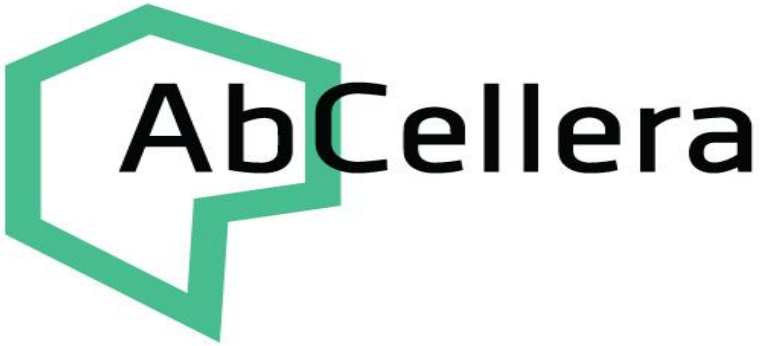


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