Antibodies to Watch in 2022

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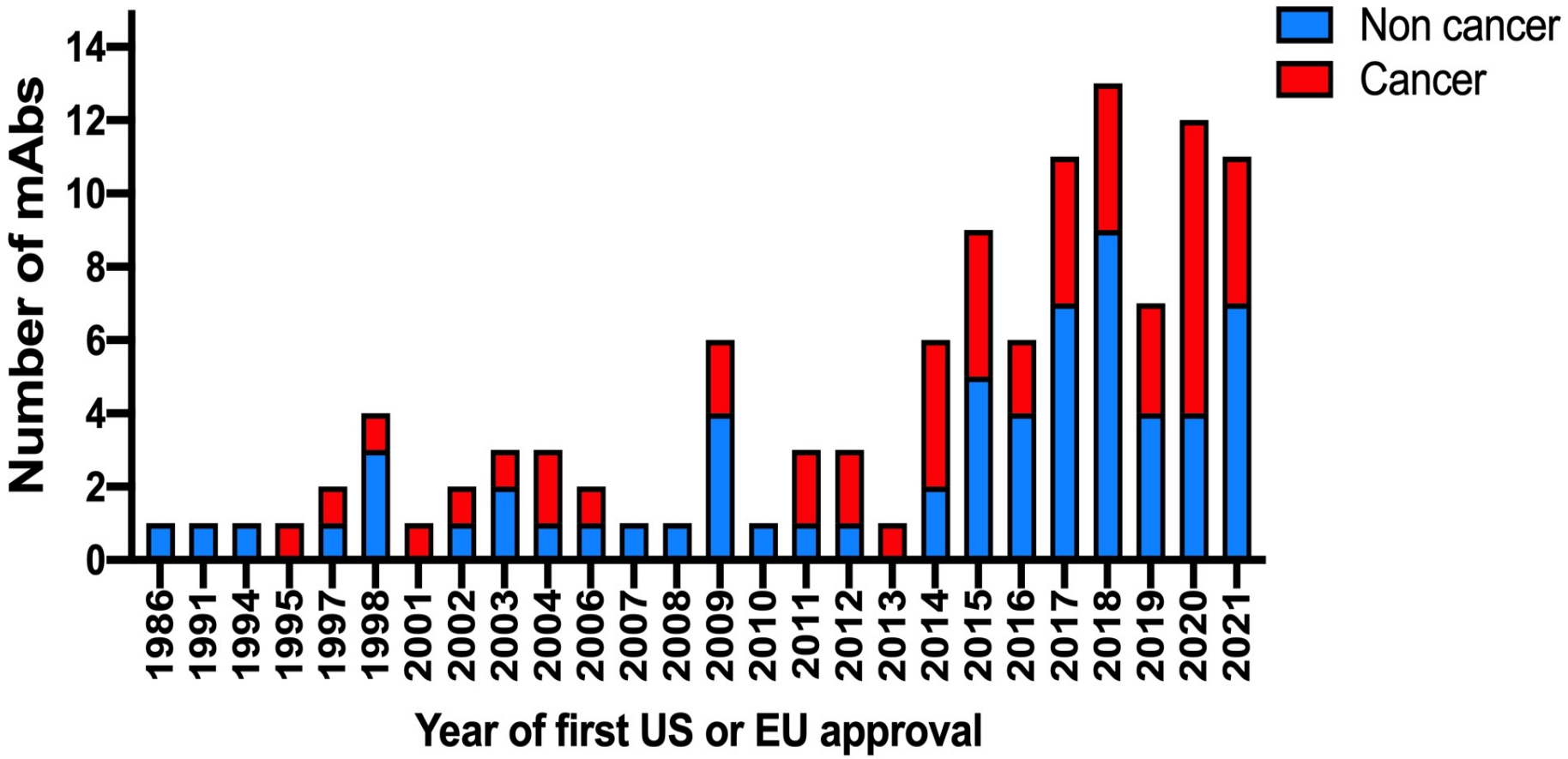
Agenda

- Trends in approvals/review of antibody therapeutics in US or EU
- First approvals of antibody therapeutics in US or EU in 2021
- Antibody therapeutics now in regulatory review in US or EU
- First approvals of antibody therapeutics granted in 2021 and those in review in the rest of the world
- Trends in late-stage development of antibody therapeutics
- “Antibodies to Watch” for possible transition to regulatory review
- Antibody therapeutics for COVID-19
  - Emergency use authorizations
  - Anti-SARS-CoV-2 antibodies in late-stage clinical development

Trends in approvals/review of antibody therapeutics in US or EU

Annual first approvals in either the EU or US



*2021 estimate as of 11/12/2021.

Tables of approved mAbs and antibodies in review available at www.antibodysociety.org/antibody-therapeutics-product-data/

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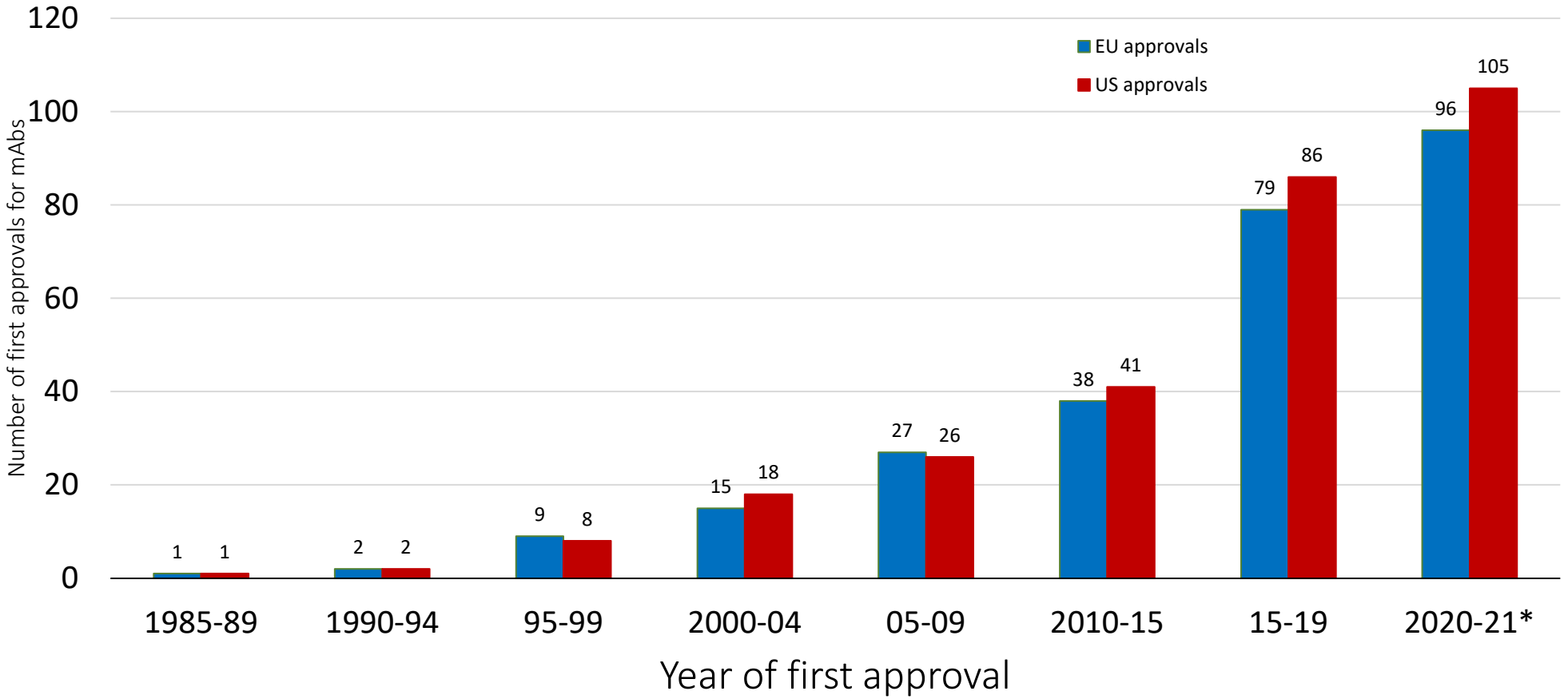
Cumulative annual first approvals: EU & US



*2021 data as of 11/15/2021. EUAs are not included.

See also: Mullard A. FDA approves 100th monoclonal antibody product. Nature Reviews Drug Discovery. May 5, 2021.

Tables of approved mAbs and antibodies in review available at www.antibodysociety.org/antibody-therapeutics-product-data/

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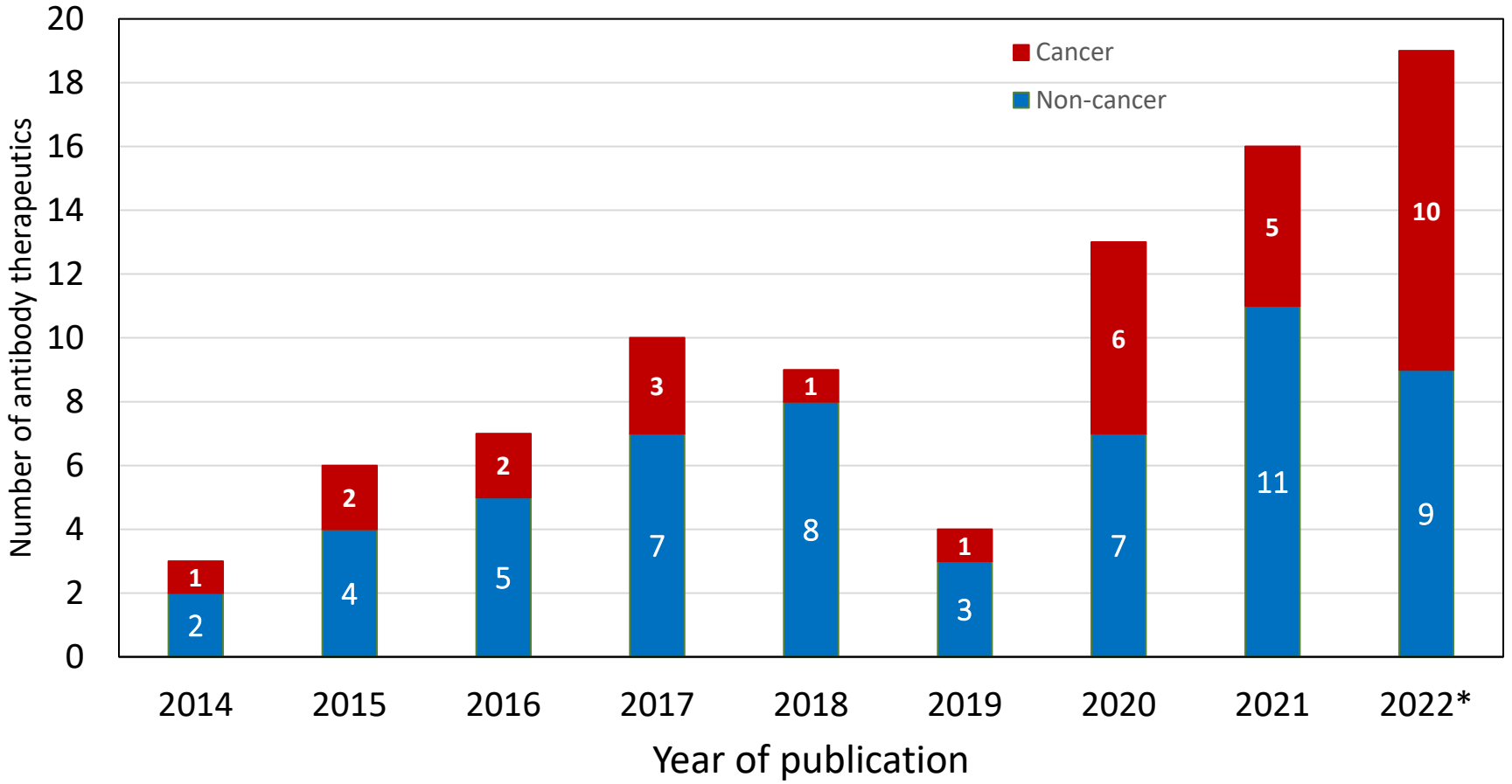
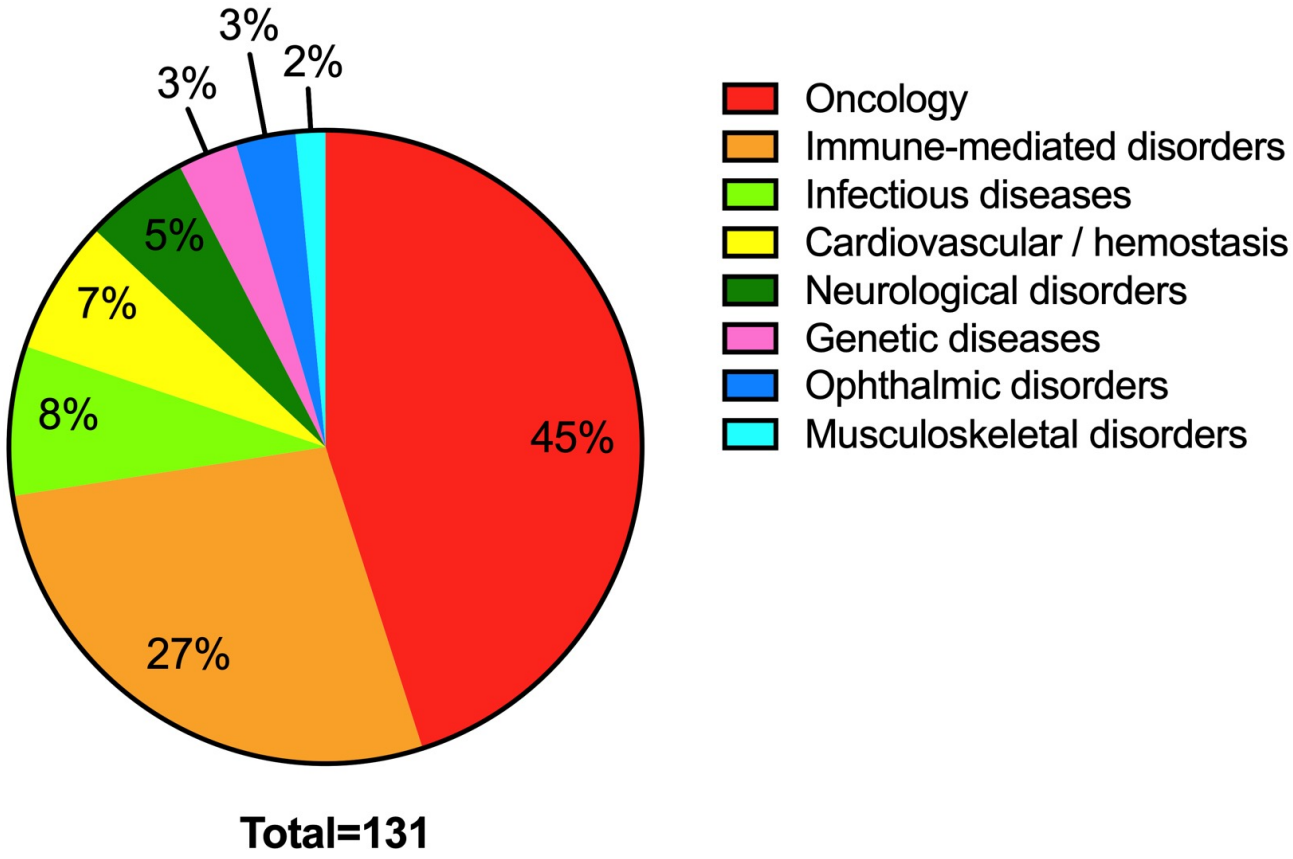
Antibodies to Watch: Number in EU/US review



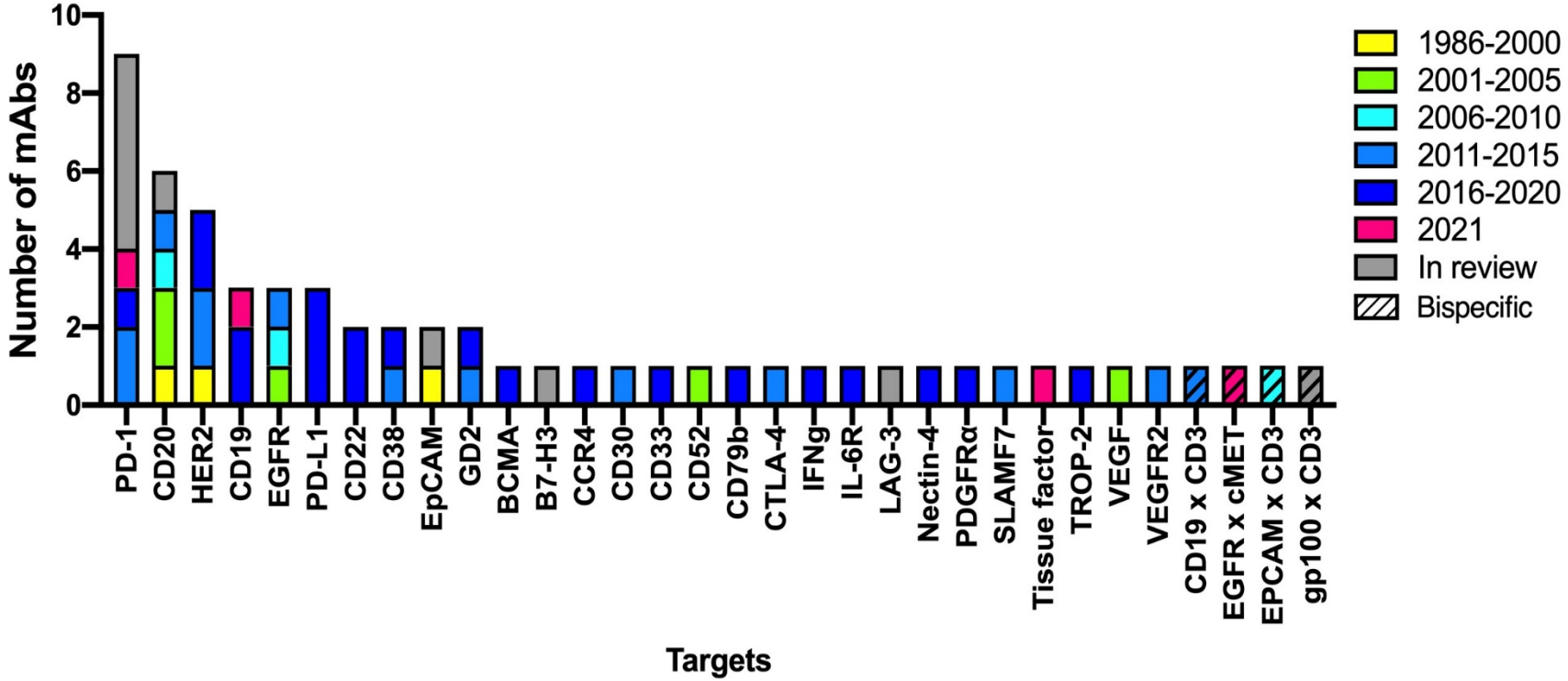
Data from 'Antibodies to Watch' articles published in *mAbs*. **As of Nov 15, 2021.*

Indications for antibody therapeutics approved or in review in either the EU or US



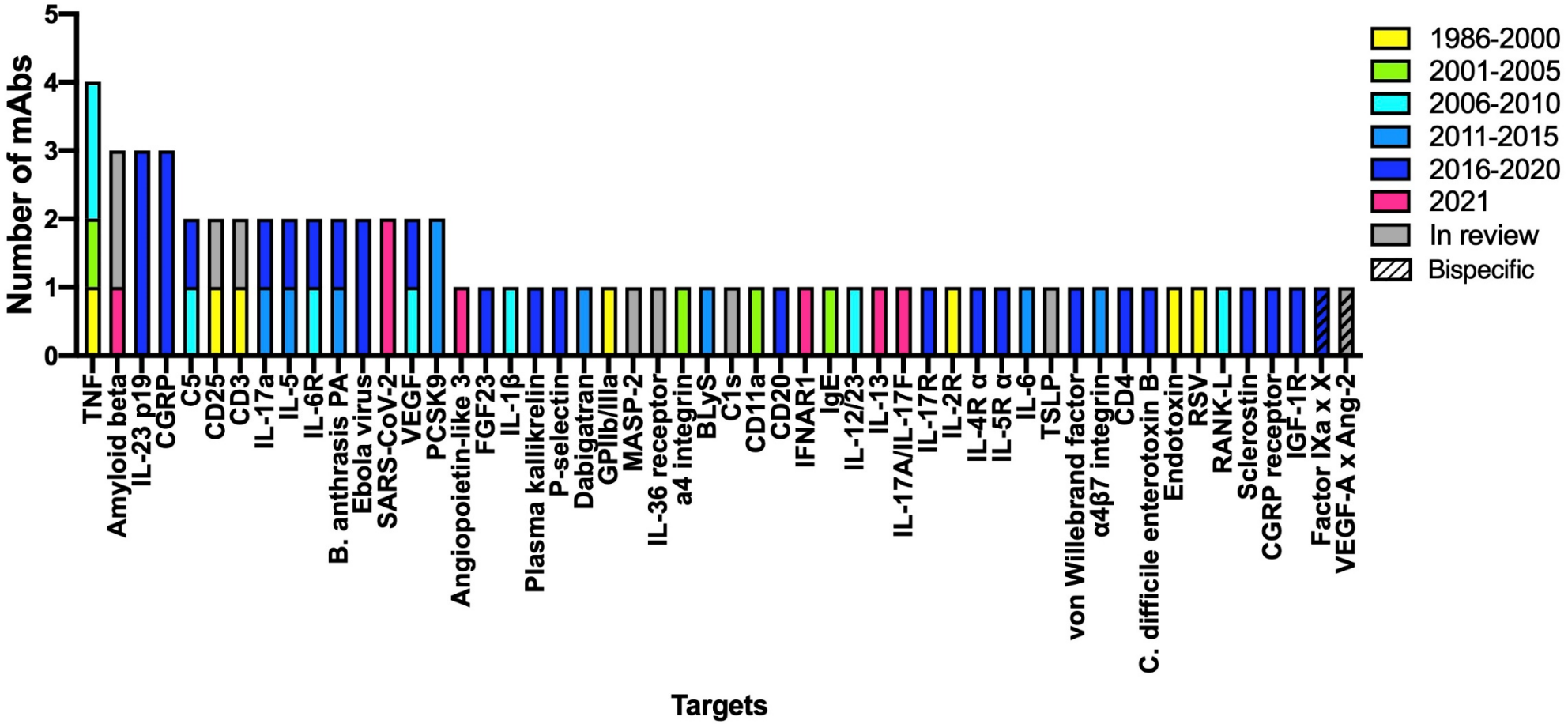
Data available as of 11/12/2021. EUAs are not included.
Tables of approved mAbs and antibodies in review available at www.antibodysociety.org/antibody-therapeutics-product-data/

Targets for antibody therapeutics approved or in review in either the EU or US: Cancer



Data available as of 11/12/2021.
Tables of approved mAbs and antibodies in review available at www.antibodysociety.org/antibody-therapeutics-product-data/

Targets for antibody therapeutics approved or in review in either the EU or US: Non-cancer



Tables of approved mAbs and antibodies in review available at www.antibodysociety.org/antibody-therapeutics-product-data/

First approvals in the EU/US in 2021
(so far)

First EU/US approvals, 2021 (so far): Cancer

INN; Brand name	Target; Format	Indication first approved	Date of first EU approval	Date of first US approval
Dostarlimab; Jemperli	PD-1; Humanized IgG4	Deficient mismatch repair endometrial cancer	4/21/2021	4/22/2021
Loncastuximab tesirine; Zynlonta	CD19; Humanized IgG1 **ADC**	Diffuse large B-cell lymphoma	In review	4/23/2021
Amivantamab; Rybrevant	EGFR, cMet; Human IgG1 **bispecific**	Non-small cell lung cancer	Positive opinion	5/21/2021
Tisotumab vedotin; TIVDAK	Tissue factor; Human IgG1 **ADC**	Cervical cancer	NA	9/20/2021

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, 2021 (so far): Non-cancer

INN; Brand name	Target; Format	Indication first approved	Date of first EU approval	Date of first US approval
Evinacumab; Evkeeza	Angiopoietin-like protein 3; Human IgG4	Hypercholesterolemia	6/17/2021	2/11/2021
Aducanumab; Aduhelm	Amyloid beta; Human IgG1	**Early Alzheimer's disease**	In review	6/7/2021
Tralokinumab; Adtralza	IL-13; Human IgG4	Atopic dermatitis	6/17/2021	In review **(2nd cycle; additional data requested)**
Anifrolumab; Saphnelo	IFN a, b, ω receptor 1; Human IgG1	Systemic lupus erythematosus	In review	7/30/2021
Bimekizumab; Bimzelx	IL-17A and IL-17F; Humanized IgG1	Psoriasis	8/20/2021	In review **(decision delayed due to travel restrictions)**
Regdanvimab; Regkirona	SARS-CoV-2; Human IgG1	**SARS-CoV-2 infection**	11/12/2021	NA
Casirivimab + imdevimab; Ronapreve, REGEN-COV2	SARS-CoV-2; Mixture of 2 human IgG1	**SARS-CoV-2 infection**	11/12/2021	In review

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 regulatory review
(excludes all approved products)

EU or US review as of November 2021

International non-proprietary name	Target; Format	Indication under review	Status in EU	Status in US
Faricimab	VEGF-A, Ang-2; Human/humanized IgG1 κ/λ **bispecific**	Diabetic macular edema and neovascular age-related macular degeneration	In review	In review
Relatlimab	LAG-3; Human IgG4	Melanoma	In review	In review
Tezepelumab	Thymic stromal lymphopoietin; Human IgG2	Severe asthma	In review	In review
Omburtamab	B7-H3; Murine IgG1	CNS/leptomeningeal metastasis from neuroblastoma	In review	NA
Spesolimab	IL-36 receptor; Humanized IgG1	Generalized pustular psoriasis	In review	NA
Retifanlimab	PD-1; Humanized IgG4	Carcinoma of the anal canal	In review	In review (2nd cycle; more data needed)

Note: Products previously approved in either region and biosimilars are excluded; 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 review only as of November 2021

International non-proprietary name	Target; Format	Indication under review	Status in EU	Status in US
Tebentafusp	gp100, CD3; Bispecific immunoconjugate	Metastatic uveal melanoma	NA	In review
Sintilimab	**PD-1**; Human IgG4	Non-small cell lung cancer	NA	In review
Ublituximab	CD20; Chimeric IgG1	Chronic lymphocytic leukemia and small lymphocytic lymphoma; Multiple sclerosis	NA	In review (C/SLL- Rolling BLA)
Penpulimab	**PD-1**; Humanized IgG1	Metastatic nasopharyngeal carcinoma	NA	In review
Tislelizumab	**PD-1**; Humanized IgG4	Esophageal squamous cell carcinoma	NA	In review
Lecanemab	Amyloid beta protofibrils; Humanized IgG1	**Early Alzheimer's disease**	NA	Rolling BLA in review
Donanemab	Amyloid beta	**Early Alzheimer's disease**	NA	Rolling BLA in review
Toripalimab	**PD-1**; Humanized IgG4	Nasopharyngeal carcinoma	NA	In review
Inolimomab	CD25; Murine IgG1	Acute graft-vs-host disease	NA	In review
Sutimlimab	C1s; Humanized IgG4	Cold agglutinin disease	NA	**Re-submitted BLA in review**
Teplizumab	CD3; Humanized IgG1	Type 1 diabetes	NA	**In review (2nd cycle; comparability issue)**
Oportuzumab monatox	EpCAM; Humanized scFv immunotoxin	Bladder cancer	MAA withdrawn	**In review (2nd cycle; more data needed)**
Narsoplimab	MASP-2; Human IgG4	Hematopoietic SCT-associated thrombotic microangiopathy	NA	**In review (2nd cycle; application deficiencies)**

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

Approvals / regulatory review in the rest of the world in 2021

First RoW approvals in 2021 (as of Nov)

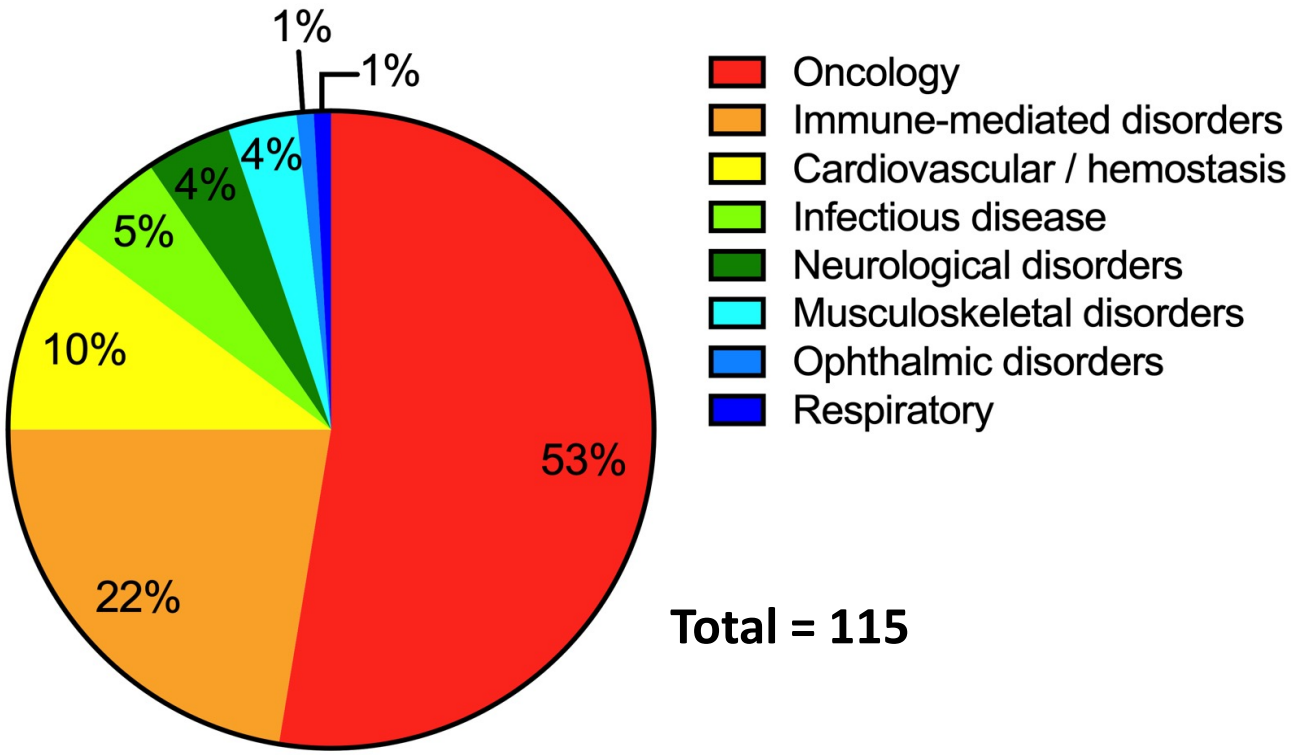
INN, Brand name	Target; Format	Indication first approved or in review	Status
Pabinafusp alfa, IZCARGO®	Transferrin receptor; Immunoconjugate	Mucopolysaccharidosis II	Approved in Japan (Mar 2021)
Disitamab vedotin, Aidixi	HER2; Humanized IgG1 **ADC**	Gastric cancer, including gastroesophageal junction adenocarcinoma	Approved in China (Jun 2021)
Penpulimab	PD-1; Humanized IgG1	Hodgkin's lymphoma	Approved in China (Aug 2021)
Zimberelimab	PD-1; Human IgG4l	Hodgkin's lymphoma	Approved in China (Aug 2021)
Envafolimab	**PD-L1; Humanized VH-Fc**	**MSI-high/dMMR solid tumors**	**Approved in China (Nov 2021)**
Sotrovimab, Xevudy	SARS-CoV-2; Human IgG1	**SARS-CoV-2 infection**	Approved in Australia (Aug 2021)
REGEN-COV2	SARS-CoV-2; Human mAbs	**SARS-CoV-2 infection**	Approved in Australia (Oct 2021)
Regdanvimab, Regkirona	SARS-CoV-2; Human IgG1	**SARS-CoV-2 infection**	Approved in Republic of Korea (Sep 2021)

RoW: Regulatory review in 2021 (as of Nov)

INN, Brand name	Target; Format	Indication first approved or in review	Status
Cadonilimab	PD-1, CTLA4; Humanized IgG1 **bispecific**	Cervical cancer	Regulatory review in China
Geptanolimab	PD-1; Humanized IgG4k	Peripheral T-cell lymphoma	Regulatory review in China
Serplulimab	PD-1; Humanized IgG4k	MSI-high/dMMR solid tumors	Regulatory review in China
Sugemalimab	PD-L1; Humanized IgG4l	Non-small cell lung cancer (Stage 3 and 4)	Regulatory review in China
Socazolimab	PD-L1; Human IgG1	Cervical cancer	Regulatory review in China
Ripertamab	CD20; Chimeric IgG1	Non-Hodgkin's lymphoma	Regulatory review in China
Ozoralizumab	TNF, albumin; Humanized **bispecific nanobody**	Rheumatoid arthritis	Regulatory review in Japan

Trends in late-stage development of antibody therapeutics

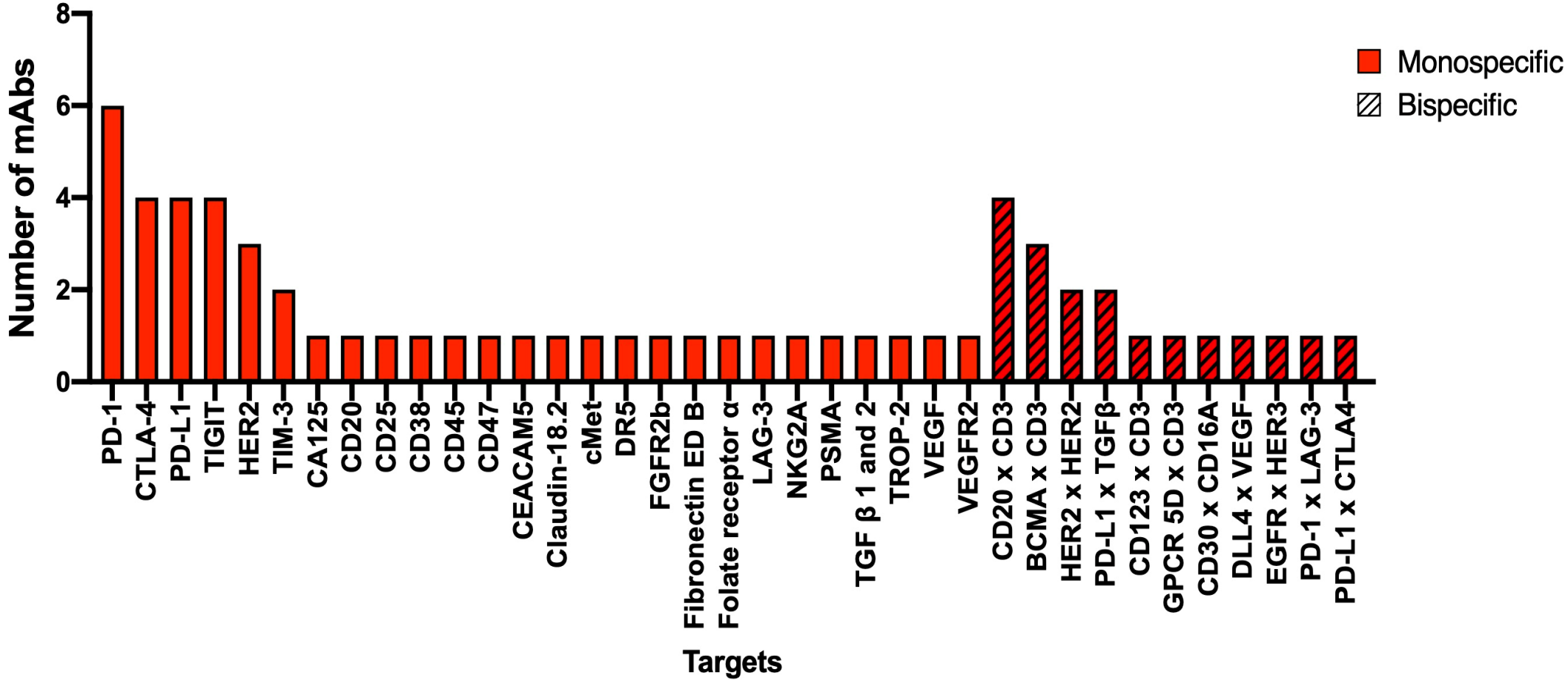
Late-stage clinical pipeline



Total = 115

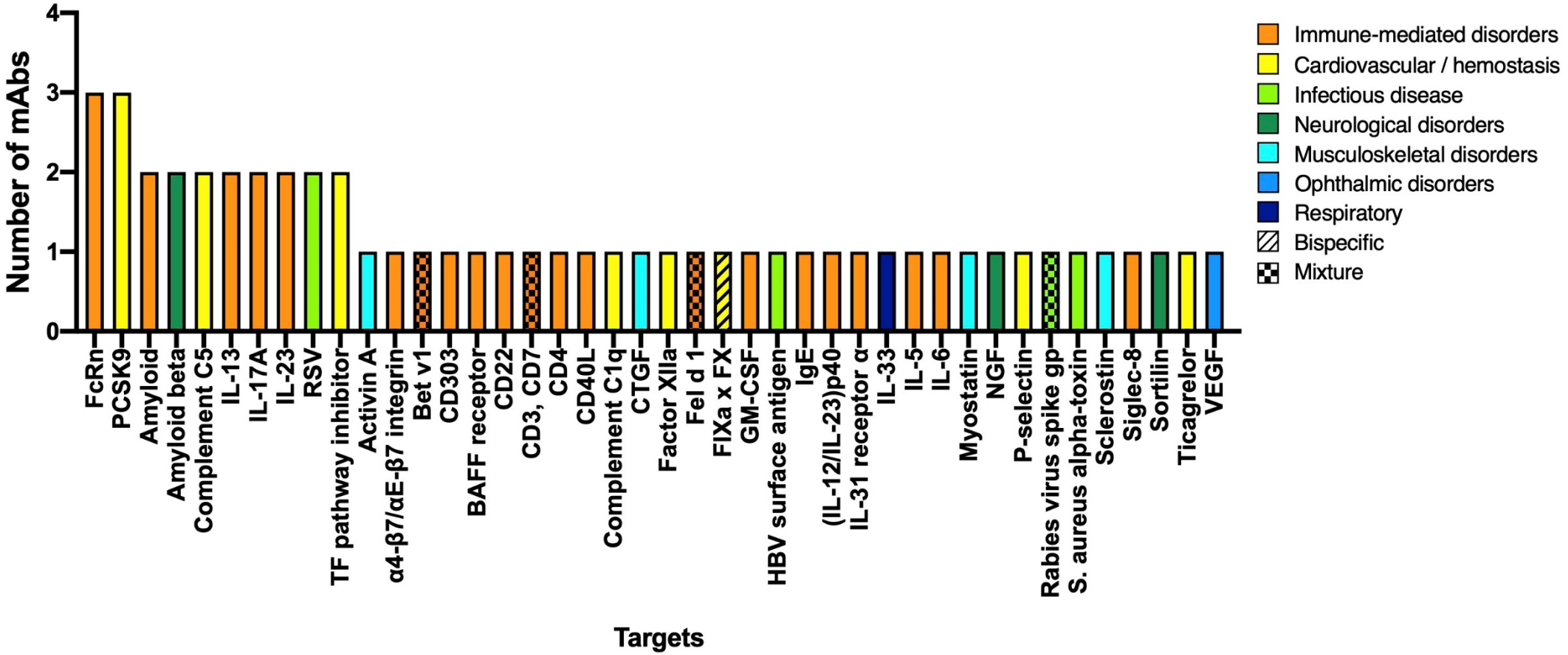
*Includes commercial development only; molecules in Phase 1/2 and 2/3 studies incorporated as Phase 2 and Phase 3, respectively. Anti-SARS-CoV-2 antibodies have been excluded. Figure based on data available as of Nov 1, 2021.

Targets, Late-stage clinical pipeline: Cancer



*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, 2021.

Targets, Late-stage clinical pipeline: Non-cancer



*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, 2021.

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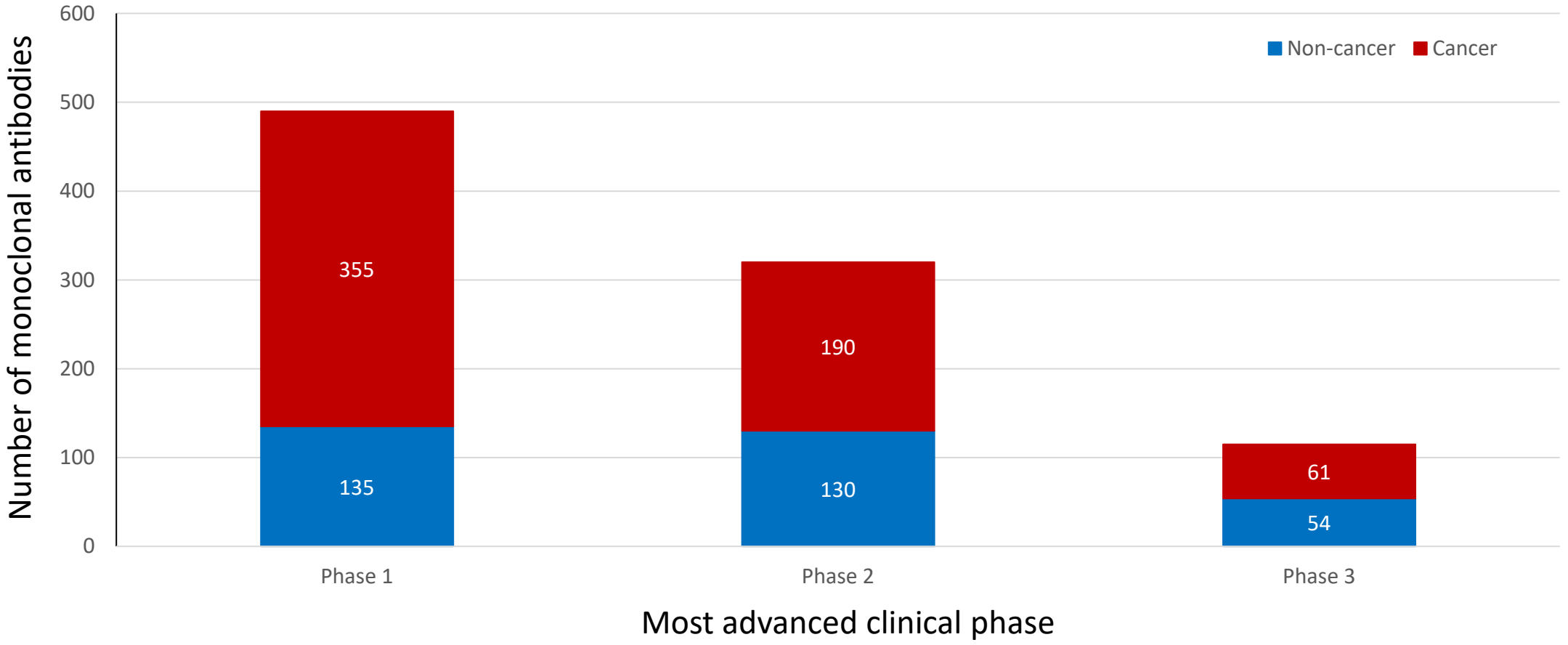
Antibody therapeutics clinical pipeline*



*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, 2021.

“Antibodies to Watch” for possible transition to regulatory review in 2022

Regulatory submission anticipated in 2022: Non-cancer

INN	Target; Format	Indication of relevant late-stage study*	Status
Bentracimab	Ticagrelor; Human IgG1 Fab	Reversal of the antiplatelet effects of ticagrelor	Phase 3
Crovalimab	Complement C5; Humanized IgG1	Paroxysmal nocturnal hemoglobinuria	Phase 3
Etrolizumab	α4-β7/ αE-β7 integrin receptor; Humanized IgG1	Crohn's disease	Phase 3
Gantenerumab	Amyloid β; Human IgG1	**Alzheimer's disease**	Phase 3
Ligelizumab	IgE; Humanized IgG1	Chronic spontaneous urticaria	Phase 3
Nirsevimab	RSV; Human IgG1	RSV infection	Phase 2/3

*Indication for which a regulatory submission is anticipated. Table includes information publicly available as of November 1, 2021.

Regulatory submission anticipated, 2021-2022: Cancer (1)

INN	Target; Format	Indication of relevant late-stage study*	Status
Mosunetuzumab	CD20, CD3; Humanized IgG1 **bispecific**	Follicular lymphoma	Phase 3
Tremelimumab	CTLA-4; Human IgG2	Non-small cell lung cancer	Phase 3
Magrolimab	CD47; Humanized IgG4	Myelodysplastic syndrome	Phase 3
Mirvetuximab soravtansine	FRα; Humanized IgG1 **ADC**	Ovarian cancer	Phase 3
Glofitamab	CD20, CD3e; IgG1 **bispecific**	Diffuse large B-cell lymphoma	Phase 3
Zolbetuximab	Claudin-18.2; Chimeric IgG1	Gastric and gastro-esophageal junction adenocarcinoma	Phase 3
Tiragolumab	TIGIT; Human IgG1	Small cell lung cancer	Phase 3
Zanidatamab	HER2, HER2; Humanized IgG1 **bispecific**	Biliary tract cancer	**Pivotal Phase 2**

*Indication for which a regulatory submission is anticipated. Table includes information publicly available as of November 1, 2021.

Regulatory submission anticipated, 2022: Cancer (2)

INN	Target; Format	Indication of relevant late-stage study*	Status
REGN5458	BCMA, CD3; Human **bispecific**	Multiple myeloma	**Pivotal Phase 2**
Talquetamab	GPRC5D, CD3; Humanized IgG4 **bispecific**	Multiple myeloma	**Pivotal Phase 2**
Teclistamab	BCMA, CD3; Humanized/human IgG4 **bispecific**	Multiple myeloma	Phase 3
Odronextamab	CD20, CD3; Human IgG4 **bispecific**	Non-Hodgkin's lymphoma	**Pivotal Phase 2**
Sabatolimab	TIM-3; Humanized IgG4	Myelodysplastic syndrome	Phase 3
Cosibelimab	PD-L1; Human IgG1	Squamous cell carcinoma	Phase 3
Iodine (131I) apamistamab	CD45; Murine IgG1, radiolabeled	Acute myeloid leukemia	Phase 3
Erfonrilimab	PD-L1, CTLA-4; Humanized/chimeric IgG1 **bispecific**	Non-small cell lung cancer	Phase 3

*Indication for which a regulatory submission is anticipated. Table includes information publicly available as of November 1, 2021.

Antibody therapeutics for COVID-19

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mAbs for COVID-19: Use granted or requested

INN or code name	Molecular format	Status for COVID-19	COVID-19 indication(s)
Etesevimab + bamlanivimab	SARS-CoV-2; Human mAbs	EUA granted	**Treatment and prevention** of COVID-19
Sotrovimab	SARS-CoV-2; Human IgG1	**Approved in Australia;** EUA granted; EMA rolling review; BLA planned in H1 2022	Mild to moderate COVID-19
Regdanvimab	SARS-CoV-2; Human IgG1	**Approved in Republic of Korea and EU**	Mild to moderate COVID-19 in adults
casirivimab + imdevimab (REGEN-COV2, Ronapreve™)	SARS-CoV-2; Human mAbs	**Approved in Australia and EU; EUA granted; BLA and MAA in review**	**Treatment and prevention** of COVID-19
Tocilizumab	IL-6R; Humanized IgG1	EUA granted; MAA in review	Hospitalized patients receiving systemic corticosteroids who require supplemental oxygen, mechanical ventilation, or ECMO
Tixagevimab + cilgavimab (AZD7442, Evusheld)	SARS-CoV-2; Human IgG1 mAbs	EUA requested	**Pre-exposure prophylaxis; Post-exposure prophylaxis**
Amubarvimab + romlusevimab (BRII-196 + BRII-198	SARS-CoV-2; Human mAbs	EUA requested	**Symptomatic non-hospitalized adults with COVID-19; Hospitalized patients with COVID-19**

Anti-SARS-CoV-2 Antibodies to Watch in 2021/2

Sponsors	Drug codes	Most advanced phase	Route(s) of administration	Use evaluated*
Mabwell (Shanghai) Bioscience Co.	MW33	Phase 2/3	IV	Treatment
Adagio Therapeutics	Adintrevimab (ADG20)	Phase 2/3	**IM**	Prevention, treatment
Sinocelltech Ltd.	Upanovimab (SCTA01)	Phase 2/3	IV	Treatment*
Bristol-Myers Squibb	C144-LS + C135-LS	Phase 2/3 (**Activ-2**)	IV, SC	Treatment
Toscana Life Sciences Sviluppo s.r.l.	MAD0004J08	Phase 2/3	**IM**	Treatment
Tychan Pte. Ltd.	TY027	Phase 3	IV	Treatment

*Protocol may include hospitalized patients

Key messages

- Projections indicate that 2021 may fall short of record levels for approvals of antibody therapeutics, due to the demands placed on the regulatory agencies by COVID-19
- Rate of entry into US or EU regulatory review has increased, but approvals have not, leading to record numbers in review
- Key lessons regarding the speed of antibody therapeutics discovery, development and regulatory review were learned during the pandemic, although the number of mAbs given authorization for emergency use has lower than expected (so far)
- Finally, watch for “Antibodies to Watch in 2022”, to be published in *mAbs* in Dec 2021/Jan 2022

Acknowledgements

- ‘Antibodies to Watch in 2022’ co-author
  - Hélène Kaplon, Servier (2018-2022)

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Thank you!

Questions?
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