Trends in the commercial development of antibody therapeutics

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Agenda

• Definitions, data sources, objectives
• Trends in FIH studies for antibody therapeutics
• Current early stage pipeline
  • Antibodies for cancer and noncancer indications:
    • formats, targets and mechanism of action
• Overall trends in the clinical pipeline
  • Trends in first marketing approvals and success rates
Definitions, Data sources, Objectives
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; **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
  • Phase transition rates
  • Overall marketing approval rates
  • Phase transition and success rates will be featured in “Antibodies to watch in 2024”
• To assess innovation in the biopharmaceutical industry
Trends in FIH studies
Antibodies starting first clinical studies*

*Data available as of Q2 2023; 2020-22 totals include anti-SARS-CoV-2 antibodies (n=20, 16, 14 for 2020, 2021, 2022, respectively, representing 29%, 19% and 15% of non-cancer pipeline, respectively)

Totals include mAbs sponsored by commercial firms only; dotted lines are 2-yr moving average.

Source: The Antibody Society.
Early-stage clinical pipeline
Status of antibodies in early-stage clinical studies

Most advanced clinical phase
Status of antibodies in early-stage clinical studies

Data as of October 2, 2023. Early-stage excludes pivotal Phase 2 studies.
TA could not be assigned for 4 molecules (undisclosed).
Status of antibodies in early-stage clinical studies

Most advanced clinical phase

Data as of October 2, 2023. Early-stage excludes pivotal Phase 2 studies.
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Status of antibodies in early-stage clinical studies

Most advanced clinical phase

Data as of October 2, 2023. Early-stage excludes pivotal Phase 2 studies. TA could not be assigned for 4 molecules (undisclosed).
Antibodies in early-stage clinical studies

Innovation: unique targets

Cancer
- Approved, in regulatory review, in late-stage studies: 59%
- Unique

Total=768

Non cancer
- Approved, in regulatory review, in late-stage studies: 60%
- Unique

Total=354
Antibodies for cancer indication
Antibodies for cancer indication

Format overview

- Monospecifics: 61%
- Multispecifics: 31%
- Immunoconjugates: 8%

Total=768
Antibodies for cancer indication

Format overview

![Pie chart showing the distribution of antibodies among Monospecifics, Multispecifics, and Immunoconjugates with percentages of 61%, 31%, and 8% respectively. The total is 768.]
Monospecific antibodies

Target overview

Top 20 targets

Number of antibodies

Claudin 18.2
HER2
TIGIT
CD73
PD-1
LAG-3
CTLA-4
4-1BB
TROP-2
CCR8
SIRPα
PD-L1
CD47
CD40
B7-H3
TNFR2
TIM-3
VISTA
OX40
FRα
Monospecific antibodies

Top 20 targets

Claudin 18.2
HER2
TIGIT
CD73
LAG-3
CTLA-4
4-1BB
TROP-2
CCR8
SIRPa
PD-L1
CD40
B7-H3
TNFR2
TIM-3
VISTA
OX40
FRα

Number of antibodies

Cancer

Target overview
Monospecific antibodies

Top 20 targets

Claudin 18.2
Her2
Tigit
Cd73
Pd-1
Lag-3
Ctla-4
4-1bb
Trop-2
Ccr8
Sipri
Pd-l1
Cd47
Cd40
B7-h3
Tnf-r2
Tim-3
Vista
Ox40
Frac

Claudin 18.2
1 in regulatory review in Japan

Number of antibodies
Monospecific antibodies

Target overview

Claudin 18.2
1 in regulatory review in Japan

HER2
14 in late stage, regulatory review or approved
Monospecific antibodies

Target overview by format subtype

Cancer

Total=465
Naked
ADC
RIC

Format subtype

68%
30%
2%

Total=465

Naked
ADC
RIC
Monospecific antibodies

Target overview by format subtype

**Popular targets - naked antibodies**

- TIGIT
- CD73
- Claudin 18.2
- PD-1
- 4-1BB
- CTLA-4
- LAG-3
- CCR8
- CD40
- CD47
- SIRP α
- TIM-3
- TNFR2
- CD39
- OX40
- PD-L1
- VISTA
- HER2

**Popular targets - ADCs**

- HER2
- Claudin 18.2
- TROP-2
- B7-H3
- cMET
- FRα
- B7-H4
- EGFR
- Nectin-4

**Format subtype**

- Naked: 68%
- ADC: 30%
- RIC: 2%

Total = 465

**Popular: for more than 3 molecules**
Antibodies for cancer indication

Format overview

- Monospecifics: 61%
- Multispecifics: 31%
- Immunoconjugates: 8%

Total=768
Multispecific antibodies

Bispecifics, trispecifics, tetraspecifics
Cancer

Multispecific antibodies

Bispecifics, trispecifics, tetraspecifics

88%
Multispecific antibodies

Bispecifics, trispecifics, tetraspecifics

Type of target overview

![Pie chart showing the distribution of multispecific antibodies by type of target.](chart.png)
Cell engagers

Multi-specific antibodies
Bispecifics, trispecifics, quadrispecifics

66%
Total=242

- Cell engager
- Tumor
- Immune cells
- Tumor, TME
- Immune cells, TME
- Undisclosed

Cancer
Cell engagers

Multispecific antibodies
Bispecifics, trispecifics, quadrispecifics

66% of multispecific antibodies are in total 242.

35% of multispecific antibodies are in total 159.

65% of multispecific antibodies are in total 159 and include cell engager, immunomodulatory.
Multispecific antibodies

Cell engagers

Tumor/fibroblast  Immune cell
Cell engagers

Multispecific antibodies

Popular targets for tumor/fibroblasts

Only engaging

Tumor/fibroblast
Immune cell

Popular targets for immune cells

Only engaging

Multispecific antibodies

Popular: for more than 2 molecules
Cell engagers

Multispecific antibodies

Popular targets for tumor/fibroblasts
- Only engaging

Popular targets for immune cells
- Only engaging

Popular targets for tumor/fibroblasts
- Immunomodulatory

Popular targets for immune cells
- Immunomodulatory

Popular: for more than 2 molecules
Multispecific antibodies

Targeting the tumor

- Cell engager
- Tumor
- Immune cells
- Tumor, TME
- Immune cells, TME
- Undisclosed

Total=242

17%
Multispecific antibodies

Targeting the tumor

Cell engager: 17%
Tumor: 57%
Immune cells: 43%
Tumor, TME: 57%
Immune cells, TME: 43%
Undisclosed: 35%
Total=242

Popular targets

Tumor only
- cMET, EGFR
- HER2 (biparatopic)
- cMet (biparatopic)

Tumor immunomodulatory
- PD-L1, CD47
- CD20, CD47
- CD38, CD47
- Claudin 18.2, CD47

Number of antibodies

Popular: for more than 2 molecules
Multispecific antibodies

Targeting the tumor

- Cell engager: 17%
- Tumor: 43%
- Immune cells: 57%
- Tumor, TME: Undisclosed

Tumor only format subtype

- Naked: 33%
- ADC: 63%
- RIC: 8%

Total=24

Popular targets

- Tumor only
  - cMET, EGFR: 4
  - HER2 (biparatopic): 1
  - cMet (biparatopic): 1

- Tumor, immunomodulatory
  - PD-L1, CD47: 8
  - CD20, CD47: 4
  - CD38, CD47: 2
  - Claudin 18.2, CD47: 1

Total=42

Number of antibodies

- cMET, EGFR: 6
- HER2 (biparatopic): 6
- cMet (biparatopic): 2
- PD-L1, CD47: 8
- CD20, CD47: 4
- CD38, CD47: 2
- Claudin 18.2, CD47: 1

Popular: for more than 2 molecules

Cancer
Multispecific antibodies

Targeting immune cells

- Cell engager
- Tumor
- Immune cells
- Tumor, TME
- Immune cells, TME
- Undisclosed

Total=242

10%
## Multispecific antibodies

### Targeting immune cells

<table>
<thead>
<tr>
<th>Number of Antibodies</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1</td>
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<tr>
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<td>3</td>
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</tr>
<tr>
<td>4</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

**Total=242**

- **Cell engager**
- **Tumor**
- **Immune cells**
- **Tumor, TME**
- **Immune cells, TME**
- **Undisclosed**

### Popular targets

- PD-1, CTLA-4
- PD-1, LAG-3
- PD-1, TIGIT
- TIGIT, PVRIG
- PD-1, TIM3

**Number of Antibodies**

- PD-1, CTLA-4: 4
- PD-1, LAG-3: 3
- PD-1, TIGIT: 3
- TIGIT, PVRIG: 2
- PD-1, TIM3: 1

**Total=242**

**Popular: for more than 2 molecules**

- Cancer
- 10%

**Targeting immune cells**

- **Cell engager**
- **Tumor**
- **Immune cells**
- **Tumor, TME**
- **Immune cells, TME**
- **Undisclosed**

**Total=242**

**Popular targets**

- PD-1, CTLA-4: 4
- PD-1, LAG-3: 3
- PD-1, TIGIT: 3
- TIGIT, PVRIG: 2
- PD-1, TIM3: 1

**Total=242**

**Popular: for more than 2 molecules**
Antibodies for cancer indication

Format overview

- Total: 768
  - Monospecifics: 31%
  - Multispecifics: 8%
  - Immunoconjugates: 61%
Format and target overview

Imunoconjugates

- Bispecific immunoconjugate: 46%
- Immunocytokine: 41%
- Immunotoxin: 7%
- Total: 61

Cancer

46%
41%
7%
Total=61

Bispecific immunotoxin
Format and target overview

**Bispecific immunoconjugate**

- Target: CD20, HER2, MAGE-A4, PRAME, TIGIT, VEGF, CD39, CD73, EGFR, PD-1, PD-L1, GPC3, CD20, albumin
- Fused protein: SIRPα, T cell receptor, TGFβ-R1I, VEGFR1, anti-4-1BB anticalin, CD19

- Total = 28

**Immunocytokine**

- Total = 61

**Immunotoxin**

- Total = 61

**Imunoconjugate**

- Total = 28

**Bispecific immunotoxin**

- Total = 61

Cancer

**Format and target overview**

- Bispecific immunoconjugate
- Immunocytokine
- Immunotoxin
- Immunoconjugate
- Bispecific immunotoxin

- Total = 28

**Immunocytokine**

- Total = 61

**Immunotoxin**

- Total = 61

**Immunoconjugate**

- Total = 28

**Bispecific immunotoxin**

- Total = 61

**Immunoconjugates**

- Bispecific immunoconjugate
- Immunocytokine
- Immunotoxin
- Immunoconjugate
- Bispecific immunotoxin

- Total = 61
Cancer

**Format and target overview**

### Bispecific immunoconjugate

<table>
<thead>
<tr>
<th>Target</th>
<th>Fused protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD20, albumin</td>
<td>SIRPα, T cell receptor, TGFβ-RII, VEGFR1, anti-4-1BB anticalin, CD19</td>
</tr>
<tr>
<td>Total = 28</td>
<td></td>
</tr>
</tbody>
</table>

### Immunocytokine

<table>
<thead>
<tr>
<th>Target</th>
<th>Fused protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD20, albumin</td>
<td>IL-10, IL-2 + IL-10, IL-12, IL-21, IL-15, IL-2 variant, TGFβ, IFNα</td>
</tr>
<tr>
<td>Total = 25</td>
<td></td>
</tr>
</tbody>
</table>

### Immunotoxin

<table>
<thead>
<tr>
<th>Target</th>
<th>Fused protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shiga-like toxin A, Cytolysin</td>
<td></td>
</tr>
<tr>
<td>Total = 4</td>
<td></td>
</tr>
</tbody>
</table>
Antibodies for non cancer indications

- Total=350
  - Monospecifics: 86%
  - Multispecifics: 12%
  - Immunoconjugates: 2%

Format:
- 86% Monospecifics
- 12% Multispecifics
- 2% Immunoconjugates
Antibodies for non cancer indications

- **Monospecifics**: 86%
- **Multispecifics**: 12%
- **Immunoconjugates**: 2%
- **Total**: 350

3% ADCs
Antibodies for non cancer indications

Format
- Monospecifics: 86%
- Multispecifics: 12%
- Immunoconjugates: 2%
- Total: 350

Primary therapeutic area
- Immune-mediated / inflammatory disorders: 46%
- Infectious diseases: 15%
- Cardiovascular / hemostasis: 13%
- Neurological disorders: 12%
- Ophthalmic disorders: 12%
- Metabolic disorders: 13%
- Respiratory diseases: 15%
- Muscular disorders: 86%
- Skeletal disorders: 12%
- Other: 3%
- Total: 350

3% ADCs
Immune mediated / inflammatory disorders

Non cancer

Total=350

46%
Mechanism of action overview

- **46%** Immune-mediated/inflammatory disorders
- **25%** Block cytokine/chemokine/allarmin/TLR signalling
- **6%** Immune cell depletion
- **5%** Checkpoint agonist
- **4%** Block CD40/CD40L pathway
- **3%** Block immune cell recruitment
- **2%** Block OX40/OX40L pathway
- **2%** Other

Total = 162

**Non cancer**

**Immune mediated / inflammatory disorders**

- Infectious diseases
- Cardiovascular / hemostasis
- Neurological disorders
- Ophthalmic disorders
- Metabolic disorders
- Respiratory diseases
- Muscular disorders
- Skeletal disorders
- Other

Total = 350

- **58%** Immune-mediated/inflammatory disorders
- **25%** Block cytokine/chemokine/allarmin/TLR signalling
- **6%** Immune cell depletion
- **5%** Checkpoint agonist
- **4%** Block CD40/CD40L pathway
- **3%** Block immune cell recruitment
- **2%** Block OX40/OX40L pathway
- **2%** Other

Total = 162
Immune-mediated /inflammatory disorders
Infectious diseases
Cardiovascular / hemostasis
Neurological disorders
Ophthalmic disorders
Metabolic disorders
Respiratory diseases
Muscular disorders
Skeletal disorders
Other

15%
Infectious diseases

Target pathogen overview

- Immune-mediated/inflammatory disorders
- Infectious diseases
- Cardiovascular/hemostasis
- Neurological disorders
- Ophthalmic disorders
- Metabolic disorders
- Respiratory diseases
- Muscular disorders
- Skeletal disorders
- Other

15%

Non cancer

- Step	15%
- Tococcus pneumoniae
- RV
- Rabies virus
- Pseudomonas aeruginosa
- Marburg virus
- Ebola virus
- Chikungunya virus
- Clostridium difficile
- Bacterium biofilm
- Influenza virus
- HBV
- SARS-CoV-2
- HIV
- CMV
- Herpes simplex
- Staphylococcus aureus
- BK virus
- Campylobacter jejuni
- Chikungunya virus
- Clostridium Botulinum
- Ebola virus
- Marburg virus
- Pseudomonas aeruginosa
- Rabies virus
- RSV

Infectious diseases

Number of antibodies

- HIV
- SARS-CoV-2
- HBV
- Influenza virus
- BK virus
- Campylobacter jejuni
- Chikungunya virus
- Clostridium difficile
- Bacterium biofilm
- Influenza virus
- HBV
- SARS-CoV-2
- HIV
- CMV
- Herpes simplex
- Staphylococcus aureus
- RSV
- Steptococcus pneumoniae

Infectious diseases
Neurological disorders

Non cancer

Total=350

12%
Neurological disorders

Target overview by indication

Total=350

Primary indication

Total=44

- Alzheimer's disease: 48%
- Parkinson's Disease: 11%
- Pain: 14%
- Other: 27%
Neurological disorders

Target overview by indication

Primary indication

Alzheimer's disease 48%
Parkinson's Disease 27%
Pain 11%
Other 14%

Total=44

Alzheimer's disease

Amyloid beta
Tau
EphA4
FAM19A5
Fibrin
MS4A4A
PD-L1
TREM2

Total=350

Non cancer

Immune-mediated/inflammatory disorders
Infectious diseases
Cardiovascular/hemostasis
Neurological disorders
Ophthalmic disorders
Metabolic disorders
Respiratory diseases
Muscular disorders
Skeletal disorders
Other
Neurological disorders

Target overview by indication

Regional distribution

Primary indication

Number of antibodies

Non cancer

Total=350

12%

Total=44

14%

27%

48%

Alzheimer's disease
Parkinson's Disease
Pain
Other

Other

11%

Immune-mediated /inflammatory disorders
Infectious diseases
Cardiovascular / hemostasis
Neurological disorders
Ophthalmic disorders
Metabolic disorders
Respiratory diseases
Muscular disorders
Skeletal disorders

Number of antibodies

12%

Total=44

Alzheimer's disease
Parkinson's Disease
Pain
Other

Target overview by indication

Primary indication

Number of antibodies

14%

27%

48%

Alzheimer's disease
Parkinson's Disease
Pain
Other

Alpha synuclein
Alpha synuclein, IGF-1R

Number of antibodies

Total=44

Alzheimer's disease
Parkinson's Disease
Pain
Other

Amyloid beta
Tau
EphA4
FAM19A5
Fibrin
MS4A4A
PD-L1
TREM2
Target overview by indication

**Neurological disorders**

- Primary indication
  - Alzheimer's disease: 48%
  - Parkinson's disease: 27%
  - Pain: 14%
  - Other: 12%

**Number of antibodies**

- NGF
- NGF, TNF
- CCL17
- Alpha synuclein
- Alpha synuclein, IGF-1R
- Amyloid beta
- Tau
- EphA4
- FAM19A5
- Fibrin
- MS4A4A
- PD-L1
- TREM2

**Non cancer**

- Total=350
- Alzheimer's disease: 44
- Parkinson's Disease: 44
- Pain: 14
- Other: 11

**Primary indication**

- Total=44
- Alzheimer's disease: 27%
- Parkinson's disease: 48%
- Pain: 14%
- Other: 11%
Non cancer

Ophthalmic diseases

Total=350

4%
Ophthalmic diseases

Target and format overview

- Immune-mediated / inflammatory disorders
- Infectious diseases
- Cardiovascular / hemostasis
- Neurological disorders
- Ophthalmic disorders
- Metabolic disorders
- Respiratory diseases
- Muscular disorders
- Skeletal disorders
- Other

Total=350

4%

Number of antibodies

Non cancer

Bispecifics
Muscular disorders

Non cancer

Total=350

2%
Muscular disorders

Target and format overview

Total=350

- Immune-mediated / inflammatory disorders: 2%
- Infectious diseases
- Cardiovascular / hemostasis
- Neurological disorders
- Ophthalmic disorders
- Metabolic disorders
- Respiratory diseases
- Muscular disorders
- Skeletal disorders
- Other

Total=6

- TfR1: 1
- MuSK: 5

Non cancer
Muscular disorders

Target and format overview

ADC/AOC targeting TfR1

2 Myotonic dystrophy (siRNA/ASO targeting DMPK)
2 Duchenne muscular dystrophy (phosphorodiamidate morpholino oligomers (PMO) for exon skipping)
1 Facioscapulohumeral muscular dystrophy (siRNA targeting DUX4)
Overall trends in the clinical pipeline
Antibody therapeutics pipeline: 2018 vs 2022*

% increase 2018 vs 2022 = 110%.

*Anti-SARS-CoV-2 antibodies excluded for historical comparison; molecules in Phase 1/2 and 2/3 studies incorporated as Phase 2 and Phase 3, respectively. 2022 data 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%.
Trends in first marketing approvals and success rates
Annual first approvals: US+EU vs ROW


Top 2 ROW countries contributing to totals in 2010-22: China and Japan.
Phase transition and approval success rates
(antibody therapeutics which entered clinical studies in 2000-2019)
Key messages

• Antibody therapeutics, particularly mAbs for cancer indications have entered clinical study in increasing numbers recently.

• For both cancer and non cancer, ~60% of the molecules is against novel targets, suggesting the biopharmaceutical industry is engaging in innovative R&D.

• Of mAbs for cancer indication:
  • The majority are monospecific, but ~1/3 are multispecific.
  • Most of the monospecifics are naked antibodies with immunomodulatory properties, and ~1/3 are ADCs.
  • Most of the multispecifics are cells engagers, of which ~1/3 have immunomodulatory properties.

• Of mAbs for non cancer indications:
  • The majority are monospecifics, only 12% are multispecifics.
  • The majority are for immune mediated / inflammatory disorders (66%), followed by infectious diseases (15%), cardiovascular / hemostasis (13%) and neurological disorders (12%).

• Trends show that antibody therapeutics are also entering late-stage clinical studies, and being granted marketing approvals world-wide, in increasing numbers recently.

• Phase transition and approval success rates increased globally and in US+EU, for antibodies which entered clinical studies after 2010 compared to those who entered in 2000-2009.
Acknowledgements

• Dr. Janice M. Reichert (Chief Operating Officer, The Antibody Society, Inc., Editor-in-Chief, mAbs)

• The Antibody Society and their corporate sponsors
Join The Antibody Society to keep up to date!

• 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
Support provided by:

- abbvie
- AbCellera
- ABLEXIS
- absci
- ADIMAB
- AlivaMab Discovery Services
- Alloy Therapeutics
- Antibody Solutions
- argenx
- AstraZeneca
- BIOINTRON
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