Life Sciences

ANNUAL BIOPHARMA REVIEW 2024

Trends in drug development and innovation

"It's both in with the old, and in with the new, but commercialisation remains king"

June 2024

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Foreword

Significant time, effort and expense goes into developing and commercialising new drug products. But are pipelines still healthy? Where are biotechs and pharmacos focusing their energy, and are regulators able to cope with demand?

Although novel drugs promise transformative change in the world's healthcare markets, they are often expensive, and may only reach small target populations. Can they really deliver?

- In this report we seek answers to these questions, looking at trends in clinical trials ('CTs') and regulatory approvals.
- We look at whether new innovative, but also older and improved technologies, can really deliver value-for-money in the real world. We consider the role of the regulator, focused on the FDA which polices the world's largest pharmaceutical market, and highlight some of the approval routes and measures the help bring innovative solutions to market.
- Our work is based on research undertaken by us, drawing on publicly available information and data, including journal articles and approvals data from the FDA website. We have also relied upon information from Evaluate Pharma.
- We have considered global commercial CTs only (10-year period 2013-23), as these typically take place on a much larger scale than academic studies.
- We have looked at trials in phases I to III only, grouping early phase I data with phase I, phase I/II with phase II, and phase II/III with phase III. Trials with any of the following statuses were excluded from our analysis: 'Approved for marketing', 'Withdrawn', or 'Unknown'. Year references relate to the calendar year that the CT started.

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Summary

72	7	65%	c.5.9k	$90bn
novel drugs approved by the FDA in 2023	C&GTs approved by the FDA in 2023	of novel drugs used one or more expedited approval route (2023)	CTs in 2023, a +2.3% CAGR (2023-23)	of M&A deals related to ADCs in 2023, a 19% share

2023 Commercial CTs volumes suggest healthy pipelines for biotechs and pharmacos, with biologics continuing to form a larger share of the total, and positive signs for both ADCs and C&GTs, two key biological technologies.

Notwithstanding this however, challenges remain around the commercialisation of ADCs and C&GTs, with the potential to address this through strategic partnerships between biotechs and pharmacos, and innovative pricing models.

Highlights from our report include the following:

- **Healthy biotech and pharmaco pipelines:** Commercial CTs are back above pre COVID levels, suggesting healthy pipelines, and greater opportunities for outsourced providers.
- **Biologics continue to rise:** CTs for biologics have been increasing at a faster rate than small molecule drugs and are forming a larger and larger share of CT volumes. Each CT typically covers multiple different drug development technologies, highlighting their complexity, and the need for greater scientific expertise across the provider and advisor community.
- **Complexity, regulatory workloads and approvals have increased:** With the complexity of drugs and manufacturing technologies increasing, regulatory complexity and workload has also increased. For example, there were record submissions to the FDA in 2023, and more advisory committees were held.
- This has translated into more new products coming to market, with 2023 novel drug approvals at their highest level for ten years - a sign of strong innovation.
- The many well-trodden routes for expedited drug approval remain popular, with volumes trending upward, and a majority of novel drugs having used one or more of the available pathways.
- Delays, due to resourcing, are occurring at the FDA however, and given new FDA powers in late 2022, there is also the potential for a crackdown on biotechs and pharmacos who are not completing confirmatory studies post approval (a widespread issue).
- This means that biotechs and pharmacos need to be better prepared, and better advised, if they want to avoid unexpected delays.
- **High confidence in ADCs:** ADCs have been attracting a lot of interest over the last year, with several large M&A deals having completed in 2023, reflecting increased investor confidence as more ADC products have been approved, and achieved commercial success.
- There remains some work to do however (e.g. combatting drug resistance and tumour heterogeneity between patients) but given ADCs' long development history (we are now into the third-generation of products), this is likely to be evolutionary not revolutionary.
- There may be further opportunities for investments in ADC portfolios, with developers who can solve the remaining scientific challenges, being highly attractive.
- **Increasing confidence in C&GTs:** CTs for C&GTs are growing, and C&GT approvals were at their highest level ever in 2023 (seven approvals).
- Products once considered part of the 'newer generation' of technologies, such as CRISPR, are now fully approved, and give confidence that new approaches can make it all the way through to commercialisation.
- **BUT challenges remain around commercialisation:** Complex manufacturing, high treatment costs, a lack of long-term efficacy data, and irregular patient treatment pathways, are all adverse factors impacting the commercial prospects of C&GTs.
- There are opportunities therefore, for outsourced providers and advisors to help identify strategic partnerships (between biotechs and pharmacos), and to explore new / innovative pricing models (e.g. outcome-based pricing) to overcome these challenges. There is evidence that C&GT asset owners are already putting plans in place and executing them.

If you would like any further information in relation to this report, please contact a member of the team (our contact details set out on the previous page).

Clinical trials: Volume and share conventional vs. biologic

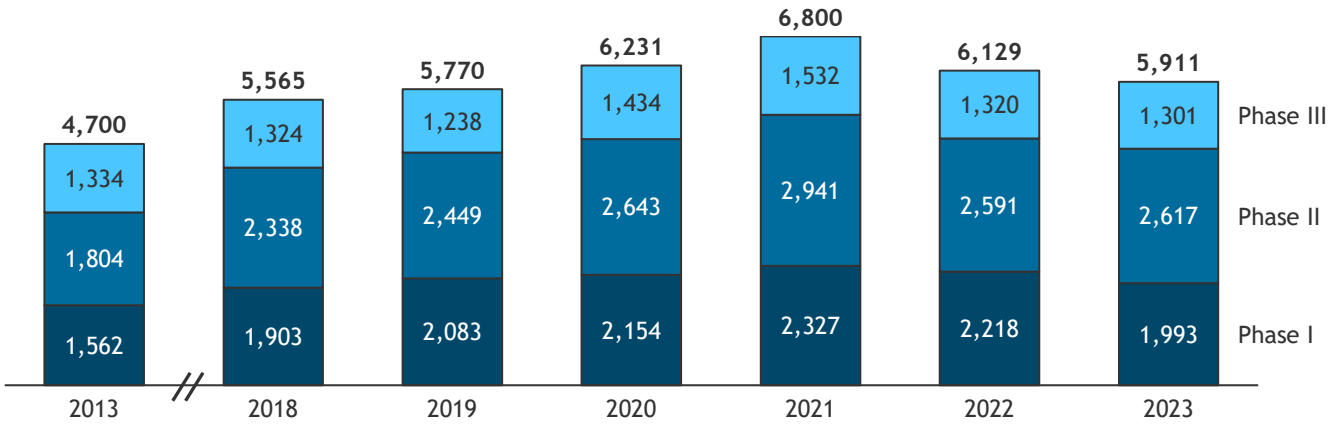
2023 CT volumes are back above pre COVID levels

- In 2023 there were around 5.9k commercial CTs in total, across phases I to III. This is now back above pre COVID levels (c.5.8k CTs in 2019).
- Of commercial CTs in 2023, c.34% of trials were in phase I, c.44% in phase II and c.22% were in phase III (see figure 1).
- This is good news for outsourced providers, suggesting more opportunities to engage with biotechs and pharmacos.

Biologics continue to be on the rise

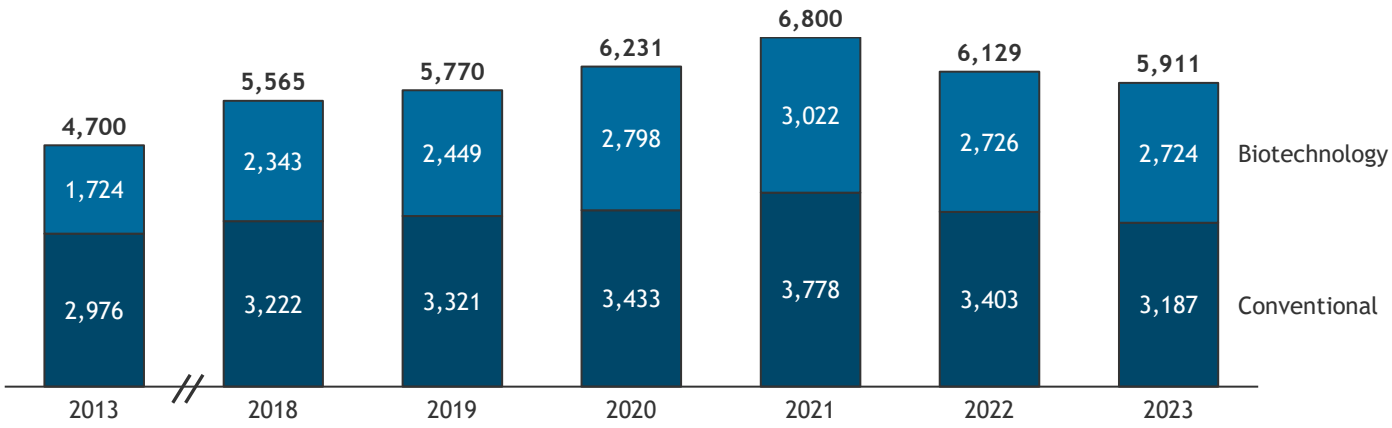
- Over the ten-year period 2013-23, CTs volumes increased at a CAGR of +2.3%. While CTs for conventional drugs have only increased at a +0.7% CAGR over that period (and remain dominated by small molecules), CTs using biologics have increased at the larger, +4.7% CAGR, from 1.7k to 2.7k CTs (see figure 2).
- Of the c.5.9k of CTs in 2023, c.3.2k were for conventional products and c.2.7k for biologics i.e. a 54:46 split. This is the largest share for biologics over the last 10 years.

Figure 1: Commercial CTs by phase



Source: Evaluate Pharma

Figure 2: Commercial CTs



Source: Evaluate Pharma

Clinical trials: Biologics share by technology

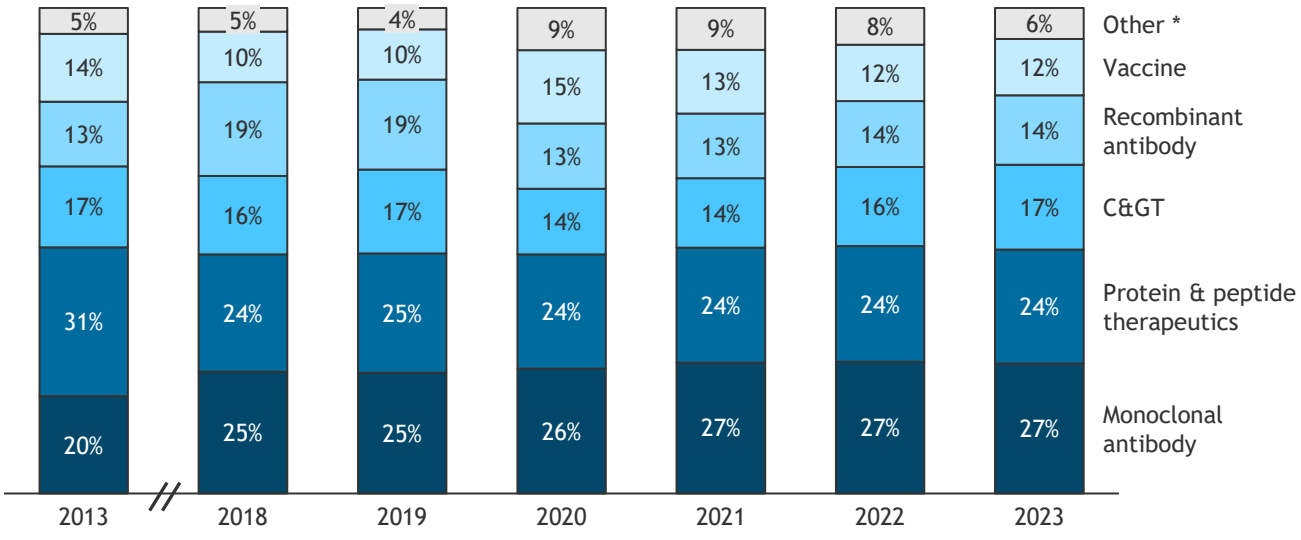
CTs for biologics are complex, covering multiple technologies

- Any given CT may cover a multiple number of technologies e.g. C&GT, monoclonal, recombinant antibodies, vaccines etc. Of the c.2.7k biological CTs in 2023, there were a total of c.5.2k investigations when factoring in all technologies i.e. an average of 1.9 technologies per CT. This average has trended upward over time (from 1.6x in 2013, but with a high-watermark of 2.2x in 2020, the middle of COVID).
- This complexity highlights the need for greater scientific expertise across the provider and advisor community.

CTs for monoclonal antibodies remain high given their wide applicability to cancer and other non-communicable diseases ('NCDs')

- Monoclonal antibodies feature in the largest share of CT investigations (27%), followed by protein & peptides (24%) and C&GTs (17%, includes cell therapies, gene therapies, and therapies with both elements).
- Whilst the share from C&GTs has remained relatively stable over the last 10 years (growing from a low of 14% in 2020 and 2021), monoclonal antibodies have been on the rise (20% share in 2013 vs. 27% in 2023), with the share from protein & peptides in decline (31% share in 2013vs. 24% in 2023) (see figure 3).
- The applicability of monoclonal antibodies to both cancer treatments (which account for a significant share of biotechs' and pharmacos' R&D budgets), and a variety of autoimmune diseases (e.g. rheumatoid arthritis, Crohn's disease) explains the focus on this technology as a potential tool for easing the rising global burden of NCDs.
- There are now c.6.5k active monoclonal antibody drugs on the market, including c.4k with oncology indications.
- This depth in inventory continues to serve the development of cancer targeting antibody-drug conjugates ('ADCs'), which combine an antibody (e.g. a monoclonal antibody (murine, chimeric, humanised, or human)) and a cytotoxic payload. The antibody attaches itself to the surface of a cancerous cell, triggering a response that absorbs the antibody and payload into the cell. The cytotoxin then gets to works killing the cancer.
- See later in our report for further commentary on ADCs.

Figure 3: Share of Biologics CTs by Technology



*Note: * Other relates to DNA & RNA therapeutics, Oncolytic Virus, Transgenic Products, Genome Editing and other biologic products*
Source: Evaluate Pharma

Approvals: Overview

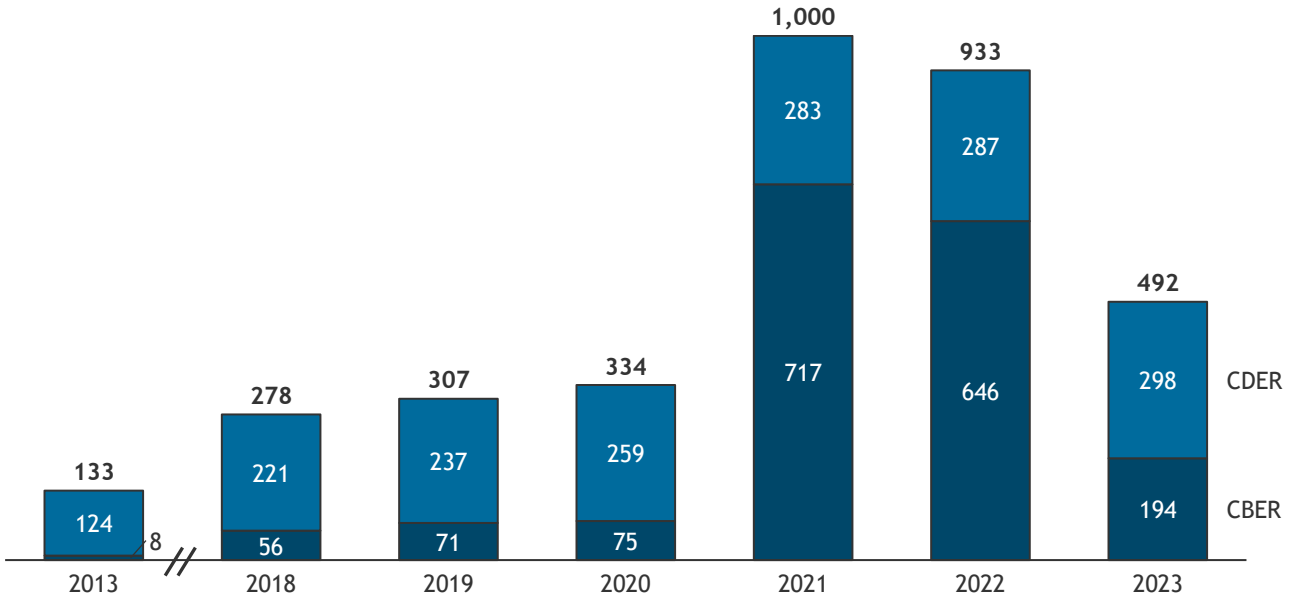
Rising drug complexity continues to increase the regulatory burden and workloads

- The pharmaceutical industry continues to see a rise in regulatory complexity, driven by factors such as increased drug technology and manufacturing complexity, the rising importance of data collection and analysis, and a greater emphasis on patient safety and drug efficacy.
- These have all put increased pressure on in-house regulatory teams and driven greater outsourcing.
- Regulators themselves have responded, scaling up teams and looking to streamline approval processes.
- In 2023, the FDA alone received 492k submissions to the CDER (298k) and CBER (194k) through its Electronic Submissions Gateway. The volume of submissions has increased by a +14% CAGR over the last ten years (2013-23), and by a +12% CAGR over the last five (2018-23) (see figure 4).
- Submissions to the CDER are at an all-time high, whereas CBER submissions are back well above pre COVID levels (75k in 2020 c.f. 717k in 2021 and 646k in 2022, reflecting the fact that vaccines fall under the remit of the CBER, alongside C&GTs and blood products).
- In addition to submissions volumes, the rising burden on the regulator is evident in a recent increase in the use of advisory committees, a tool the FDA uses to obtain independent expert advice covering scientific, technical and policy matters, and which, in the past, have given the market early insights into its thinking on certain drug applications. They also serve to build trust by making the FDA's thinking more transparent.
- There were 55 such meetings in FY23 (the FDA's financial year ends on 30 September), back above pre COVID levels (52 meetings in FY19, c.f. 25 in FY20, 36 in FY21 and 35 in FY22).

FDA approvals were at a five year high in 2023

- Measured in output, there were c.6k approvals by the CDER in 2023 (c.4k for labelling), the highest in the last five years. Of these, c.1k were in respect of original applications covering NMEs, new dosage forms, new combinations and indications (as opposed to supplementary submissions e.g. for labelling, manufacturing and efficacy changes etc.).

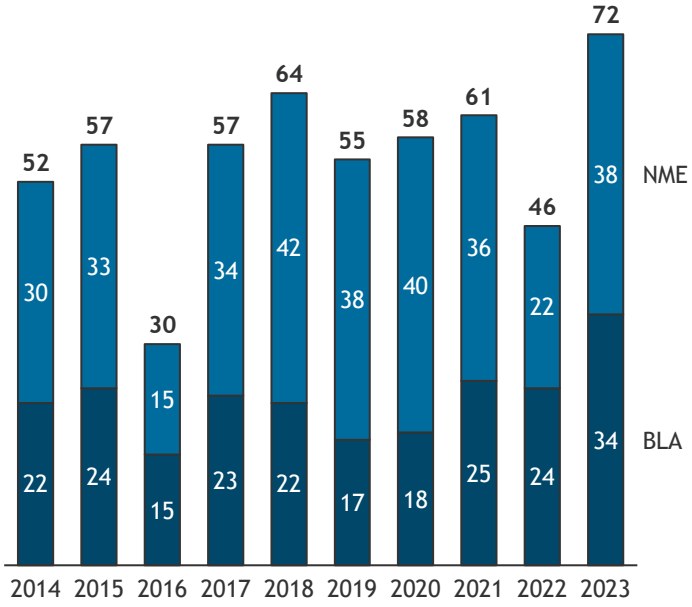
Figure 4: Submissions received by the FDA (CDER and CBER)



Source: FDA.gov

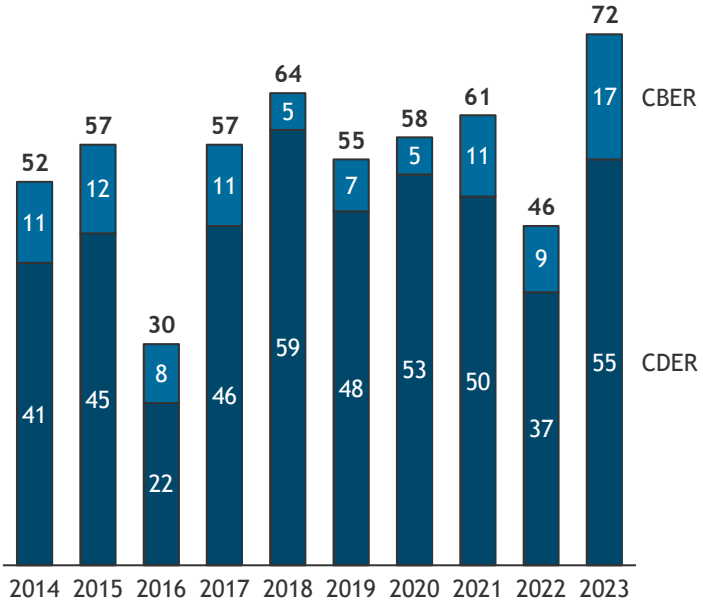
Approvals: Novel drug approvals by type

Figure 5: FDA novel drug approvals by type



Note: CBER BLA approvals exclude assays, reagents and source plasma
Source: FDA.gov

Figure 6: FDA novel drug approvals by office



Note: CBER BLA approvals exclude assays, reagents and source plasma
Source: FDA.gov

Record novel drug approvals are a sign that innovation remains strong

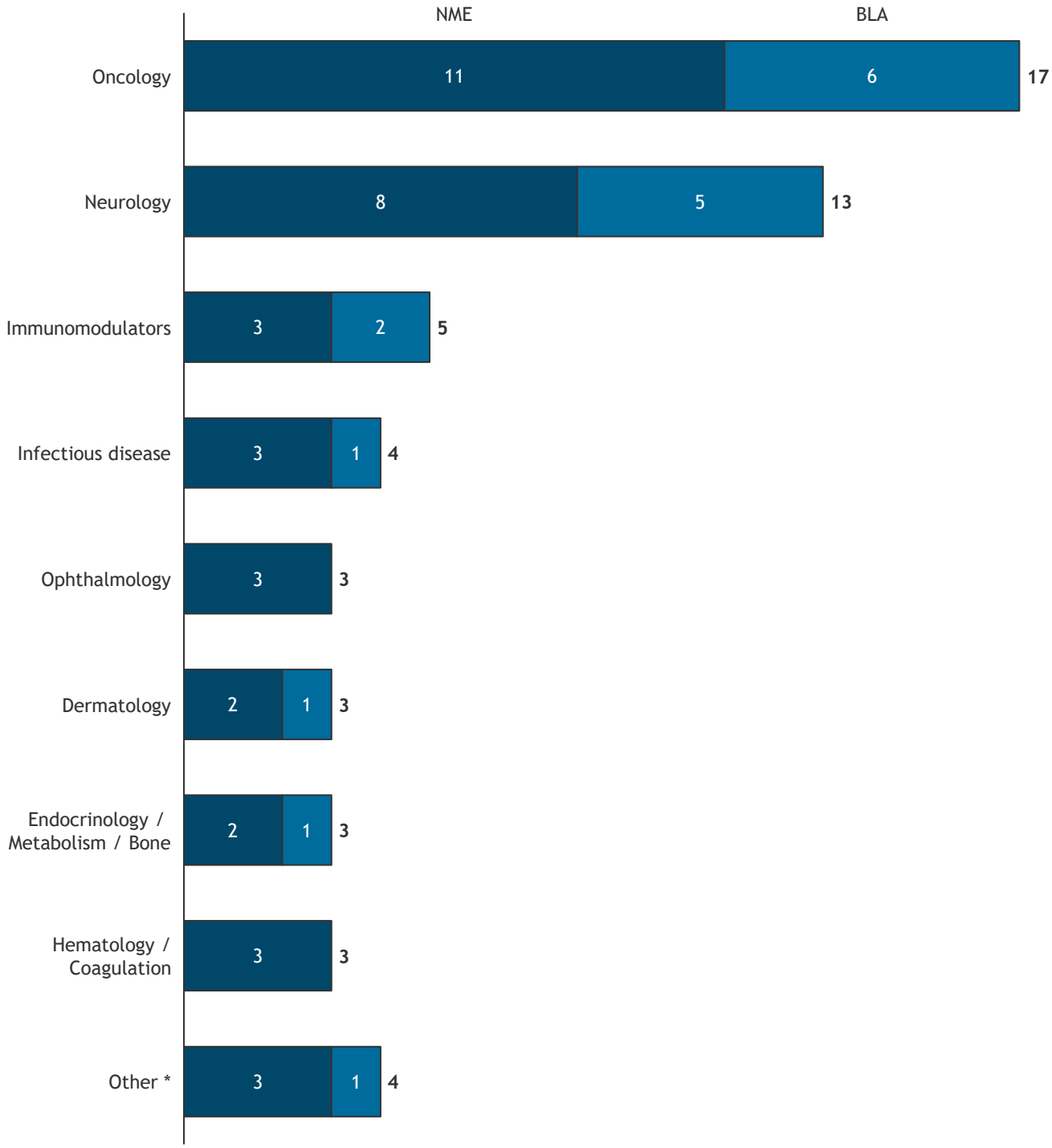
- The total number of novel drugs approved by the FDA was 72 in 2023, a ten-year high (see figures 5 and 6), demonstrating that innovation remains high in the drug development sector.
- The 72 approvals included 38 conventional drugs (NMEs approved by the CDER) and 34 biologics (17 new BLAs approved by the CDER, and 17 new BLAs approved by the CBER).
- The CBER's 17 new BLA approvals are its highest over the ten-year period.

Oncology remains the dominant indication

- CDER novel approvals only (55) reflected a wide range of therapeutic areas including infectious diseases (COVID-19, HIV-1), neurological conditions (ALS, Alzheimer's) and cancers (prostate, lung, colorectal). Oncology dominated with c.31% of the approvals, followed by neurology with c.24% (see figure 7).

Approvals: Novel drug approvals by therapeutic area

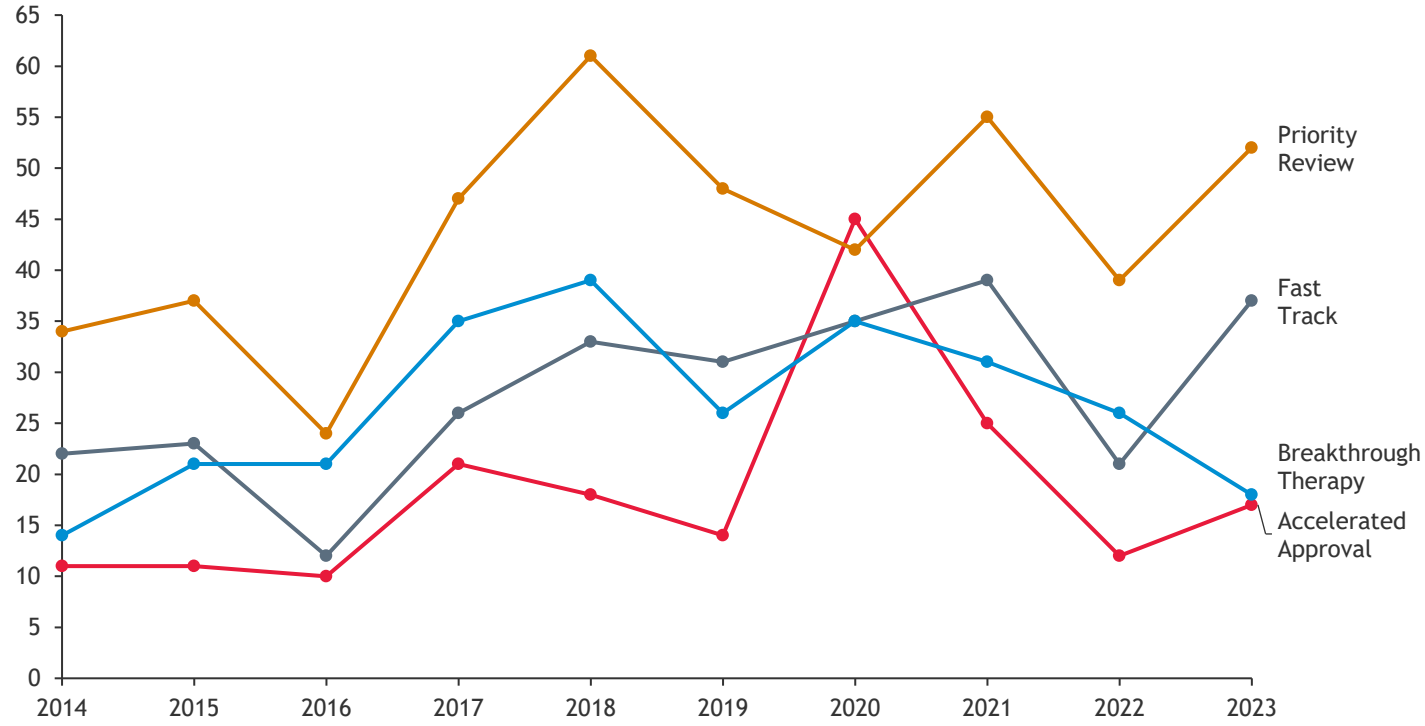
Figure 7: CDER novel drug approvals by therapeutic area



*Note: * Other includes Cardiovascular, Respiratory and Urologic*
Sources: FDA.gov, Evaluate Pharma

Approvals: Expedited pathways

Figure 8: FDA's expedited pathways for new drug approvals



Source: FDA.gov

There is an upward trend in the use of expedited pathways

- The numerous approval pathways for an expedited review, including, accelerated approval, breakthrough therapy, fast track, and priority review, are all now well-established routes (see box 1 on the next page for an overview of the different routes).
- Broadly speaking, they work well, and over the last nine years (period 2014-23) total approvals using expedited routes have increased, albeit with some fluctuation (due to COVID). In 2023 for example, there were 17 accelerated approvals by the CDER (including nine novel drugs), compared to 11 in 2014.
- There were 18 breakthrough therapies (nine novel drugs) compared to 14 in 2014, and 37 fast track approvals (25 novel drugs) compared to 22 in 2014 (see figure 8).

The FDA is looking to expand the use of expedited pathways

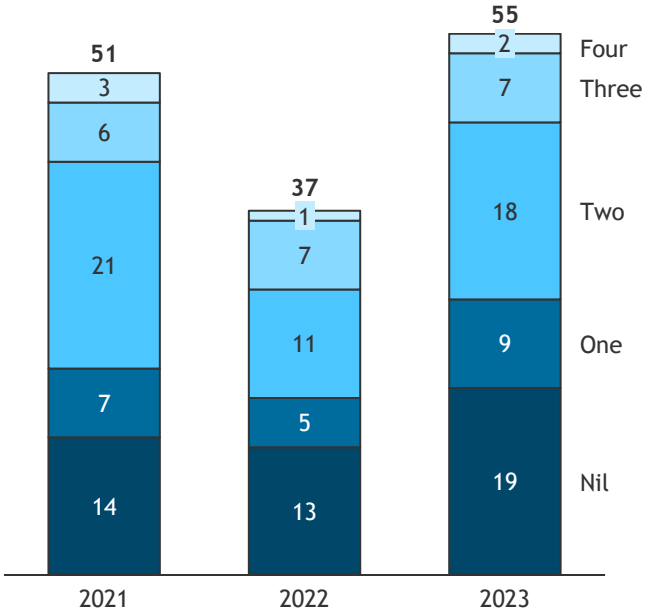
- The FDA continues to push and develop the use of expedited pathways with a variety of initiatives, including *Project Confirm* (a program to develop greater transparency regarding accelerated approvals for cancer treatments), *RTOR* (Real-Time Oncology Review, a program to bring forward an FDA evaluation by allowing earlier submission of efficacy and safety results) and *STAR* (Split Real Time Application Review, a 2023 pilot program designed to reduce FDA review times for efficacy supplements in respect of certain NDAs and BLAs).
- However, practice does not always match the ambition. For instance, Amtagvi's eventual approval in February 2024, under a Priority Review, followed a delay due to 'resource constraints' at the FDA. This is not an isolated case either, with six of the CDER's 55 novel drug approvals in 2023 having been subject to an FDA delay.
- Biotechs and pharmacos need to be better prepared, and better advised, if they want to avoid unexpected delays.

Approvals: Expedited pathways

Box 1: Overview of the FDA's expedited pathways

- **Priority Review:** designed in 1992 to reflect the FDA's goal to ***take action on an application within six months*** for drugs that treat ***serious conditions and, if approved, would provide a significant improvement*** in safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions
- **Accelerated Approval:** designed in 1992 to allow drugs for ***serious conditions that fulfil an unmet medical need*** to be brought to market on a faster timeline than traditional approaches
- **Fast Track:** designed in 1997 to facilitate the development, and expedite the review of, ***drugs to treat serious conditions and that fulfil unmet medical needs***
- **Breakthrough Therapy:** designed by US Congress in 2012 to expedite the development and review of drugs which may ***exhibit substantial improvement over other available therapies***. It includes all the Fast Track program features and offers intensive FDA guidance during drug development

Figure 9: CDER novel drug approvals - number of expedited pathways taken



Source: FDA.gov

Biotechs and pharmacos appear to hedge their bets, with applications across multiple expedited pathways

- A significant share of novel drug approvals use one or more of the expedited pathways. For example, 36 out of the 55 novel drugs approved by the CDER in 2023 i.e. 65% (see figure 9) used one or more pathways, with nine using as many as three (seven novel drugs) or four (two novel drugs) pathways.
- For novel drugs coming through on two pathways (21 in 2021, 11 in 2022 and 18 in 2023), a priority review in combination with either fast track or breakthrough therapy was the most common combination.
- There are no novel drugs approved in the period 2021 to 2023 under an accelerated approval only, and although accelerated approvals were up in 2023 (17 vs. 12 in 2022) there are concerns that future approvals via this route may reduce.

The FDA is looking to clamp down on biotechs and pharmacos who fail to undertake confirmatory studies

- Concerns regarding future accelerated approvals reflect new powers granted to the FDA in late 2022, following wide-spread evidence that many biotech and pharmacos were failing to complete confirmatory studies, despite these being an important approval condition.
- The new powers give the FDA the ability to impose a requirement for a confirmatory study to be well underway ahead of approval, for six-monthly progress updates to subsequently be issued to it, and for it to be able to withdrawal an approval where studies fall short.
- There are signs that the FDA is applying these powers, with it having recently (end of March) declined an accelerated approval for odronextamab (for blood cancer) due to concerns related to enrolments into confirmatory trials.
- Biotechs and pharmacos in response have complained that the FDA's requirements are too vague, lacking a clear definition of what "well underway" confirmatory trials are, and that this drives uncertainty.
- Regulatory affairs specialists are well placed to help manage this uncertainty on behalf of biotechs and pharmacos.

Approvals: Other routes

Without FDA verified therapeutic equivalence ('TE'), drugs approved via the 505(b)(2) route may face commercialisation challenges

- The majority of the FDA's work does not relate to novel drugs, but new formulations, indications, dosages, or routes of administration for existing products.
- For such small molecule products, the 505(b)(2) pathway offers a shorter and cheaper route to approval, allowing submissions to rely on existing data from a Reference Listed Drug ('RLD'), with no need for extensive and repetitive CTs.
- According to FDA data, there were 58 approvals via the 505(b)(2) pathway in 2023 (compared to 50 in 2021 and 59 in 2022). 2017 was the high-watermark over the nine-year period 2014-22, with 73 approvals.
- Products approved via a 505(b)(2) route are not automatically considered to be therapeutically equivalent to their RLD. Historically however, all products approved via this route were assigned the same average sales price as the RLD, notwithstanding TE. Since late 2022, this only happens where the FDA has verified TE.
- This poses a challenge for commercialising these products, as products without a TE determination from the FDA will be assigned a unique, potentially lower sales price. In the past the FDA has been very slow at getting around to completing TE determinations, and although measures have been introduced to speed this up (with a requirement to assess this within 180 days of approval) it is too early to say definitively what the impact has been on approval numbers.
- There therefore needs to be greater focus on, and certainty that pharmacos can demonstrate TE, if they are to avoid this issue.

Antibody-drug conjugates: Investor confidence

Investors appear to have high confidence in antibody-drug conjugates (ADCs), with significant investments in ADC assets over 2023

- Although ADCs promised a lot in terms of better targeted therapies, their development has not been without its issues (see box 2).
- Currently however, they are attracting significant interest, with recent research from IQVIA (*IQVIA Institute for Human Data Science. Global Trends in R&D 2024: Activity, Productivity, and Enablers. February 2024*), indicating that over 2023, there were six M&A deals related to ADCs, for a total deal value of c.$90bn.

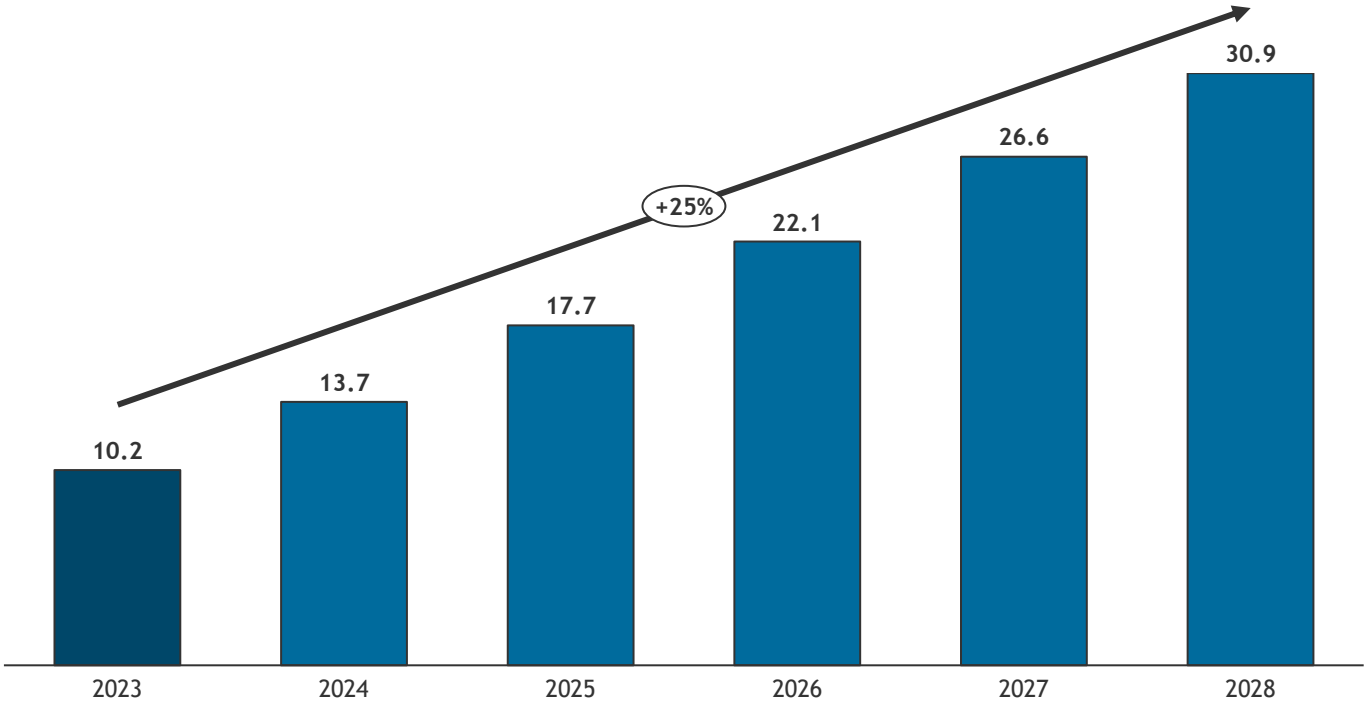
- This compared to a total 2023 deal size across all products of c.$200bn, comprising 31 deals (only disclosed deal values above $2bn were counted). ADCs therefore represented 19% of deal volume (6 out of 31) and 45% of deal value, a significant share. Key deals included Pfizer's acquisition of Seagen, a world-leader in ADC technology ($43bn deal size), and AbbVie's acquisition of ImmunoGen (completed 12 Feb-24), whose portfolio includes the first-in-class ADC, ELAHERE for ovarian cancer ($10.1bn deal size).
- The commercial success of Enhurtu (approved by the FDA in December 2019 for the treatment of breast cancer, with indication extensions in May 2022 and August 2022) has been touted as a key reason for resurgent interest in ADCs, as well as an overall increase in confidence in the technology, as more and more products have been granted approval.
- ADCs also appear to offer an investment opportunity that is well protected from competition, given longer exclusivity periods for biologics (than small molecules), the complexity of ADCs, and therefore, difficulty of manufacturing a biosimilar, as well as what is seen to be a complex and ill-defined regulatory pathway for biosimilar approvals.

Box 2: Overview of the development of ADCs

- **1990s to 2000s:** The first-generation of ADCs were developed. However, their linkers were found to be unstable in blood flow.
- Instability in the linker (leading to a premature release of the payload) was found to be the cause of a fatal adverse event in connection with the ADC Mylotarg, which was withdrawn in 2020, ten years after its original FDA approval. Mylotarg has subsequently been re-approved (September 2017) however, following changes in the dosing regimen to improve its safety profile.
- The payloads of the first-generation of ADCs were found to have weak concentrations, and together with linker instability issues, only a very small portion of the intended dose typically reached the target site (c.1-2%). Consequently, a number of CTs were discontinued.
- **2010s:** Second-generation ADCs (e.g. Adcetris (approved August 2011) and Kadcyla (approved February 2013)) improved upon all key ADC components i.e. monoclonal antibodies with a better coupling ability to small-molecule payloads, linkers with better plasma stability, and more effective cytotoxic drugs.
- **Current:** Third generation ADCs (e.g. Polivy (approved June 2019)), Padcev (approved December 2019) and Blenrep (approved August 2020)) saw the introduction of fully humanised antibodies, more potent payloads, and site-specific conjugation technology. As a result, unwanted immunogenicity and off-target toxicity has reduced (improved conjugation means that products are more homogenous, with a smaller drug-antibody ratio distribution).

Antibody-drug conjugates: Commercial potential

Figure 10: Forecast global ADC sales ($bn)



Source: Evaluate Pharma

Global ADCs sales are expected to show significant growth over the next five years

- There are now 16 approved ADCs on the global market, with world-wide sales of ADCs (including development candidates) of c.$10bn in 2023, rising to over $30bn by 2028 (see figure 10 (Evaluate Pharma estimates)).

Further development of ADCs may be required to realise their full commercial potential

- Notwithstanding the positive developments (and recent increased investor confidence in the technology), challenges remain. For example, Blenrep (for relapsed and refractory multiple myeloma), a third-generation ADC approved via an expedited FDA route, was withdrawn in November 2022 following the failure of a confirmatory trial designed to show outperformance against another product (we note that GSK have recently announced (7 March) positive results for Blenrep in combination with another drug, PomDex).
- Some of the remaining challenges for the technology include drug resistance, tumour heterogeneity and adverse events, with innovations such as dual-drug and bispecific (i.e. two antigen binding options) ADCs looking to address these issues, as well as better identification of suitable patient populations using biomarkers.

Cell & gene therapies: Approvals and pipeline

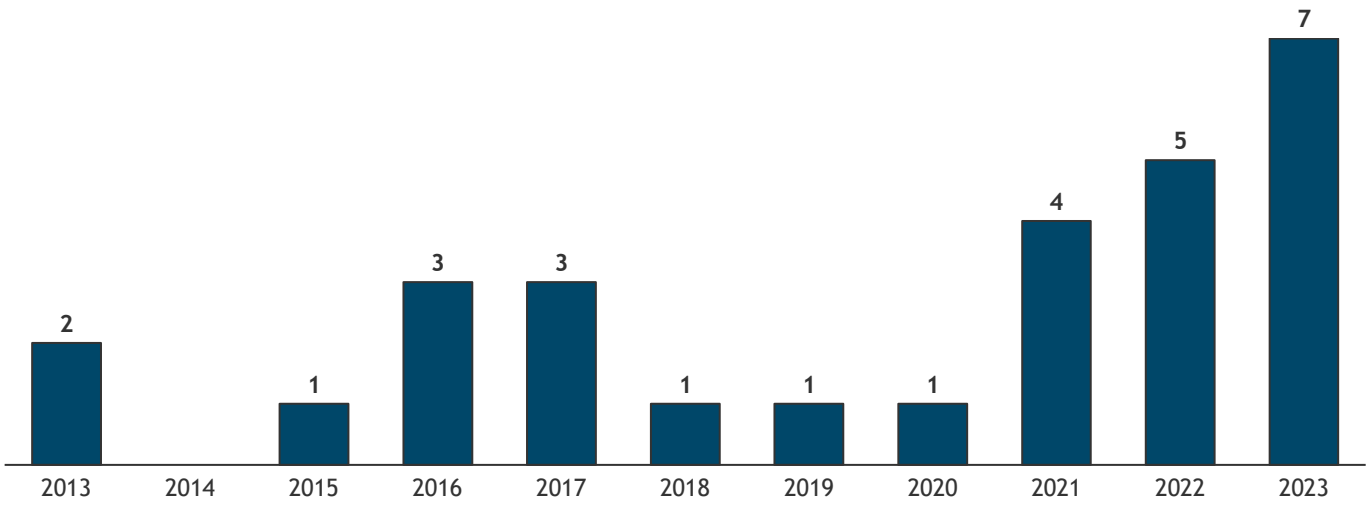
A record number of C&GTs were approved in 2023

- Gene therapies treat diseases by replacing, inactivating or introducing genes into cells to compensate for abnormal genes or make a beneficial protein.
- Cell therapies (which have a significant oncology focus) treat diseases by restoring or modifying cells or using them to deliver a therapy into the body.
- Cells are cultivated or altered outside of the body before being injected, grafted or implanted into the patient to treat disease. The cells may originate from the patient (autologous cells) or a donor (allogeneic).
- There are now 36 C&GTs that have been approved by the FDA, with seven approvals in 2023, a record (see figure 11).
- 2023 approvals included CASGEVY, the first CRISPR-Cas9-edited gene therapy, and Lyfgenia, a lentiviral vector gene therapy, both of which are new treatments for sickle cell disease.
- C&GT approvals have been gaining momentum, with the seven approvals in 2023 following five in 2022, four in 2021, and one in each of the years 2018 to 2020. Already in 2024, two new C&GTs have been approved, including Amtagvi, the first treatment for cancer (melanoma) that uses tumour-infiltrating lymphocytes, and Lenmedly, which uses stem cells to treat metachromatic leukodystrophy.

There is a healthy pipeline of C&GTs in pre and clinical development, that will feed into further approvals in the future

- Many more C&GTs are expected to gain approval in the future with commercial C&GT trials of c.0.9k in 2023 - more than doubling over the last ten years (c.0.5k CTs started in 2013) (see figure 12).
- There are also a significant number of C&GTs in pre-clinical development (c.2.2k gene therapies and c.2.1k cell therapies, with c.1.2k of these classified as both).
- Most gene therapies in development (pre-clinical and clinical) utilise viruses as vectors for performing gene insertions, with adeno-associated viral vectors dominant, followed by lentiviral vectors and adenoviral vectors. The majority of gene therapies focus on inherited diseases.
- Most cell therapies in development use T cells, followed by stem cells. However, there are a wide variety of different cell types being investigated e.g. blood, bone marrow, skin, tumour, connective tissue etc.
- High numbers of C&GTs in pre-clinical development, clinical development, and being approval, feed into higher sales forecasts, with sales from C&GTs expected to increase from $6.5bn in 2023, to $38.8bn by 2028 (see figure 13) i.e. growing at a CAGR of +43%.

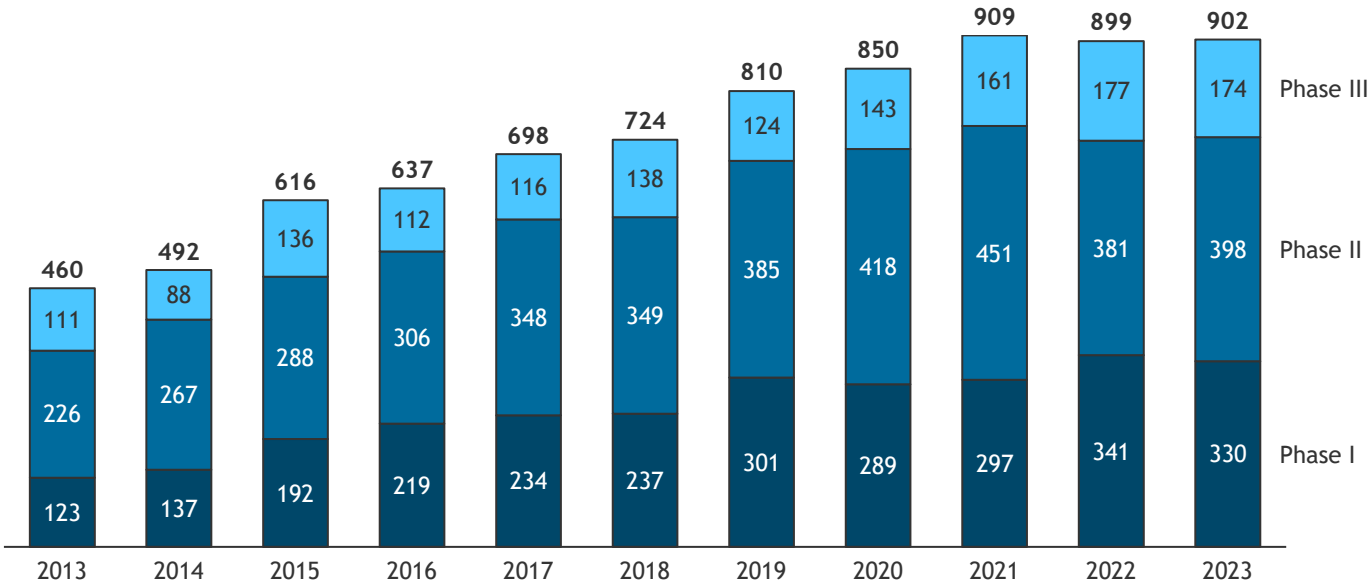
Figure 11: FDA C&GT product approvals



Source: FDA.gov

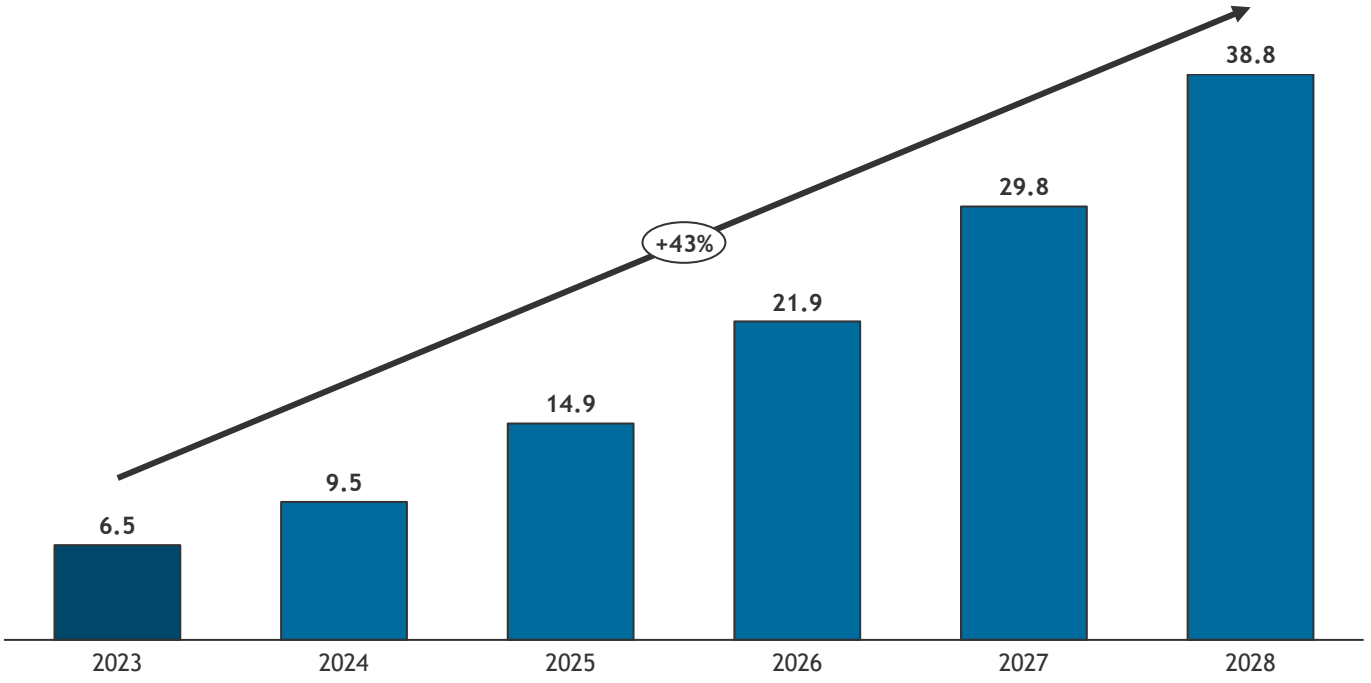
Cell & gene therapies: Approvals and pipeline

Figure 12: C&GT CTs by phase



Source: Evaluate Pharma

Figure 13: Forecast global C&GT sales ($bn)



Source: Evaluate Pharma

Cell & gene therapies: Commercialisation

Commercialising C&GTs remains challenging

- Although forecast sales for C&GTs suggest rapid growth over the next five years, they face a number challenges to their commercialisation, including:
  - Single dosing: although single dosing reduces side-effects from repetitive administration, typical C&GT treatments are highly personalised (e.g. based on an individual patient's own cells) increasing costs
  - Safety and efficacy: long-term safety and efficacy data for C&GTs is limited, and therefore, they carry more uncertainty and financial risk for payers
  - Just-in-time dosages: cellular products require cold-chain logistics for transfers between the laboratory and treatment sites, which increases distribution costs
  - Small patient populations: most current C&GTs only treat conditions with relatively small patient populations, and consequently, costs (including manufacturing) are relatively high
  - Non-recurrence: assuming long-term efficacy, once a patient has been treated there is no follow-up re-treatment, and as C&GTs are focused on oncology, an NCD, the prospective patient population will reduce overtime, limiting population-wide demand

High C&GT treatment costs require innovative thinking to address payers' concerns

- The cost of a one-off treatment of CASGEVY in the UK is estimated to be around £1m per patient, with an estimated list price in the US of around $2.2m.
- Lyfgenia, another recently approved C&GT (December 2023) that uses lentiviral vectors and is indicated for sickle cell disease, also has a very high estimated cost, at around $3m.
- Costs at these levels present a real challenge for payers and bodies such as the Institute for Clinical and Economic Review ('ICER') in the US, and the National Institute for Health and Care Excellence ('NICE') in the UK, who both assess the expected value-for-money from new health technologies.
- The ICER, which US healthcare insurers use as a reference when deciding whether or not to cover certain drugs, have suggested that CASGEVY and Lyfgenia need to be in the price range $1.4m to $2.1m. Both therapies fall outside of this range.
- NICE, who evaluate new health technologies for NHS use, have just released draft guidance (March 2024), indicating that it does not yet recommend the use of CASGEVY. It has asked for further data from its developer, Vertex, citing concerns with both the clinical and economic evidence provided. In particular, NICE refer to uncertain efficacy given a lack of testing against a reference drug, there having been only a small clinical study, and a lack of clarity on the long-term impacts of using the drug.
- New innovative payment methods for C&GTs, allowing costs to be spread overtime, and potentially linked to clinical outcomes, may be the solution. In the UK for example, the NHS recently committed to look at the options for introducing new C&GT drugs, committing to conduct two pilot studies into outcomes-based pricing as a part of the 2024 Voluntary Scheme for Branded Medicines Pricing, Access, and Growth ('VPAG'), published in November 2023.
- Given all the above, there is likely to be significant demand from C&GT asset owners for market access specialists who can help overcome payer concerns, and those that can bring innovative thinking to payment solutions, will be in the greatest demand.

Strategic partnerships with pharmacos help C&GT biotechs with commercialisation

- Even where payers' concerns can be addressed, complex manufacturing processes, a lack of manufacturing scale, limited capacity in hospitals/ treatment centres, and irregular patient pathways may prove challenging.
- Licensing deals between C&GT biotechs and large pharmacos, who have greater resources and commercialisation expertise, are a potential solution for some of these challenges.
- Although data from Evaluate indicates that the total value of C&GT licencing deals fell in 2023 compared to 2022, there has been an upward trend in its share of all licensing deals over the last 5 years (period 2018 to 2023), from c.12% by number (2018) to c.16% by number (2023).
- This indicates that licencing is an important strategic option for this technology.

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1. At constant exchange rate

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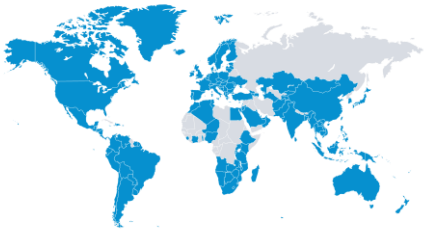

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