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CGT Landscape: Recent Approvals, Deals And 2024 Catalysts

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The last quarter of 2023 was an exciting one for the cell and gene therapy sector – with the first-ever approval for a CRISPR-based therapeutic in the US and an increase in Phase III trials in the overall CGT pipeline.

In the fourth quarter of 2023, Casgevy (exagamglogene autotemcel) – a CRISPR-based therapeutic developed by *Vertex Pharmaceuticals Incorporated* and *CRISPR Therapeutics AG* – was approved by the US Food and Drug Administration for sickle cell disease and in the UK for both sickle cell disease and transfusion-dependent β-thalassemia (TDT). In January 2024, the FDA followed the sickle cell approval with a green light for Casgevy in TDT as well. The TDT endorsement arrived more than two months early as a regulatory decision had been slated for 30 March.

The first thumbs-up stateside for Casgevy came on the same day (8 December, 2023) that the FDA also approved bluebird bio's gene therapy Lyfgenia (lovotibeglogene autotemcel) for sickle cell disease. Casgevy has unsurprisingly garnered the most interest as its approval signifies a new era for genetic medicine. (Also see "*Vertex/CRISPR Nab First-Ever Gene Editing FDA Nod, Overshadow Bluebird's Same-Day Win*" - Scrip, 9 Dec, 2023.)

Commenting on the UK approval for Casgevy, Jennifer Doudna, who alongside Emmanuelle Charpentier was the recipient of the 2020 Nobel Prize in Chemistry for the discovery of using CRISPR Cas9 for gene editing, wrote on X (formerly Twitter) that she was "a bit overwhelmed with emotion at the news [and] going from the lab to an approved CRISPR therapy in just 11 years is a truly remarkable achievement."

At the 2024 J.P. Morgan Healthcare Conference in January, Vertex CEO Reshma Kewalramani said Casgevy, which comes with a price tag of $2.2m in the US, represents a multibillion-dollar market opportunity. She told investors the company had hit the ground running, claiming that "physicians prefer gene editing therapy to gene therapy."

While Casgevy is expected to be a blockbuster, Evaluate Pharma's consensus forecasts suggest Lyfgenia could reach just $355m in revenues by 2028 – a fairly modest return, especially given the high overheads that come with manufacturing and administering the therapy in specialized treatment centers.

There were a number of CGT approvals in 2023 (see *Exhibit 1*). While some cell and gene therapies are forecast to be $1bn-plus earners, many others are expected to have more modest revenues. (Also see "*The 'Haves And Have-Nots' Are Becoming Clearer In Cell And Gene Therapy*" - Scrip, 16 Jan, 2024.)

Exhibit 1.

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Subtle Pipeline Shifts

According to data from Citeline and the American Society of Gene and Cell Therapy (ASGCT), for the first time since Q3 2022 (*see Exhibit 2*), the number of gene therapies (gene therapy and genetically modified cell therapies) in Phase III increased from the previous quarter, growing by 10% in Q4 2023.

Exhibit 2.

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Oncology and rare diseases remained the top areas of gene therapy development in both the overall pipeline (preclinical to pre-registration) and in the clinic (Phase I to pre-registration; *see Exhibit 3*). For the 1,038 pipeline gene therapies being developed for rare diseases, eight out of the top 10 rare diseases were oncological, a trend seen throughout 2022 and 2023. Citeline and ASGCT's Q4 analysis showed that development in acute myelogenous leukemia overtook development in non-Hodgkin's lymphoma for the first time in the past nine quarters.

The top five rare diseases for which gene therapies are being developed are:

1. Myeloma
2. Acute myelogenous leukemia
3. Non-Hodgkin's lymphoma
4. B-cell lymphoma

5. Ovarian cancer

Exhibit 3.

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The proportion of gene therapy trials for non-oncology indications has increased by 1% since the previous quarter, to 39%, continuing the trend of an increasing proportion of non-oncology gene therapy trials initiating each quarter since Q4 2022. 56 gene therapy trials were initiated in Q4 2023.

CGT Deal-Making

10 acquisitions of advanced molecular therapy companies occurred in Q4 2023, up from Q3 2023's nine deals. The biggest acquisition, announced just before the quarter's end, featured *AstraZeneca PLC* acquiring autologous and allogeneic cell developer *Gracell Biotechnologies Inc.* for $1.2bn.

M&A activity also included two reverse mergers — NAYA Biosciences with *INVO Bioscience, Inc.*, and *Selecta Biosciences, Inc.* with *Cartesian Therapeutics, Inc.* — and three acquisitions of CDMOs: Applied StemCell, Forge Biologics, and ABL Europe.

Exhibit 4.

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More To Come

Looking ahead in 2024, there are a number of expected critical events in the CGT pipeline.

Exhibit 5.

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