LIFE SCIENCES

CELL & GENE THERAPY

INVESTING IN A NEW TOMORROW?

APRIL 2021
## CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOREWORD</td>
<td>3</td>
</tr>
<tr>
<td>WHAT ARE CELL AND GENE THERAPIES AND HOW ARE THEY DIFFERENT?</td>
<td>4</td>
</tr>
<tr>
<td>THE CELL AND GENE THERAPY MARKET</td>
<td>5</td>
</tr>
<tr>
<td>REGULATORY LANDSCAPE</td>
<td>7</td>
</tr>
<tr>
<td>KEY PLAYERS AND CLINICAL TRIALS</td>
<td></td>
</tr>
<tr>
<td>▶ Gene therapy</td>
<td>9</td>
</tr>
<tr>
<td>▶ Cell therapy</td>
<td>11</td>
</tr>
<tr>
<td>THE FUTURE</td>
<td>13</td>
</tr>
<tr>
<td>ABOUT BDO</td>
<td>14</td>
</tr>
</tbody>
</table>
Anand has a Masters in Chemical Engineering from Cambridge University, and over 8 years’ experience in Healthcare and Life sciences. He has specialist skills in portfolio strategy, product development, forecasting and launch strategy for pharma and biotech companies.

Ashley is an Executive in BDO’s Life Sciences team. She holds a Masters degree in both Biology and Chemistry. Prior to BDO, she worked in research for alternative cancer therapy, and in industry in the health & personal care sector.

Dodi is an Assistant Manager in BDO’s London Corporate Finance team. He is a former pharmacist having graduated with a Masters in Pharmacy from the University of Nottingham.

Gurpal is a former surgeon. He has been published and is a reviewer of a well known journal. He has over 15 years’ experience in Healthcare and Life Sciences covering growth strategy, operational strategy and commercial due diligence.

Cell and gene therapies are widely considered to be the future of treating several, often life-threatening conditions, and are hence a growing area for pharma and biotech companies alike. In this paper we take a look at the landscape for cell and gene therapies, highlighting some of the key assets in the field.

Cell and gene therapies are emerging technologies and form the cornerstone of “next-generation” therapies. There are currently a handful of approved treatments on the market (e.g. Yescarta, Kymriah, Zolgensma and Imlygic), but several hundred in the development pipeline.

As shown in this report, cell and gene therapies are exciting technologies, with rapid market revenue growth of 64% p.a. forecast between 2020-26. A large proportion of the therapies in clinical trials are being developed by small to mid-size biotechs, providing plenty of opportunities in this space for M&A, product licensing deals and investment.

We have worked with businesses at every stage of the business life-cycle and understand the challenges and opportunities they face. We also have a particular interest in next-generation therapies, backed up by experience and knowledge in the space within the team.

We have drawn on publicly available sources, as well as conversations with industry leaders and key opinion leaders, to produce this report.

This paper also includes a section on the regulatory pathway for the development of cell and gene therapies, written by Scendea. We would especially like to thank the Scendea team for their contribution and insights in this report.

Scendea is a leading product development and regulatory consulting practice serving the pharmaceutical and biotechnology industry. They are committed problem solvers, redefining the meaning of customer service, with a focus on reducing time-to-market and minimising development costs.

Dr Gavin Edwards is a business leader with expertise in regulatory affairs and medicinal product development. Dr Edwards’ expertise includes pre-licensing services relating to biotechnology-derived products. Dr Edwards is a Director of Scendea.

Dr Richard Turner is a Principal Consultant & Director at Scendea, and has been working in biopharmaceutical development for over 30 years. A former Pharmaceutical Assessor at the UK MHRA he is a recognised expert in regulation and development of biotechnology products.

Dr Rehma Chandaria is a Consultant at Scendea with experience of US and EU regulatory affairs and drug development. Rehma has previously worked as a scientist in the biotechnology industry, and has a PhD in tissue engineering.

This paper also includes a section on the regulatory pathway for the development of cell and gene therapies, written by Scendea. We would especially like to thank the Scendea team for their contribution and insights in this report.

Scendea is a leading product development and regulatory consulting practice serving the pharmaceutical and biotechnology industry. They are committed problem solvers, redefining the meaning of customer service, with a focus on reducing time-to-market and minimising development costs.
WHAT ARE CELL AND GENE THERAPIES AND HOW ARE THEY DIFFERENT?

Cell and gene therapies are some of the most revolutionary advances in treatment in recent years, potentially leading to the next paradigm shift in therapies. Although initial drug approvals have been for relatively small patient groups and rare diseases, the significant pipeline of cell and gene therapy studies currently underway will significantly expand the impact of these treatments, and unleash their genuine, unprecedented potential.

INTRODUCTION

Cells are the smallest structural units of living organisms. They differ in size, shape or function, depending on their role in different tissues and organs. Some are highly specialised or differentiated for specific tasks. For example, red blood cells are specialised to carry oxygen, whilst nerve cells are specialised to transmit electrical signals.

Genes are small segments of DNA within cells which encode a gene function, such as the synthesis of a protein. These gene products are used to help the cell carry out its vital activities, for example, some proteins act as chemical messengers in signalling pathways.

Disruptions to the DNA sequence of genes can lead to a loss or change in a cell’s ability to carry out its role in the body. This often leads to widespread changes that manifest as disease, such as genetic disorders and cancers.

Cell and gene therapy are different, yet intersecting fields of biomedical research which aim to treat the disease at its cause through restoration or exploitation of genetic or cellular functions.

HOW DO GENE THERAPIES WORK?

Gene therapy aims to treat diseases by replacing, inactivating or introducing genes into cells in order to compensate for abnormal genes or make a beneficial protein. Most approved approaches utilise viruses as vectors for performing gene insertions, although the introduction of clustered regularly interspaced short palindromic repeats (CRISPR) gene editing technology has opened new doors for its application in gene therapy.

HOW DO CELL THERAPIES WORK?

Cell therapy aims to treat disease by restoring or modifying cells or using them to deliver therapy in the body. Cells are cultivated or altered outside of the body before being injected, grafted or implanted into the patient to treat disease. For example, transplanting of immune cells modified to fight cancer cells, or grafting on stem cells to regenerate a diseased cornea in the eyes. The cells may originate from the patient (autologous cells) or a donor (allogeneic cells).

WHERE ARE WE NOW?

- Globally, the first cell therapy was approved in 1997 (TranCyte), and the first gene therapy was approved in China in 2003 (Gendicine)
- In Europe, the first cell therapy was approved in 2009, and the first gene therapy was approved in 2012

The milestones credited not only the years of research and scientific advancements that had been made to achieve viable treatment, but also the willingness of regulators to accept the advancement of cell and gene based therapy. Past success has now paved the way for further approvals, continued research and an explosion of clinical trials:

- Could potentially treat a vast range of medical conditions
- Potentially curative treatment of complex genetic diseases
- One-time therapy minimizes side-effects due to repetitive administration
- Minimal risk of autoimmunity or Graft-versus-Host Disease (GvHD)
- Cost effective in comparison to annual treatments taken over the span of a lifetime.

Note: *As of January 2021
Source: Novartis, Nature, clinicaltrials.gov, ema.europa.eu, research & analysis
THE CELL & GENE THERAPY MARKET

The cell and gene therapy market is forecast to grow at an impressive CAGR 64% to reach $45.3Bn by 2026. Growth is driven by a number of factors including increasing investment into next-generation therapies, experimental therapies moving through clinical trials as well as from regulatory bodies such as the FDA to support approvals and aid transition of therapies to commercial stage products.

MARKET DYNAMICS

1/3 OF BIOPHARMA’S PIPELINE IN PRECISION MEDICINE

- Precision medicine means ensuring delivery of the right intervention to the right patient at the right time
- The cost and health risk associated with traditional, trial-and-error or ‘one size fits all’ medicine makes precision medicine imperative for targeted therapy
- Recent scientific and technological advances have helped reduce development times for personalised treatment making it more available and accessible
- The drug development industry is moving rapidly towards precision medicine and leading pharma companies are expecting to increase investment in the area by an additional 1/3 over the next few years.

10-20 NEW PRODUCT APPROVALS EACH YEAR*

- The US Food and Drug Agency (FDA) stated in 2019 that it was preparing for a coming wave of experimental cell and gene therapies
- This year, the FDA are expecting more than 200 applications requesting permission to begin cell and gene therapy trials and subsequently expect to hire ~50 additional clinical reviewers to handle the surge
- The successful approvals of cell therapies Kymriah (Novartis), Yescarta (Gilead) and gene therapy Luxturna (Novartis) marked a transition for the field from experimental to commercial.

IMPRESSIVE GROWTH FORECAST OVER NEXT FEW YEARS

- The global cell and gene therapy market generated ~$2.3 billion in 2020 and is predicted to grow at a CAGR rate of 64.0% during the forecast period 2020-2026.

ESTIMATED CELL & GENE THERAPY GLOBAL MARKET SIZE REVENUE ($BN)

Note: **FDA Commissioner Scott Gottlieb prediction to 2025
Source: BIS research, Evaluate Pharma, Cell&Gene, BDO interviews, research & analysis
Global market leaders
- Planned R&D cycles and large budgets
- Large and diversified portfolios covering multiple therapy areas
- More than 10,000 employees and revenues over £10 billion.

Lean, nimble and take on more R&D risk
- Sector specialist portfolios with focussed pipeline in specific therapy area/technology
- Typically less than 10,000 employees and under £10 billion revenue.

Focus on scientific challenges, fundamental and early stage research
- Generally funded through government, public funding or industry partnerships
- Activities often in a specific therapy area/technology.

Typically dedicated to a specific therapy area, medical need or patient group
- Focussed on delivery of care
- Generally funded through government, public funding or industry partnerships.

The future of these therapies is driven by improvement and refinement of the underpinning technologies and cellular mechanisms, such as improvements in the safety of gene editing tools, fine-tuning of regulating mechanisms designed into cells, or the use of cells to deliver drugs in a controlled and targeted way.

Increased automation to accelerate the production process and eliminate human error and variability in batches, and use of artificial intelligence in the field is also expected to aid future cell and gene clinical development. Powerful new technologies will aid analysis of correlated studies, product and process development, and could be considered for determining which patients may be more likely to benefit from which advanced therapy.

Innovations to closed, automated manufacturing systems will also aid in reducing cost of production for what are highly personalised therapies and assist in the re-imagining of cold chain logistical models. Both will help widen access to treatment to a greater numbers of patients in future.

The implications of emerging technologies and the requirements for adoption means we will likely continue to see regulations and policies be revised and adapted to allow the advancement of cell and gene therapy. The requirement for payment and reimbursement schemes for treatments seen as ‘one-time’ will also revolutionise traditional healthcare provision in multi-payer countries such as the US.

Source: Clinicaltrials.gov, Cell&Gene, Chemical & Engineering News, BDO interviews, research & analysis
There are numerous regulatory milestones in Europe and the US that a company developing an ATMP may target. Many of these can accelerate and streamline the development process, and help get the product on the market sooner, whereas others provide incentives such as reduced Agency fees and market exclusivity after the product is approved.

**INTRODUCTION**

Before a cell and gene therapy (CGT) product can be approved for use, a company must show that it is safe and effective in the target disease. This is done by first testing the medicine in animals or ‘test-tube’ experiments (pre-clinical studies), and then in humans in clinical trials.

Once the company has data to prove that the product is safe and works in the disease, they must apply to regulatory agencies to obtain approval to market the medicine. In the US, the regulatory agency is the FDA. Cell and gene therapies are regulated under section 351 of the Public Health Service (PHS) Act, and the Center for Biologics Evaluation and Research (CBER) is the center within FDA which is responsible for regulating cell and gene therapies. In Europe, Regulation (EC) 1394/2007 provides the overall legal framework for advanced therapy medicinal products (ATMPs), comprising cell therapies, gene therapies and tissue engineered products. The Committee for Advanced Therapies (CAT), part of the EMA provides the expertise required to evaluate ATMPs and plays a central role in their scientific assessment and authorization.

In 2009 the EMA recommended ChondroCelect, the first ATMP, for approval in the European Union for the repair of cartilage defects in the knee. In the US, the first approved ATMP came a year later with Provenge, a cell therapy for the treatment of some prostate cancers. In total, there are currently 9 cell and gene therapy products licensed in both regions.

**INTERACTING WITH REGULATORY AGENCIES**

During the pre-clinical stage of development, there are several methods of interacting with FDA and EMA.

In the US, FDA offer Initial Targeted Engagement for Regulatory Advice on CBER products (INTERACT) meetings to Sponsors of CGT products. The programme allows companies to meet with the agency before any major commitments are made for early stage activities.

In the EU, the EMA’s Innovation Task Force (ITF) briefing meetings provide an informal forum allowing companies to interact with the Agency at an early stage in development to discuss regulatory, technical and scientific issues arising from the development of innovative medicines such as CGT products. ITF briefing meetings sit alongside more formal procedure such as ATMP Classification, whereby companies can consult EMA to receive confirmation that the product meets scientific criteria for defining an ATMP. EMA also provides an ATMP Certification procedure for products being developed by micro-, small- and medium-sized enterprises (SMEs). This allows companies to receive scientific evaluation of the available quality and non-clinical data at any stage in a product’s development in order to identify any potential issues early on.

**CLINICAL TRIALS**

In order to study a medicinal product in human clinical trials, companies are required to submit a Clinical Trial Application (CTA) in Europe, or an Investigation New Drug (IND) application in the US. Although the processes in the different regions vary, the primary aim of the application is to show that there is enough evidence to proceed with testing the product in humans.

*The CAR-TCR drug development field has achieved huge success over the past year with regulatory approvals in the U.S., Europe, Japan and Australia proving the potential these drugs have to successfully cure patients around the globe.*
In order to accelerate patient access to medicinal products intended to treat serious unmet medical needs, EMA and FDA offer expedited procedures for marketing authorisations (MA). In Europe, a MA with Exceptional Circumstances may be granted subject with specific obligations if the applicant can demonstrate it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use. Further, a Conditional MA can be granted on the basis of early clinical trial data. Ongoing or additional clinical studies must then be conducted to demonstrate the product’s benefits and the MA must be renewed annually. Similarly, in the US, FDA may offer Accelerated Approval based on demonstration of an effect on a surrogate or intermediate clinical endpoint, where further studies are needed to show an effect on a relevant clinical outcome. After gaining an accelerated approval, additional clinical trials are required to confirm clinical benefit. If the results confirm clinical benefit, the drug is converted from accelerated approval to “regular” approval.

If a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation, applicants can request Accelerated Assessment of the MAA in the EU, so that it is assessed in 150 days instead of the normal 210 days. Similarly, in the US, Priority Review designation can be awarded so that FDA reviews the licence application in 6 months instead of the normal 10 months.

---

**DEVELOPMENT TIMELINE**

<table>
<thead>
<tr>
<th>PRE-CLINICAL</th>
<th>CLINICAL TRIALS IN HUMANS</th>
<th>LICENCING</th>
</tr>
</thead>
<tbody>
<tr>
<td>NON-HUMAN / IN VITRO</td>
<td>PHASE I</td>
<td>PHASE II</td>
</tr>
</tbody>
</table>

**KEY REGULATORY DESIGNATIONS**

Following proof of principle as a consequence of early-stage nonclinical and clinical studies, a number of incentive schemes exist, that companies developing ATMPs for serious conditions with an unmet medical need may apply for. The Priority Medicines (PRIME) scheme is available in Europe, and Fast Track Designation (FTD), Breakthrough Designation (BTD) and Regenerative Medicine Advanced Therapy (RMAT) designations are offered in the US. These designations provide companies with opportunities for increased interactions with the Agencies in order to discuss data requirements at an early stage and help to expedite development of promising products.

For companies developing products for rare indications, Orphan Drug Designation (ODD) is another consideration in both jurisdictions. ODD provides financial benefits in terms of EMA fee reductions during development, and market exclusivity post licensing. Furthermore, in the US, Rare Paediatric Designation (RPD) is a consideration for Sponsors developing therapies for serious or life-threatening rare diseases that primarily affect children. When a product with RPD is approved, the Sponsor can apply for a ‘Priority Review Voucher’ (PRV), which can be redeemed for a marketing application for a different product, providing the FDA accepts use of the voucher on the chosen drug. The voucher may be sold or transferred, and there is no limit on the number of times it can be transferred. As an example, BioMarin’s voucher, the first ever to be sold, was purchased for USD 67 million.

**LICENSING**

In order to accelerate patient access to medicinal products intended to treat serious unmet medical needs, EMA and FDA offer expedited procedures for marketing authorisations (MA). In Europe, a MA with Exceptional Circumstances may be granted subject with specific obligations if the applicant can demonstrate it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use. Further, a Conditional MA can be granted on the basis of early clinical trial data. Ongoing or additional clinical studies must then be conducted to demonstrate the product’s benefits and the MA must be renewed annually. Similarly, in the US, FDA may offer Accelerated Approval based on demonstration of an effect on a surrogate or intermediate clinical endpoint, where further studies are needed to show an effect on a relevant clinical outcome. After gaining an accelerated approval, additional clinical trials are required to confirm clinical benefit. If the results confirm clinical benefit, the drug is converted from accelerated approval to “regular” approval.

If a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation, applicants can request Accelerated Assessment of the MAA in the EU, so that it is assessed in 150 days instead of the normal 210 days. Similarly, in the US, Priority Review designation can be awarded so that FDA reviews the licence application in 6 months instead of the normal 10 months.
Much of the innovation and development in the space is being driven by smaller biotech companies or research universities, sometimes in partnership with big pharma or an entity specialised in the targeted therapy. As the technology matures, large pharma companies are expected to shift focus towards owning the technology versus partnering, as demonstrated by recent large acquisitions. The majority of assets under trials target cancers, sensory organs and blood disease as well as rare, genetic conditions across multiple therapy areas. A high number of trials are currently at Phase II, where safety and efficacy is assessed.

### Analysis of Key Players & Clinical Trials

#### Key Players

- Orchard Therapeutics
- Helixmith
- Spark Therapeutics
- Gensight Biologics
- Sibiono
- AveXis (Now Novartis Gene Therapies)
- Bluebird Bio

#### Clinical Trials

<table>
<thead>
<tr>
<th>Therapy Area</th>
<th>Key Assets Under Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>600</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>500</td>
</tr>
<tr>
<td>Neurology</td>
<td>400</td>
</tr>
<tr>
<td>Ophthalmological</td>
<td>300</td>
</tr>
<tr>
<td>Osteoarticular</td>
<td>200</td>
</tr>
<tr>
<td>Infections</td>
<td>100</td>
</tr>
<tr>
<td>Blood</td>
<td>100</td>
</tr>
<tr>
<td>Skin</td>
<td>100</td>
</tr>
<tr>
<td>Immunology</td>
<td>100</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>100</td>
</tr>
<tr>
<td>Other</td>
<td>100</td>
</tr>
</tbody>
</table>

#### Split by Therapy Area

- Oncology: 600
- Psychiatry: 500
- Neurology: 400
- Ophthalmological: 300
- Osteoarticular: 200
- Infections: 100
- Blood: 100
- Skin: 100
- Immunology: 100
- Cardiovascular: 100
- Other: 100

#### Split by Phase

- Phase I: 600
- Phase II: 500
- Phase III: 400
- Phase IV: 300

---

Note: Source: Evaluate, ClinicalTrials.Gov, BDO interviews, research & analysis
### TOP 5 GENE THERAPY PIPELINE ASSETS BY FORECAST REVENUE 2021-26

<table>
<thead>
<tr>
<th>COMPANY</th>
<th>PRODUCT</th>
<th>INDICATION</th>
<th>PHASE</th>
<th>FORECAST SALES (SM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2021</td>
<td>2022</td>
</tr>
<tr>
<td>Sarepta</td>
<td>SRP-9001</td>
<td>Duchenne muscular dystrophy</td>
<td>Phase III</td>
<td>12</td>
</tr>
<tr>
<td>CRISPR Therapeutics</td>
<td>CTX001</td>
<td>Thalassaemia &amp; Sickle cell disease</td>
<td>Phase II</td>
<td>-</td>
</tr>
<tr>
<td>Biomarin</td>
<td>Valoctocogene Roxaparvovec</td>
<td>Haemophilia A</td>
<td>Filed</td>
<td>3</td>
</tr>
<tr>
<td>Homology</td>
<td>HMI-102</td>
<td>Phenylketonuria (PKU)</td>
<td>Phase II</td>
<td>-</td>
</tr>
<tr>
<td>Rocket Pharma</td>
<td>RP-A501</td>
<td>Danon Disease</td>
<td>Phase I</td>
<td>-</td>
</tr>
</tbody>
</table>

### TOP 5 GENE THERAPY ASSETS RATED MARKET LEADERS

<table>
<thead>
<tr>
<th>DEVELOPER</th>
<th>ACQUIRER / LICENCEE</th>
<th>PRODUCT</th>
<th>INDICATION</th>
<th>PHASE</th>
<th>IMPORTANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarepta</td>
<td>Roche</td>
<td>SRP-9001</td>
<td>Duchenne muscular dystrophy</td>
<td>Phase III</td>
<td>Forecast to become a blockbuster therapy upon successful launch, with sales of $2.3b in 2026</td>
</tr>
<tr>
<td>AveXis (Now Novartis Gene Therapies)</td>
<td>Novartis</td>
<td>Zolgensma</td>
<td>Spinal Muscular Atrophy</td>
<td>Approved</td>
<td>Only one-time, curative treatment approved for SMA, which is the leading genetic cause of infant mortality</td>
</tr>
<tr>
<td>Biomarin</td>
<td>N/A</td>
<td>Valoctocogene Roxaparvovec</td>
<td>Haemophilia A</td>
<td>Filed</td>
<td>Potential to be first approved gene therapy in the haemophilia A space and received accelerated assessment and Orphan Drug designation</td>
</tr>
<tr>
<td>FKD</td>
<td>Ferring</td>
<td>Adstiladrin</td>
<td>Bladder Cancer</td>
<td>Filed</td>
<td>Set to be the next approved gene therapy Adstiladrin eliminates the need for the complete removal of the bladder in aggressive forms of bladder cancer</td>
</tr>
<tr>
<td>Bluebird Bio</td>
<td>N/A</td>
<td>Zyntelgo</td>
<td>Beta thalassamia</td>
<td>EMA Approved</td>
<td>Eliminates need for lifelong blood transfusions and provides a solution for patients who do not have matching donors for stem cell transplantation - the therapy is also accessible through an outcome-based payment agreement</td>
</tr>
</tbody>
</table>

### EVALUATING COMMERCIAL ADVANTAGES

Gene therapies that will become market leaders will be those that can provide a cure to debilitating diseases, which can otherwise only be managed with current available treatments and therefore require life-long supportive care and administration of drugs. Because of their potential to provide a cure and their convenience as an one-time intervention, gene therapies can have great commercial advantages.

*Source: Evaluate, fda.gov*
KEY PLAYERS & CLINICAL TRIALS
Cell therapy

The therapeutic action underlying cell therapy makes it attractive for treatment of cancers and for use in immunotherapy. As such, a high number of assets are being developed in these areas as well as for the central nervous and cardiovascular systems. The high potential number of patients that could be treated by these therapies has gained interest from the healthcare sector, Government and public bodies alike with many acting as key stakeholders in the R&D and leaders on clinical trials for pharma held assets. Many cell therapies are at early and pre-clinical phases, as recent scientific advances generate a wave of new experimental treatments entering trials.

ANALYSIS OF LEAD SPONSORS IN CELL THERAPY CLINICAL TRIALS

<table>
<thead>
<tr>
<th>SMALL/MEDIUM PHARMA &amp; BIOTECH</th>
<th>UNIVERSITIES &amp; RESEARCH INSTITUTES</th>
<th>HOSPITALS, GOVERNMENT &amp; PUBLIC BODIES</th>
<th>BIG PHARMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRIAL ACTIVITY</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28%</td>
<td>29%</td>
<td>37%</td>
<td>1%</td>
</tr>
<tr>
<td>EXAMPLES OF KEY PLAYERS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allife Medicine</td>
<td>University of Pennsylvania</td>
<td>CHU</td>
<td>Novartis</td>
</tr>
<tr>
<td>Juno Therapeutics (Acquired by Celgene)</td>
<td>UCLA</td>
<td>City of Hope</td>
<td>GSK</td>
</tr>
<tr>
<td>Celgene (Acquired by Bristol Myers Squibb)</td>
<td>Baylor College of Medicine</td>
<td>Mayo clinic</td>
<td>Bristol Myers Squibb</td>
</tr>
<tr>
<td>Hrain Biotechnology</td>
<td>Icahn School of Medicine Mount Sinai</td>
<td>Memorial Sloan Kettering Cancer Centre</td>
<td>Gilead</td>
</tr>
<tr>
<td>Centogene</td>
<td></td>
<td>CHU</td>
<td></td>
</tr>
</tbody>
</table>

SPLIT BY THERAPY AREA

<table>
<thead>
<tr>
<th>KEY ASSETS UNDER TRIAL</th>
</tr>
</thead>
</table>

SPLIT BY PHASE

Source: Evaluate, ClinicalTrials.Gov, BDO interviews, research & analysis
Cell therapies that will become market leading regimens, will be those that will cover an unmet need, and will provide a treatment solution for patients with limited options. They will be expected to offer longer-term responses in comparison to currently available therapeutic options. Therapies are currently showing promise in tough-to-treat, multifactorial disorders that also tend to be leading causes of mortality, such as cancer. While cell therapies such as chimeric antigen receptor T-cell (CAR-T) therapy are in the spotlight of oncology treatments, having shown strong efficacy data, other types of cell therapies, such as mesenchymal stem cell therapy, seem to be more suited for diseases characterised by weakening of muscles, tissues or bones that can benefit from regeneration, such as heart failure. Similar to the gene therapies, the COVID-19 outbreak may negatively impact the development of such therapies and cause delays.

Source: Evaluate, FDA.gov
Cell and gene therapies are a rapidly growing area within the biopharmaceutical landscape, with rapid growth forecast between 2020-26. Growth is driven by pipeline products which will require investment in the area. We have highlighted some of the key future themes expected below.

**CONSOLIDATION / FURTHER DEALS**

As shown earlier in this paper, several assets under development are currently owned by small-mid sized pharma and biotech companies:

- These companies will require funding to progress to the next phases of development, running trials which are more complex and expensive than more traditional therapies.
- Cell and gene therapies are also typically far more expensive than traditional therapies, and will require additional investment in sales and marketing to successfully commercialise them.

This will drive increased requirement for fundraising and increased investment. This may come from:

- Big pharma / biotech: acquisition of smaller companies and assets to increase presence in the space - such acquisitions may range in size from a few million to several billion (e.g. Novartis’s acquisition of Zolgensma through $8.9B acquisition of AveXis in 2018).
- Mergers and acquisitions of larger pharma and biotech to access more innovative products and next-gen therapies, e.g. Bristol-Myers Squibb’s $74B acquisition of Celgene in 2019.
- PE/VC investment in larger businesses with developed pipelines.

**INVESTMENT IN OUTSOURCED SERVICES**

Manufacturing is the major challenge in cell and gene therapies:

- **Increased specialist CDMO demand:** This has led to certain players building their own manufacturing capability. However, in the majority of cases they would contract with specialist contract development and manufacturing organisations (CDMOs) and contract manufacturing organisations (CMOs).
- This drives growth in the spend on CMO and CDMO services in cell and gene therapies: growth is estimated to be ~25% p.a., and forecast to continue at this rate.
- **CDMOs investing more in cell and gene therapy capability** by acquiring smaller specialist providers (e.g. Catalent’s $1.2B acquisition of Paragon Bioservices in April 2019 and Thermo Fisher’s $1.7B acquisition of Brammer Bio in March 2019).
- **Larger CMO deals have also been occurring in the space,** e.g. Danaher’s $21B acquisition of GE Healthcare’s business, to further bolster its capability for manufacturing of next-generation therapies.

Cell and gene therapies will also require complex logistics needs:

- The need for **specialist cold chain logistics** will increase the requirement for investment into infrastructure across the whole spectrum, and helps to provide a differentiator for healthcare logistics.

Complexity of running trials is also expected to increase the requirement for **clinical and regulatory services:**

- This is expected to drive growth in demand for specialist CRO providers: they are expected to understand the key challenges to do with running trials in cell and gene therapies.
- **Specialist regulatory and technical advisory firms** with know how in working with ATMPs will also become more important as biotech and pharma bring additional products through the pipeline.

Finally, bringing these products to market will require specialised **commercial pharma services:**

- A need to better educate and inform stakeholders in the market will increase the potential market for medical communications, market access, commercial and pharmacovigilance services.

*Capability and knowledge of next generation therapies in smaller specialist outsourced pharma services businesses will hence make them highly attractive targets for PE/VC funds, in addition to larger CROs looking to increase their capabilities.*
ABOUT BDO

BDO’S M&A AND STRATEGY TEAM HAS UNRIVALLED EXPERIENCE OF ADVISING COMPANIES IN THE LIFE SCIENCES AND PHARMA SECTOR.

INTERNATIONAL REACH
Access to large international buyers, entrepreneurial businesses and private equity investors across the world through our international network

DEEP SECTOR KNOWLEDGE
BDO’s team incorporates specialists from a wide range of backgrounds with a strong understanding of the sector, including former scientific researchers, doctors, pharmacists and advisers who focus exclusively on the sector

INTEGRATED TEAM
We have the ability to pull a wide range of experts within the firm to deliver a solution to your problem

YOUR OBJECTIVES ARE OUR PRIORITY
We tailor our approach to maximise successful outcomes for our clients and remain flexible to their requirements throughout the process

HANDS-ON STYLE
Our project management approach allows management to remain focused on the business
Our partners are engaged throughout the process so you receive full benefit of their experience

STRONG CREDENTIALS
We are one of the most active advisers in the UK and globally with deep experience of marketing and advising mid-cap businesses

BDO INTERNATIONAL - A SINGLE NETWORK WITH GLOBAL REACH

US$10.3 billion
2019/2020 revenue
A year on year increase of 7.8%1

167
Countries

1,600
Offices

91,000
Staff

1. At constant exchange rate.

1,546
Completed deals in 2020

WITH A TOTAL DEAL VALUE OF $83.5bn

32% Private equity deal involvement

23% OF OUR DEALS ARE CROSS BORDER

ONE OF THE MOST ACTIVE ADVISERS GLOBALLY*

2,500 Corporate Finance Professionals

120 COUNTRIES PROVIDING DEDICATED CORPORATE FINANCE SERVICES

*2nd leading Financial Due Diligence provider globally
– Mergersmarket global accountant league tables 2020
2nd most active globally, 2019 M&A Adviser by deal location - Pitchbook