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AUTOMATION: THE SILVER BULLET OF BIOTHERAPEUTIC MANUFACTURING?

"We should not only pioneer a transformational approach to treating cancer, but also aim at decreasing production time and streamlining distribution processes, that is our end goal"– Earl Wayne, CorsairBio

Earl Wayne, Executive Vice President of process and the manufacturing facility at CorsairBio, entered the Cell Therapy Manufacturing Facility with several questions spinning around in his mind. As he passed through the decontamination room, he considered the complexity of the 14-day 30-step process the facility was using to manufacture a biotherapeutic cancer treatment; the last resort when all other therapies failed. He watched several technicians in full body suits and masks perform the various tasks; quality assurance, quality control, and logistics to ship the product to other sites for study. Earl arrived at his office and considered why the biotech industry continued, for the past 40 years, to rely on highly labor-intensive processes and lagged in automation compared to other industries. Wayne understood that the process would be difficult to scale-up, could result in too much variability across batches, and relied heavily on skilled technicians. The impact of the solution loomed over his shoulders, which was the delivery of products to thousands of patients for approval by the Food & Drug Administration (FDA).

Wayne was losing skilled expertise at a rate of 10% annually. He knew that losing staff at this rate put millions of dollars and potentially thousands of patients at risk if they could not get the product to market. The issues facing Wayne and CorsairBio were low wages, labor intensive processes, and limited investment in technology which could improve employee lives while driving a more efficient supply chain. Consistent feedback from the manufacturing center employees was that, considering the labor-intensive processes, they were overworked and overwhelmed, and the company did not holistically plan or invest well in human capital.

How was Wayne going to retain skilled staff? Given the tight deadlines and regulatory requirements, was it possible to automate manufacturing and reduce reliance on human resources while increasing operational efficiency? Could this reduce the burden on staff and decrease time-to-market? These and other questions swirled through Wayne's mind as he contemplated how to get buy-in from his Board. Wayne was feeling the pressure, especially with thousands of lives and millions of dollars at risk.

Editor: Grandon Gill

Biotherapy

Biotherapy, also called biological response modifier therapy (BRM therapy) and biological therapy, is a type of cancer treatment that uses substances from living organisms to treat cancer among other diseases. These substances can either occur naturally in the body or are produced in a laboratory. In fighting cancer, some biotherapies stimulate or suppress the immune system to help the body fight the disease. Other biotherapies attack specific cancer cells to keep them from growing or kill them; they may also lessen some side effects caused by chemical cancer treatments. Types of biotherapies include immunotherapy and other targeted therapies (Biotherapy, n.d.).

Immunotherapy

Immunotherapy is a type of cancer treatment that helps the human body's immune system fight cancer. The immune system, made up of white blood cells, organs, and tissues of the lymphatic system, helps the body fight infections and other diseases. The immune system detects and destroys abnormal cells, and in certain instances, it even prevents or curbs the growth of cancer cells, as part of its normal function. An instance where this may occur is clusters of immune cells found in or around tumors. These T cells, infiltrated around tumors, are a sign that the immune system is naturally responding to the development and growth of a tumor. People who have T cells in or around their tumors respond better to immunotherapy treatment than people without T cells (Immunotherapy, n.d.).

Although the immune system prevents and slows down cancer growth, cancer cells can get around the immune system in various ways:

- Genetically modified cancer cells can be less visible to the immune system,
- Cancer cells that contain protein on their surface turn off the immune cells, and
- Cancer cells that change normal cells around the tumor to suppress/interfere with how the immune system responds.

In these instances, immunotherapy helps the immune system to better respond against cancer.

Types of Immunotherapies

The most common types of immunotherapies used to treat cancer included:

- Immune checkpoint inhibitors: drug treatment that blocks checkpoints. These checkpoints are part of the immune system and prevent it from responding too strongly. Blocking these checkpoints with drugs allows immune cells a stronger response on cancer cells.
- TILs (most known as T-cell transfer therapy): treatment where the most active immune cells around the tumor were extracted, enhanced, and multiplied in a laboratory then intravenously inserted back into the body to fight the cancer.
- Monoclonal antibodies: immune system proteins created in a lab that mark cancer cells for destruction.
- Treatment vaccines: designed to enhance the immune system response to cancer cells.
- Immune system modulators: agents that enhance the immune system response against cancer, some in a more general way and others affect specific parts of the immune system (Immunotherapy, n.d.).

Current Immunotherapy Research

Immunotherapy research has been focused on several areas, including:

- Resistance research: focused on overcoming cancer resistance to immunotherapy treatments,
- Immunotherapy response predictions: a small portion of the population; scientists have been attempting to determine why particular people responded well to treatment,
- Cancer cells evasion/suppression of immune system: focused on how cancer cells evaded or suppressed the immune system for development of better drugs and treatments, and
- Reduce immunotherapy side effects: focused on reducing the common side effects of pain, swelling, soreness, redness, itchiness, rash and flu-like symptoms (Immunotherapy, n.d.)

T cell Therapy: Six Things to Know

According to an interview, Six Things to Know About T cell Therapy, conducted by Clayton Boldt, PHD with Jason Bock, PHD at the University of Texas MD Anderson Cancer Center on April 15, 2021, T cell therapy is also a topic of discussion at CorsairBio which focused on:

1. T cells are white blood cells made of T and B cells that survey the body for abnormal cells. As a tumor grows, T cells recognize these cells as abnormal and penetrate the tumor.
2. T cells can be used for cancer therapy in two ways, 1) expanding the T cells and 2) reengineering them with certain attributes to fight the tumor which they already recognized as they exit the tumor.
3. The treatment process for T cell therapy begins by taking a biopsy of the tumor, isolating the T cell for expansion and engineering which takes about a month. When the T cells are ready, the patient is prepped for infusion by first going through a chemotherapy regimen to prepare the body. Afterward, the patient will receive immune modulating therapies to stimulate the T cell activity.
4. There are no side effects from the T cell infusion itself, whereas most patients of chemotherapy do experience them.
5. Clinical studies have yielded encouraging results with T cell therapy. Most studies thus far have treated patients with melanoma, but other potentials are being explored. T cells appear to be long lasting, meaning evidence has been found of them patrolling the body years after an infusion, potentially preventing a recurrence prior to detection.
6. T cells offered a promising option for patients with solid tumors that other cell therapies had not delivered (TIL Therapy: 6 things to know, 2021)

FDA Drug Approval Process

Per the U.S. FDA website, the drug approval process undergoes nine steps; listed below and illustrated in Exhibit 1.

1. **Preclinica**l (Animal Testing): testing done in laboratories with results submitted through the Investigational New Drug Application (IND). At this stage, the FDA decides if the process is reasonably safe to move forward to clinical trials and human testing.
2. **Clinical Trials** (Human Testing): this phase begins after the IND has been reviewed by the FDA and a local institutional review board (IRB) made up of scientists and non-scientists in hospitals and research institutions with oversight of clinical research.
3. **Phase 1 Testing**: this phase is usually conducted in healthy volunteers. With a goal of determining the side effects of the drug, how often they occur, and how the drug is metabolized and excreted. In this phase there are between 20 and 80 participants.

4. **Phase 2 Testing**: this phase begins when Phase 1 Testing results reveal acceptably low levels of toxicity. While the focus of phase 1 testing is on safety, the focus of this phase is on effectiveness. The goal is to generate preliminary data of treatment on people who have the disease the drug is being developed for. Participants in this phase range from a few dozen to 300 subjects.
5. **Phase 3 Testing**: at the end of Phase 2, one of two meetings occur between the FDA and the Sponsors to agree on the scale of the studies that should happen in phase 3. Studies in this phase begin when drug effectiveness has been demonstrated in phase 2.
6. **Review Meeting**: in this step the FDA and the Sponsors meet to agree on post market requirements and commitment studies as agreed to by the Sponsors to be conducted after the FDA has approved the drug for delivery on the market.
7. **New Drug Application (NDA) or Biologics License Application (BLA)**: in this step, the drug sponsor formally requests that the FDA considers approving a new drug for marketing.
8. Steps 8 and 9 are combined in **Application Reviewed**: at this step, the FDA has 60 days to decide if it will file the application for review. The review period is 10 months or less for standard drugs and six months for priority drugs (The FDA's Drug Review Process, 2017).

Cell Therapy Market

According to a PR Newswire article published on March 3rd, 2022, in 2021 the global cell therapy market size was valued at $7.2B and expected to expand at a compound annual growth rate of 20.4% from 2022 to 2030, reaching a market worth of $34.69B. This growth is attributed to numerous factors including fast adoption of cancer immunotherapies, development of bioinformatic tools, the rising number of cancer cases worldwide, and increased demand for personalized medicine.

The rising number of research and funding activities in this space and a robust focus on research activities from government health institutions and giant pharmaceutical companies in immuno-oncology therapy development was expected to drive the market growth over the forecasted period. On the other hand, the high cost of immuno-oncology therapies, stringent regulatory requirements for biomarkers, and poor reimbursement policies are expected to hinder market growth during the forecasted period (Immuno-oncology Cell Therapy Market worth $34.69 Billion by 2030 - Exclusive Report by InsightAce Analytic, 2022).

Competitors

The number of cell therapy options in development increased by over 700 between 2021 to 2022 (Exhibit 2). This increase is attributed to the substantial number of centers and institutes that are engaged in stem cell therapy R&D. An increased number of companies have received FDA approvals for stem cell therapies for various diseases and infections.

Some of the prominent players in the cell therapy market include:

- Kolon TissueGene, Inc.
- Anterogen Co., Ltd.
- JCR Pharmaceuticals Co., Ltd.
- Castle Creek Biosciences, Inc.
- The Future of Biotechnology, MEDIPOST
- Osiris Therapeutics, Inc.
- PHARMICELL Co., Ltd
- Tameika Cell Technologies, Inc.
- Cells for Cells
- NuVasive, Inc.

- Vericel Corporation
- Celgene Corporation (Cell Therapy Market, n.d.)

CorsairBio at a Glance

Cell and gene therapy have historically been manufactured by the NCI (National Cancer Center) and other academic centers for research purposes. To date, these site-specific processes have not been scalable or standardized to serve larger patient populations. CorsairBio was founded to deliver broad access to cell therapy for people with cancer by developing clinical trials and centralized, scalable manufacturing processes to enable regulatory approvals and commercial launches. CorsairBio maintains cell therapy manufacturing with a product completion rate of greater than 90% (Exhibit 3). It currently supplies investigational cell therapy for clinical trials at various sites with a streamlined manufacturing process. To date, several patients have been treated with CorsairBio products and have completed safety and efficacy trials in cancer patients. Discovery research team at CosrsairBio is developing pipeline projects to increase this efficacy. Commercial-scale manufacturing will begin after initial product approval from the FDA.

Cell therapy has become a multi-billion dollar per year industry globally (Brindley, Culme-Seymour, & Davie, 2011)[OBJ] Biotherapeutics and gene therapy as a business has grown rapidly and will be increasingly competitive due to the demands of intellectual property rights and patents on processes and products. Competition has been fierce, with clinical trials as the equivalent of the trophy at the end of the race, and the playing field comprising hospitals and clinics across the country, and in some cases around the world. CorsairBio has fared better than most in this regard, with the success rates of their production processes and the ongoing successes of those therapies proving out. Currently CorsairBio is a step away from approval by the FDA, while most competitors are still in the Wayney phases of their clinical trial process, waiting for efficacy data. This provided CorsairBio a large benefit in terms of time and placement ahead of the nearest threat to market share. CorsairBio was considered the first company to launch personalized cell therapy products specifically tuned to each cancer patient. The competition uses a similar concept but focuses on modified cell therapy products which require data of safety, feasibility, and tolerability in patients prior to FDA approval, which may take years.

CorsairBio attracted patients as much as it attracted hospitals, clinics, and insurance companies. Historically the patients enrolled in clinical trials, community outreach projects, collaboration efforts with non-profit organizations, hospitals, and in partnership with oncologists to educate patients about CorsairBio cell therapy options. Patients who were successful examples of the CorsairBio clinical trials advocate for CorsairBio's specific cell therapy products in cancer forums through their stories. CorsairBio invited patients to share their stories and conducted various educational workshops for prospective and potential cancer patients. CorsairBio had a strong medical public-affairs team who were constantly travelling to various national and international conferences for researchers, physicians, oncologists and scientists to present data and clinical trial results, further broadening and advancing the CorsairBio message and marketing throughout the industry. With over 1.7 million potential patients in the U.S. alone CorsairBio, as a leader in the market, had the potential to positively affect many patients before other treatments were available.

The core competencies that CorsairBio had been able to employ were encapsulated within the ability to treat a wide type of cancers with proprietary techniques, with better clinical response and additional products in the development pipeline. CorsairBio has established an in-house cell manufacturing process with over 18 lines of production for unique treatments of various forms of cancer, in close partnership with the research and development arm of the company to collaborate with their scientific teams to design

new and innovative products for as-yet unmet medical needs. CorsairBio invested in building the capabilities, talent, expertise and technology.

The flagship product of CorsairBio trials was a treatment for melanoma. With over 325 thousand new cases annually worldwide, there was a staggering number of potential patients who could benefit from the treatment. At the core of CorsairBio' advantages over their competitors were the intellectual innovations driving their product line, which were directly attributed to the human resources the company had at their disposal. With that in mind, the tribulations CorsairBio experienced with respect to skilled talent retention could identify a major problem in the corporation.

Three main drivers:

- Fasttrack launch to market - speed up the process to bring the product to market,
- Operational efficiency - find and exploit options to improve operational efficiency, and
- Reduction of risk - how a company can reduce the inherent risk of new biotherapeutic products.

Biotherapeutic product commercialization was challenging since very few approved therapies were on the market. CorsairBio was a leader in pioneering personalized biotherapeutics to treat patients with cancer. CorsairBio laid the foundation for launch readiness through the establishment of a timeline and strategy to win the race to market. To navigate the market space, CorsairBio identified the return based on the number of patients they could treat. There was a very narrow window within which to create, deliver and capture the market portion targeted. Once the product moved onto the market, revenue and net income would increase exponentially over the first few years. However, with several biotherapeutic companies near the same position in the race, CorsairBio would need to investigate additional therapies for production to build a sustainable business and guarantee financial success. Parallel to those goals was the need to ensure there were no gaps between products in the pipeline; stagnation never won a race.

CorsairBio had worked with urgency at every step to develop a product. Time had played an important role in planning for the commercial end-to-end patient support model. Due to its unique nature, critical attention to detail needed to occur early to avoid potential downstream launch delays. If CorsairBio could maintain the required level of fine tuning, being early to the market could provide a massive advantage.

Key Challenges

- Quality - open system, human dependent process involving multiple steps from initiation to final product,
- Scale - capable of producing thousands to ten thousand units within the manufacturing process,
- Sustainability - supply chain unable to support the industry,
- Risk Mitigation - need to assess the full range of supply chain inputs; reagents, consumables, equipment, and human resources, ensure the viability and safety of every element, and
- Capabilities and Resources - consider how to mitigate any gaps; rethink the engagement model with health systems, policy makers and funding sources.

What value is created: the novel treatment of cancer for patients with unmet needs.

Exploring Technology

Compliance

In the reality of cell manufacturing, Wayne found himself up against some of the toughest restrictions and regulations above and beyond any other manufacturing sector in the world. This was for good reason; if

any inconsistencies in the biotherapeutics were to find their way to a patient, the results could be devasting. For FDA regulated industries, there were specific compliance guidelines manufacturers must follow commonly referred to as GMP and a guide the industry uses called the IQ, OQ, and PQ guide. (Installation Qualification, Operational Qualification, and Performance Qualification. Reference Exhibit 4) This guide provided specific instructions on the machinery in place to ensure it could produce the desired product outcomes throughout the manufacturing process. Additional design qualifications and validation layers exist under each respective IQ, OQ, and PQ umbrella to ensure 100% consistency with each machinery change or update (The FDA Group, LLC, 2022). With Wayne having to operate a closed facility (an air-tight facility requiring HAZMAT suites and decontamination procedures prior to entry) there were also required security compliance protocols. CorsairBio followed typical HIPAA security standards with security management processes to evaluate risk analysis, access management (building and cloud), and cyber security. The HIPPA guidelines were just as, if not more important than those for production. Of reported violations of HIPPA 50% were of data that was physically stolen and 20% were data that was disclosed without authorization from the patient, reference Exhibit 5 (Wikipedia, 2022). For these reasons, Wayne needed to explore options that would fit the environment and the governing regulations.

The Gaps

The technology CorsairBio had in place was basic API scripts tying together multiple custom-built systems with basic capabilities for ERP, CTMS (clinical trials management software), and AAS-based CTMS's. (Atomic absorption spectroscopy). The gaps within the current solution included a process with extensive complexity and heavy reliance on human input. Due to the lack of in-line monitoring, many of the processes were 'open' and prone to errors and those mistakes could lead to contamination of the product. Additionally, the QC release testing process was very long and expensive; moreover, the QC process accounted for over 30% of the cost. These errors added to an already overloaded supply chain nightmare made worse when sourcing raw materials amidst a global shortage of medical grade plastics, consumables and computer hardware.

The Needs

The board of directors expected that an investment in automation would decrease the operational cost to 30% and save on labor in two ways, 1) retain existing talent and minimize onboarding and training costs and 2) reduce the headcount needed by lowering the complexity in many processes. CorsairBio needed an Advanced Planning and Scheduling (APS) Software integrated with an ERP to monitor standard operational efficiency, IQ/OQ/PQ compliant machinery, ensure inventory accuracy, eliminate product downtime, increase product quality, and drive capacity utilization. The software would need to support general SOP to manage deviations and promote adherence to protocol. They were looking to incorporate a DOE (design of experiments) as a part of the IQ portion of the compliance requirements. The software would also need to provide comprehensive electronic batch records along with a unified digital space to monitor all facility operations in real-time with priority notifications and AI to proactively identify threats to operations that could result in production downtime. This type of solution would reinforce GMP compliance and improve the security of patients' samples through increased traceability. Wayne's main goal was to achieve mature manufacturing to integrate the production layer through a distributed control system.

Cellular Gene Therapy Manufacturing Technology

As Wayne researched the market to arrive at a solution and fulfill the organizational needs, he continued to ask himself: who was the leading innovator in closed cellular manufacturing? What solutions were out there? How could I limit the number of partnerships we have? Could one vendor supply all the needs? A

vendor would have to not only provide the bioprocessing machinery to accomplish scientific clinical manufacturing, testing, quality management, and production; but also, would need to provide the software to fully integrate with that technology and provide actionable data in real-time. The environment also needed to be air-tight and decompressed to prevent any contamination requiring an individual entering the facility to be wearing HAZMAT suites. This included machinery like counterflow centrifugation systems, biological safety cabinets, culture machinery, centrifuges, CryoMed freezers, and electroporation systems that meet GMP requirements for cell and gene therapy facilities. See Exhibit 6 (ThermoFisher Scientific, n.d.).

Coupled with the machinery, the software would need to flow through all stages of gene therapy production The generic patient specific cell therapy workflow manufacturing process consisted of the following (Exhibit 7):

- Patient sample collection
- Sample transportation
- Sample processing and expansion
- Conditioning and infusion preparation
- Sample transportation back to hospital
- Infusion

Overall, the transportation of patient samples and final products is a critical component of the cell therapy manufacturing process and must be carefully coordinated and executed to ensure the safety and efficacy of the therapy.

Organizational Development

Recruitment, Retention, and Upskilling

CorsairBio experienced a labor shortage during the COVID-19 pandemic due in part to an increased desire in the labor market for telework. One-third of establishments increased telework for some or all employees during the COVID-19 pandemic (Dalton, 2022). However, it is impossible to manufacture cell therapy products from home. In fact, 87.6% of manufacturing jobs are non-telework positions according to U.S Bureau of Labor Statistics, 2021 Business Response Survey to the Corona Virus Pandemic (Exhibit 8).

To recruit talent, CorsairBio collaborated with various universities to identify candidates and training and internships to retain skilled staff. The various training programs were offered at the undergraduate and graduate levels with the intent to upskill workers. The organization also instituted an All-Employee Meeting to help eliminate knowledge gaps for non-technical users.

In addition to training and upskilling, the organization created retention bonuses and flexible work schedules to help reduce employee turnover.

Change Management

Leadership recognized that employees were in one of two categories, the first embraced automation and the second feared that automation would eliminate their jobs. Leadership teams had limited understanding of automation or digital transformation and therefore feared that the company might underestimate the complexity of the change process. This resistance to and uncertainty of change were barriers that CorsairBio attempted to overcome by using the Prosci® ADKAR® change management model (Exhibit 9).

Prosci® research has shown that for changes to be successful, organizations must prepare, equip, and support individuals moving through changes so that change is successfully adopted. Without adoption, change would likely be unsuccessful and desired outcomes would not be delivered (Prosci®, 2022).

Besides the All-Employee Meetings being used as a forum to upskill, it was used as part of the change management plan to educate employees on the benefits of digital transformation, clarify the company vision, and create transparency for the demand of the change.

Employee Engagement

Organizational development theory suggests that companies are ineffective when there are gaps in representation within the levels of leadership during the decision-making and planning process. Effective leadership should be engaged in a critical feedback process as necessary to understand the amount of effort required to adopt change.

When feedback was received by the leadership, the impression from employees was that CorsairBio leaders were unapproachable and that any suggestions were dismissed without consideration.

CorsairBio hired a new VP of HR who introduced a SWOT analysis to look at internal and external threats. In response to the analysis, CorsairBio launched an employee appreciation platform called Kazoo (Exhibit 10) to share and appreciate employee achievements and coordinate organizational team building events and exercises.

Previously, most business decisions at CorsairBio were made by one person, essentially as a directive, with the rest of the organization expected to support the decision and comply. The new VP of HR saw the value of a more collaborative decision-making approach and elicited feedback from the employees to enhance the company's decision-making processes.

Decision Summary

Clearly labor shortages were not the only problem CorsairBio faced. Supply chain and logistic challenges, operational issues and lack of proper equipment and bioprocessing technologies which proved unsuited to support scalability were creating bottlenecks. Wayne had to make an informed decision on the manufacturing strategy and consider the benefits and risks of each. As he considered the extraordinary path of a CorsairBio biotherapeutic product from bench to bedside for the benefit of the patients, Wayne had to keep in mind the importance of quality of product, sustainability and scalability of process, and robustness of supply chain and logistics. The conversion of complex processes from manual labor to machine automation not only required regulatory approval but also had an impact on quality and possibly stability of the product. The various equipment used for cell expansion, storage and transportation are extremely sensitive to even the smallest of changes. Wayne considered the following options:

1. **Fully automate the process.** Convert end-to-end cGMP production to avoid any risk of human error and minimize repetitive manual work. The results expected included a reduction in operating costs for controlled biotherapeutic manufacturing and improved monitoring for the benefit of patients with unmet needs. It would reduce cleanroom requirements and space requirements, which could reduce operational costs of the facility and the number of operators while increasing potential throughput. However, this would require IQ, OQ and PQ validation as per FDA regulation and compliance, which would extend the timeline for federal approval and delivery to market.
2. **Convert to semi-automated**. Conversion of manual processes to automation requires a robust and cumbersome validation and performance qualification process which would require more full-time employees. There were a few complex procedures that would not require a closed system or automation. With an advanced software system integrated to monitor operational efficiency, it would help move towards automation in step-by-step process. In addition, a partial automation system could eliminate some of the labor-intensive processes which reduce long-term costs and risk and eliminate the positions that still needed to be filled.
3. **Externalize manufacturing.** Seek out an external vendor or outsource automated manufacturing. This could be quicker, less expensive and minimize risks while easing the burden on quality control and monitoring systems while providing support to regulatory submissions. Most of the external vendors were previously FDA registered as well as ISO 13485- and 9001-certified. The vendors were equipped with clinically relevant software, including traceability documentation for product master and regulatory support.
4. **Do nothing.** As the cell therapy field evolved with more novel approaches, automation alone might not resolve the issue and could require more specialized and skilled laborers. Additionally, automation alone might not fill the gap between the human element and the machine capability. Given the employee turnover rate of >20% and the assessed workforce requirement to fulfill the complicated, labor-intensive manufacturing process, CorsairBio was forced to invest time and money in improving hiring strategies and develop internal training programs. Collaboration with academia and internships for fresh prospects, in addition to job opportunities, had the potential to resolve the labor shortage.

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Authors

Justin Roberts draws on his 17 years of people-leadership experience with a variety of tech and communication companies. He is currently leading the Public Sector organization at Verizon. In this position, he leads remote teams across the United States to support the company's Public Sector initiatives inclusive of Cyber Security, Network Architecture, Network Design, Deployment, Service & Customer Success Management, and Business Strategy & Transformation across every contract vehicle Verizon owns with State, local, and Education entities. In his prior roles with Verizon, Justin worked in an international capacity leading and working across teams around the globe with Verizon Connect, and Verizon's SaaS Telematics business unit. Roberts has also held roles with organizations such as Microsoft, Tesla, & AT&T; coupled with, several years in market-level leadership roles in national big box retail. His IT career consists of management- and director-level roles that primarily helped influence product roadmap and architected-applicable IT implementations across some of the biggest corporations on the planet. His successful career is attributed to his ability to adapt to change, which, he says, "requires a mentality that is rooted in a desire to learn."

Krithika N. Kodumudi is a dedicated researcher who fills a direct leadership role in implementing studies aimed at better understanding the functional activities and immune correlations of various cell therapy products to treat cancer. Krithika has over 15 years of research experience in cancer immunology and immunotherapy. She has previously held positions in the Moffitt Cancer Center as a senior scientist and within the USF as an Assistant Professor contributing to cancer research. She was also actively involved in teaching Ph.D. cancer biology students. She has extensive experience in preclinical development for immunotherapy-based clinical trials and has published research in various high-impact-factor, peer-reviewed journals.

James H. Wilkendorf is a veteran of the US Navy of 20 years. His career was spent on special projects and in locations across the Pacific from Alaska to Japan and Hawaii, with his final duty station at the National Cryptologic School in Maryland. His recent roles include contract work for US Central Command as a Senior Analyst, and within the Project Management Office of a billion-dollar contract with the Army for training and readiness. With his experience in analytical skills, critical thinking and structured analysis, and his experiences in diverse cultures, he has a depth of perspective rarely found and highly sought after. His education includes a Bachelor of Science in Global Business and Public Policy from the University of Maryland, University College, and he carries several certificates including multiple military technical schools, Master Training Specialist, Lean 6 Sigma: Yellow Belt, and a Certified Higher Education Professional Certificate in Leadership.

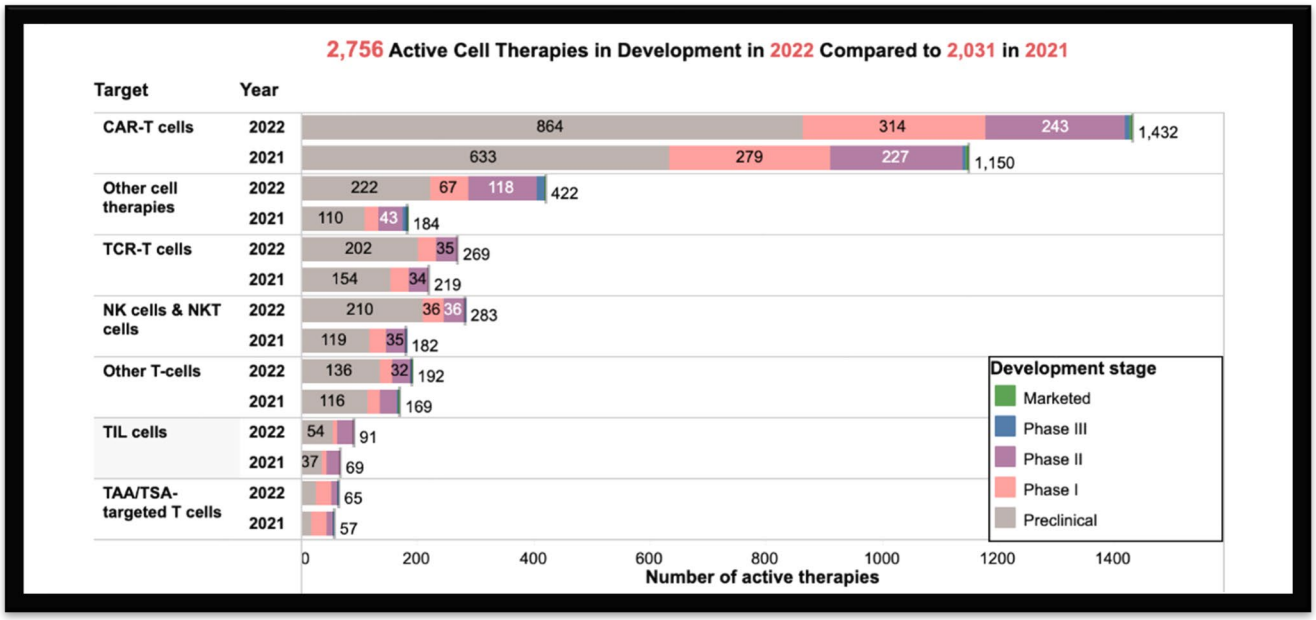
Heath Harlan Campbell is responsible for driving Cigna's affordability programs through contract negotiation and establishing effective business-to-business engagement models. As Assistant Vice President, Campbell plays a lead role for several ancillary benefits within Cigna and is accountable for financial performance of vendor relationships. Prior to his current position, Campbell spent time in Health Plan Operations and Provider Network Contracting and Management. He received a Bachelor degree in Business from Florida State University and earned certificates in Post-Crisis Leadership and Diversity, Equity and Inclusion in the Workplace from the University of South Florida. He is a Prosci Certified Change Manager, a Certified Scrum Master and a Project Management Professional.

Adela Mustafaraj works in the finance industry as a Sr. Compliance Officer and is responsible for establishing internal strategies, policies, procedures, processes, and programs to prevent violations of law, rule, or regulation and design and deliver a risk management framework that maintains the risk levels within the firm's risk appetite and protects the franchise. Responsibilities include the design, development, delivery and maintenance of Compliance programs, policies and practices, investigate and respond to compliance risk issues, and review materials to ensure compliance with various regulatory and legal requirements. Mustafaraj received a bachelor's degree in international business and management Information Systems from the University of South Florida.

Exhibit 1: DA Drug Approval Process

Source: https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-ensuring-drugs-are-safe-and-effective

Exhibit 2: Cancer Cell Immunotherapy Pipeline 2022

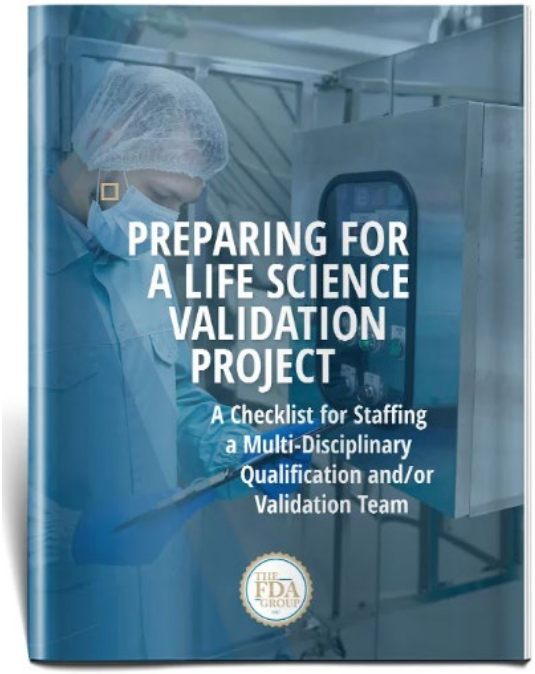


Source: https://www.cancerresearch.org/en-us/scientists/immuno-oncology-landscape/cancer-cell-therapy-landscape

Exhibit 3: Example of automated Cell Therapy manufacturing

Source : NCI

Exhibit 4: Guide to IQ, OQ, PQ



GET OUR FREE GUIDE

Preparing for a Life Science Validation Project

A Checklist for Staffing a Multi-Disciplinary Qualification and/or Validation Team

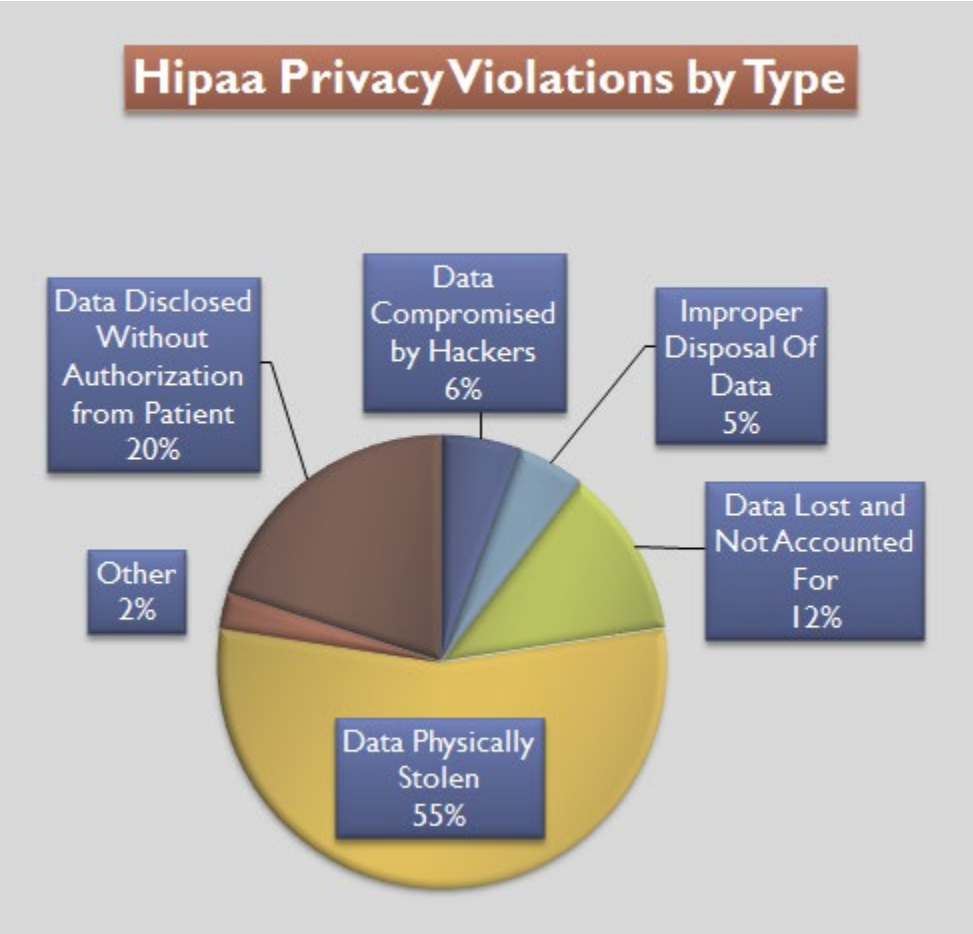
Building a multi-disciplinary team to support Qualification and/or Validation of new or modified facilities, systems and processes have become a cGMP expectation of the FDA and many other regulatory agencies in ICH markets.

Carrying out these activities across all stages of a product lifecycle –– from research and development, through to manufacture and distribution, or throughout a period of change –– continues to be one of the top challenges for pharmaceutical, medical device, diagnostic, and other FDA-regulated life science companies.

This guide will help you overcome these challenges and save valuable time locating and evaluating Validation specialists who can see your program through to success on time and on budget.

Source: Preparing for a Life Science Validation Project: A Free Guide & Checklist (thefdagroup.com)

Exhibit 5: Breakdown of the HIPPA violations



Source: Health Insurance Portability and Accountability Act - Wikipedia

Exhibit 6: Equipment Examples

Thermo Scientific Heracell Vios CR and Steri-Cycle CR CO_2 incubators – CTS series are the first third-party certified cleanroom compatible CO_2 incubators on the market, suitable for use in ISO Class 5 and GMP Grade A/B environments. The incubators provide optimal cell growth conditions, enhanced cleaning compatibility and an active particle control system.

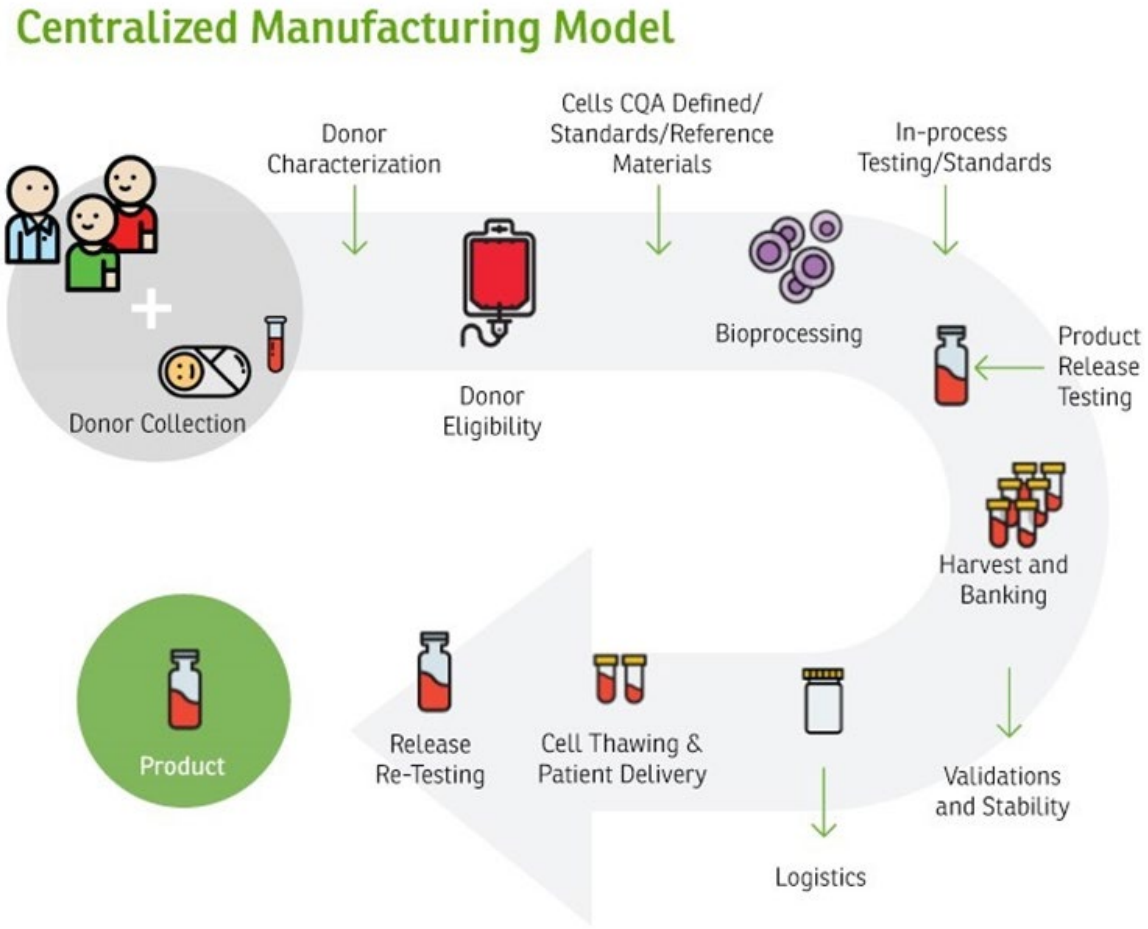
Thermo Scientific General Purpose Pro Centrifuges - CTS Series are designed to meet the needs of today's rapid-fire discoveries, with updates to help you perform research more quickly, consistently and with powerful reliability. The CTS Series of our 4L range (benchtop and floor model) satisfies not only the need for an essential separation equipment, but also the necessary compliance documentation and validation services

Thermo Scientific Herasafe 2030i Biological Safety Cabinet - CTS Series is designed to maximize sample protection and user safety, with an emphasis on containment, comfort and convenience, all day, every day. The CTS Series combines a comprehensive documentation package saving valuable time and giving piece of mind

Source: Cell & Gene Therapy Lab Equipment | Thermo Fisher Scientific - US

(ThermoFisher Scientific, n.d.)

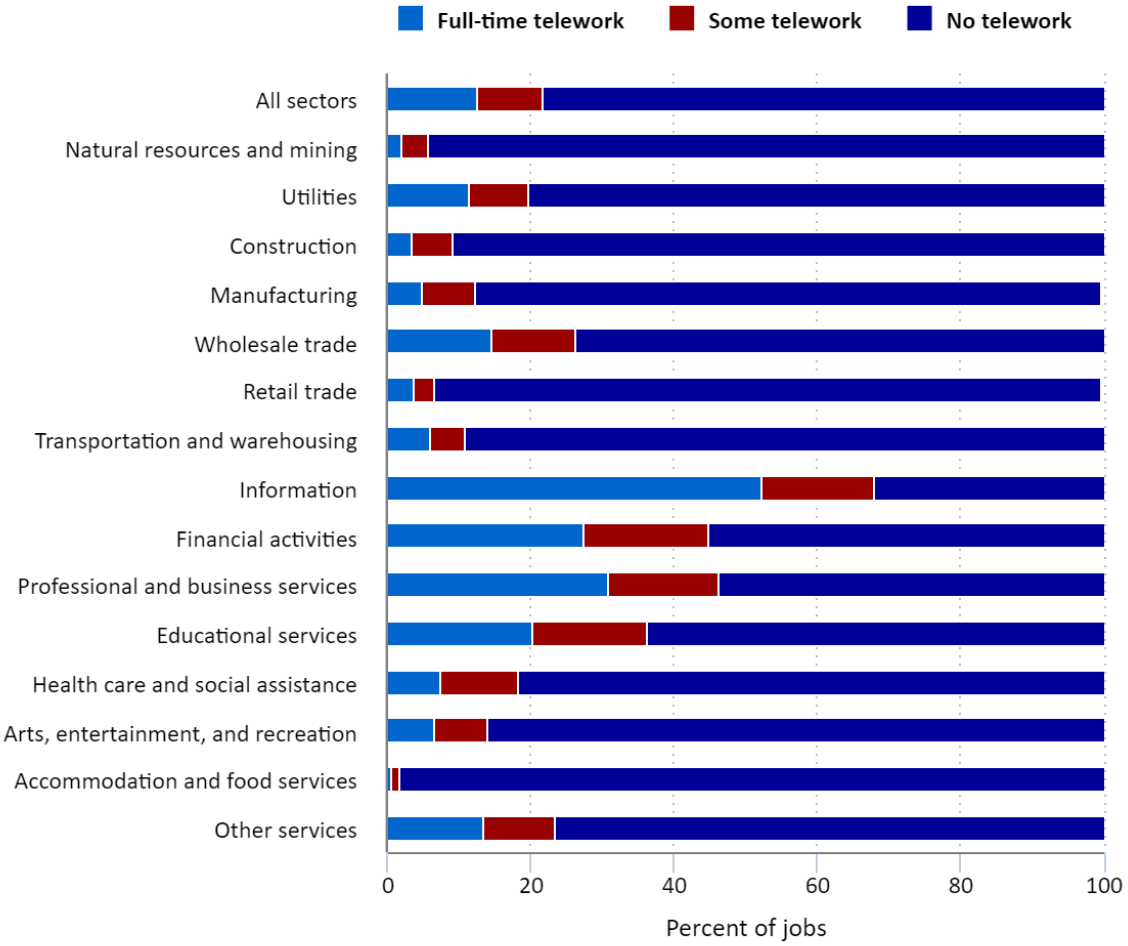
Exhibit 7: Cell Therapy Manufacturing Process



Source: https://nam.edu/manufacturing-cell-therapies-the-paradigm-shift-in-health-care-of-this-century/

Exhibit 8: Telework Patterns by Industry

Chart 1. Telework patterns by industry



Click legend items to change data display. Hover over chart to view data.
Note: Definitions of industry sectors correspond to codes from the 2017 North American Industry Classification System.
Source: U.S. Bureau of Labor Statistics, 2021 Business Response Survey to the Coronavirus Pandemic.

Exhibit 9: Prosci® Change Management Model

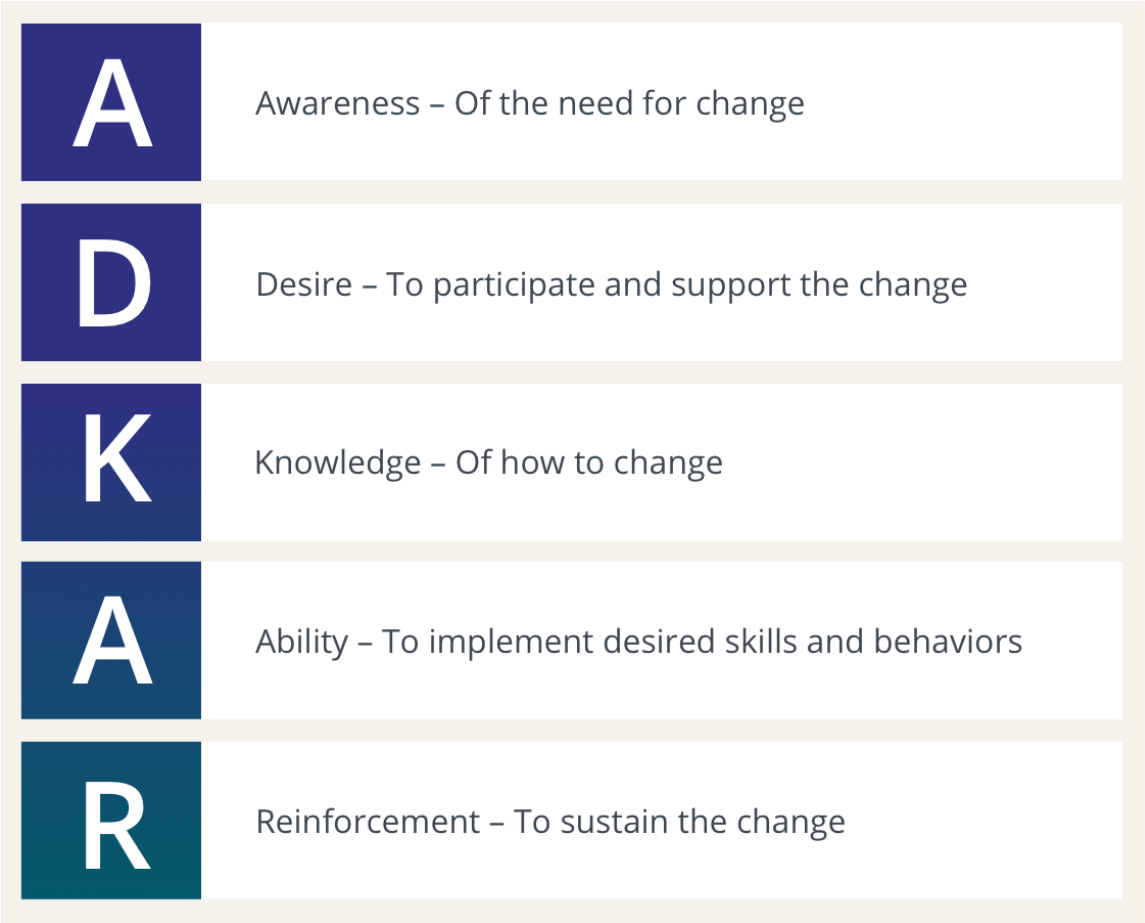
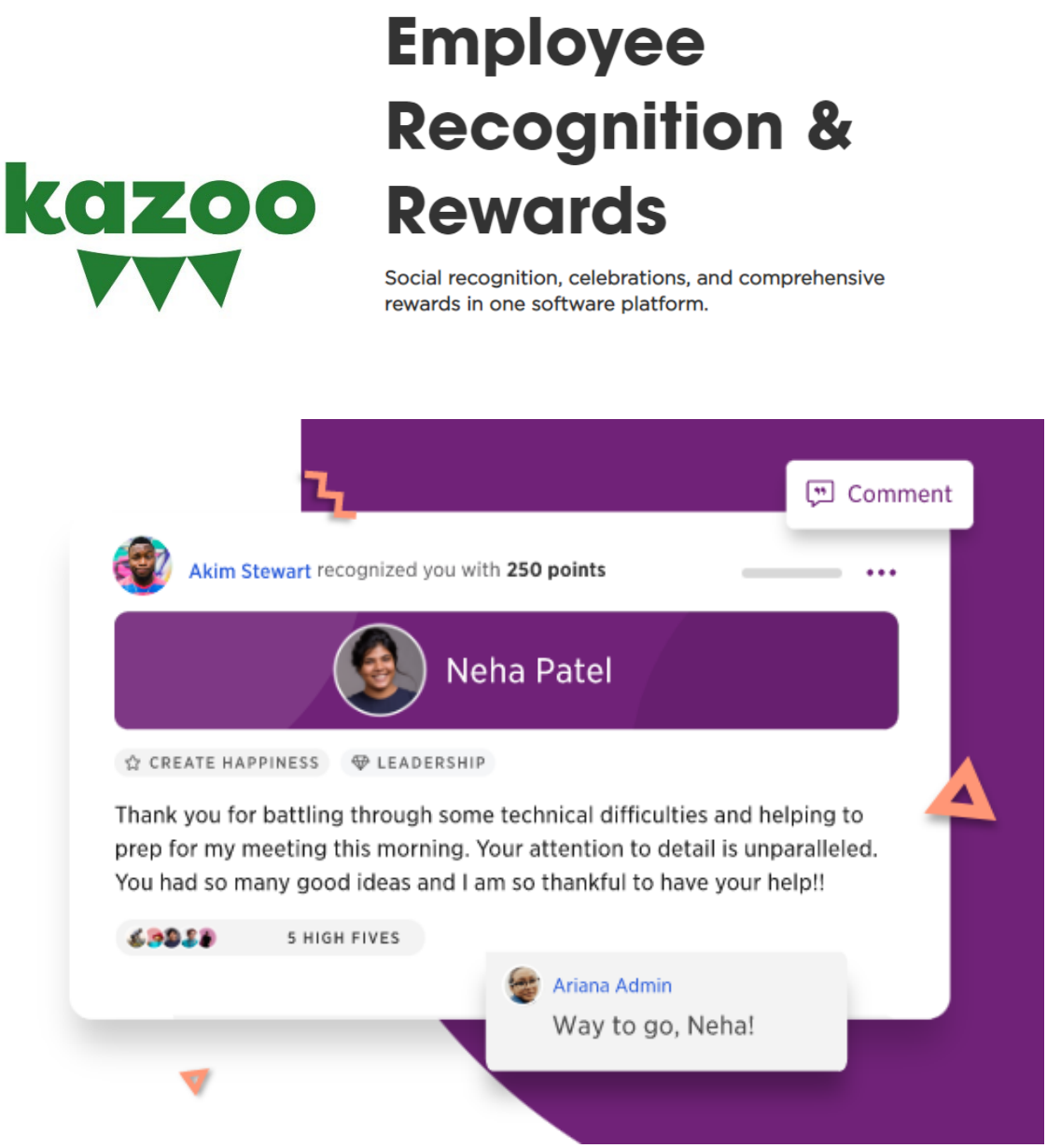


Exhibit 10: Kazoo Software Platform



Source: [Employee Recognition and Rewards | Kazoo (kazoohr.com)]