POSITIONING BIOBANKING ASSETS FOR MAXIMUM VALUE

Leveraging the Precision Medicine Opportunity for Biobanks

CROSSTREE

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Introduction

Over the past seven decades, the concept of biobanking has grown significantly, from simple biological sample repositories to complex and dynamic units belonging to large infrastructure networks. Since the 1950s, technological advances such as automated sample processing, computerization, and the advent of the internet revolutionized biobanks, increasing their number, complexity, and interconnectivity exponentially. Modern biobanks enable large-scale analysis for individuation of specific disease biomarkers starting from biological or digital material (i.e., bioimages) with well-annotated clinical and biological data. These features are essential for improving personalized medical approaches, where effective biomarker identification is a critical step for disease diagnosis and prognosis.

Today, a seismic shift is taking place in the pharmaceutical development and diagnostics industry which will transform biobanking even further. As therapies and assays continue to migrate towards precision medicine, so too must the traditional biobanking model, which is a key component in the supply of both physical samples and the data necessary to achieve patient-specific treatments. The Journal of the National Institute of Cancer states: "As the source of molecular information, human biospecimens, such as tissue or blood, are both the foundation of personalized medicine and the fuel that drives the basic and translational research needed to achieve this vision." As precision medicine grows, so, too, does demand for biobanking services, offering both strategic and financial investors a significant opportunity for value creation.

Biobanking and Precision Medicine

Biobanks, and the genetic insights they provide, form an essential bridge from traditional to precision medicine and its promise of new, more effective therapies tailored to precise genomic signatures. Precision medicine has blossomed into one of the highest growth market segments of the healthcare industry, valued at ~$60 billion today and projected to grow to ~$100 billion over the next five years and close to $800 billion by 2028.[3]

However, research must become more efficient for precision medicine to realize its full potential. Today's computing power allows for certain applications such as the fast discovery of new disease biomarkers, but there remains a large, ever-growing amount of unanalyzed patient population data. Regardless of the type of sample, the most important portion of population data needed for the development of precision medicine comes directly from human biospecimens. These specimens are a key bridge from traditional medicine to the promise of new therapies tailored to precise genomic signatures. In addition to the high volume of specimen data, a high level of biospecimen specificity is required by customers. Precision research begets precision medicine and requires distinctive biospecimens for researchers in close alignment with their highly focused and specialized needs. The demand for specifically characterized and annotated biospecimens is on the rise.

Learn more in Crosstree's *Inorganic Growth Strategies in Precision Medicine*.

Based on the traditional biobanking service and asset model, there are generally two directions where growth can occur in the direction of precision medicine: those centered around data and those centered around physical specimens (Fig. 1). These two directions are not mutually exclusive. However, there needs to be a focused effort on which route to pursue, as each pathway positions certain traditional assets better than others to take advantage of evolving customer needs.

Biobanking Value Continuum

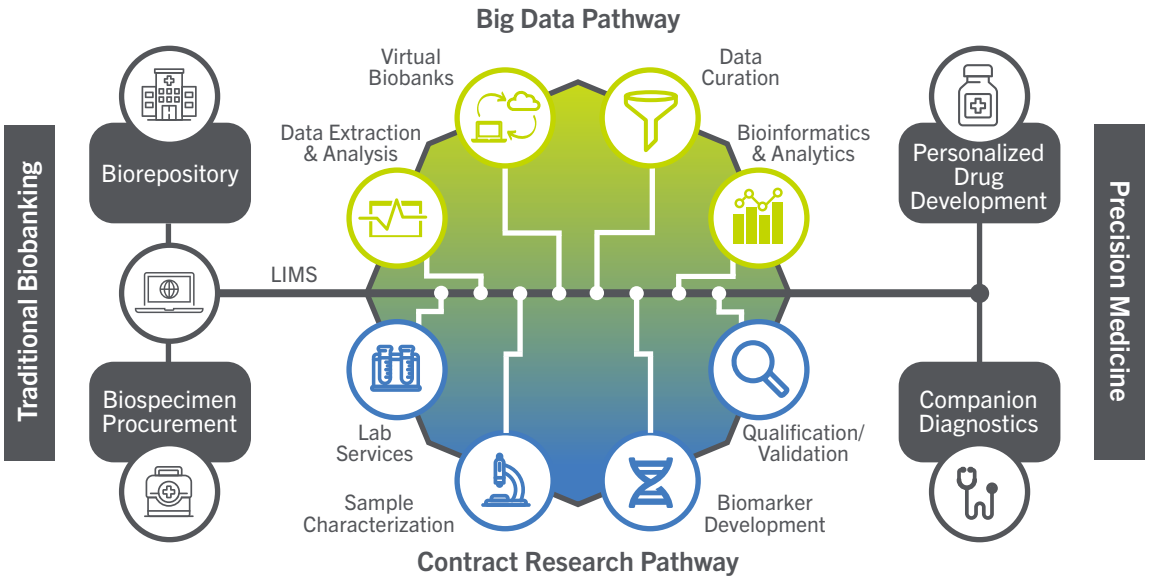

Figure 1: Biobanking Value Continuum

There is an existing and growing demand in the market for high-quality physical specimens along with their respective patient annotated data – the more detailed and characterized the data, the greater the demand and relative value. Demand for biospecimens and their data is outstripping the currently available supply, and this high demand will continue until (or if) a pure-data paradigm shift emerges.

Like the clinical research marketplace of 12-15 years ago, many pharma, biotech, and diagnostic companies are conducting their own in-house translational medicine and biomarker development studies. Many of the large commercial participants have created internal infrastructures along with the requisite bureaucracy, systems, and processes in order to execute at large and diverse scales of development.

Much like the clinical research development space, there is an ever-growing need and desire by large sponsor organizations to outsource specialty services and take advantage of third-party resources in order to reduce costs, create economies of scale, and mitigate risk by leveraging specialized expertise on a contracted basis. The ability for traditional biobanking services to expand into specialty contract service offerings on a larger one-stop-shop scale has the potential to both accelerate timetables and provide more cohesive scientific research, mitigating issues that may arise between multiple third-party vendors.

UNDERSTANDING BIOBANKING'S CUSTOMER PAIN POINTS

For decades, biobanks have created capital-intensive assets in order to compile and store large volumes of human biospecimens, often speculatively, in the hope of satisfying a pipeline of medical research for both current and future consumption.[4] It has been incredibly difficult for biobanks to effectively scale the flow of specific specimens into the hands of researchers in quantities and quality sufficient to satisfy demand and has led to significant industry consolidation attempts, as demonstrated by the BioIVT and Discovery Life Sciences roll-ups. This "doubling-down" on traditional business models by biobanking leaders results in customers having to limit the scope of their work due to difficulties in procuring specimens in sufficient quantity and quality from a limited number of suppliers.

Customers are calling for increasingly robust patient data regarding each sample (annotated data), further complicating the biospecimen procurement market. The traditional biobanking business model of specimen stockpiling in the form of mass collections has, historically, rarely considered the need for associated patient data, and as such patient data has infrequently been captured. This leads to a lack of properly annotated specimens in older inventories (estimated at 42% of all inventoried specimens) to fulfill the growing supply demand for the precision medicine research pipeline and have therefore lost much of their usefulness and requisite value.

Further exacerbating the lack of patient data associated with most of the world's inventoried biospecimens is the fact that many biospecimens, even current samples with data, are missing the proper consents and the ever changing regulatory adherence goal posts necessary to fully realize the usefulness of the samples and its annotated data for current demand and use. These drivers of specimen obsolescence handcuff researchers who require samples for specific use cases that may not have been collected or properly pre-consented by the specimen donor.

Value Creation Pathways

THE 'BIG DATA' PATHWAY

Biobanking of the future will be more agile, finding a way to intelligently understand and act upon the research and development community's needs for highly specified biospecimens from highly specified patient populations and to deliver, in a near on-demand environment, the exact specimens and associated patient data needed to advance precision medicine research needs. This type of intelligent process will require a data-driven "just-in-time" business model.

The Big Data Pathway (Fig. 2) follows a data collection and analysis route, leading towards what has been recently referred to as virtual biobanks or data repositories (e.g. GenoSpace, M2Gen). The collection and analysis of specimen data combined with patient clinical data, laboratory data, molecular data, and genetic data, leads to the big data platforms necessary to perform the bioinformatics and analytics needed to promote precision medicine targeting, lead generation and digital biomarker and formulation

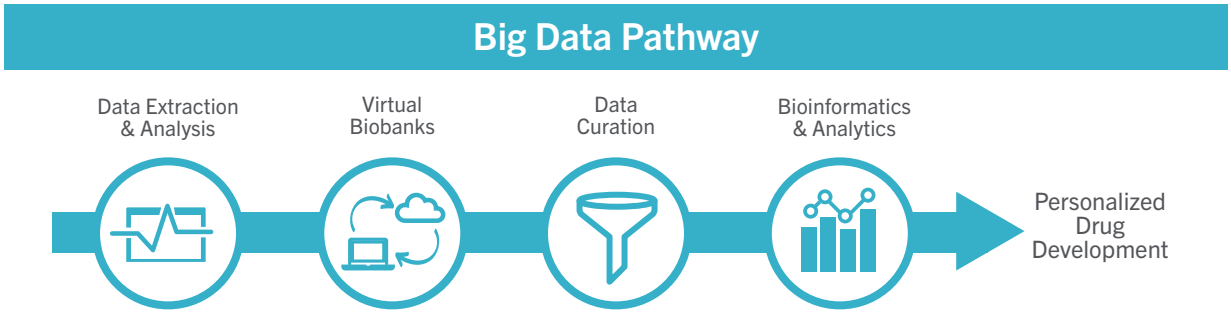

Figure 2: Big Data Pathway

development. Additionally, big data platforms combined with other longitudinal data sets (clinical trial data, EMR/EHR data, and patient registries) can lead to a trove of virtual data collection and analysis that allows for highly specialized patient recruitment activities, furthering advancements in the future development of personalized medicines based on real-world evidence and population group studies.

In the relative near- to mid-term, specimens with highly characterized data generated through various molecular sequencing processes, especially whole genome sequencing (WGS) could be monumental in identifying patients and patient groups eligible for sophisticated precision medicine and diagnostics trials and development work. Sequencing (WGS in particular) is a significant data producing activity creating huge sets of data (Big Data) from which extensive bioinformatic and genetic analysis could be conducted.

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The main benefit of the Big Data Pathway is a future state where physical samples may no longer be required by researchers. Given the industry's current inability to supply enough high-quality, fully characterized and annotated samples, a shift to data repositories could allow instantaneous access by researchers around the world and reduce or eliminate

upkeep of physical specimen inventories, as the physical sample becomes a single point in the data collection process, part of a global big data set. Computational analytics would then further supplant the need for physical specimens with digital samples and a single patient's specimen now feeds a theoretically infinite set of research needs both in the present and future.

Although the movement towards digital-only development remains substantially futuristic in nature, the market is beginning to materialize some tangible examples gaining traction in the form of virtual placebo arms of clinical studies (e.g. Flatiron Health), the digital development of biomarkers used in the creation of diagnostic tests for COVID-19 (e.g. Seegene Technologies), and even leading vaccine development efforts (e.g. GeoVax Labs).

CONTRACT RESEARCH PATHWAY

The second biobanking precision pathway, the Contract Research Pathway (Fig. 3), follows the route of value-added and contract services such as drug target identification, validation, and biomarker discovery services including various types of laboratory operations, characterization studies, specimen processing, assay and biomarker development services, validation, testing, and regulatory services. The core of these services is associated with pathology and histopathology laboratory services and, more recently, those with molecular characterization services.

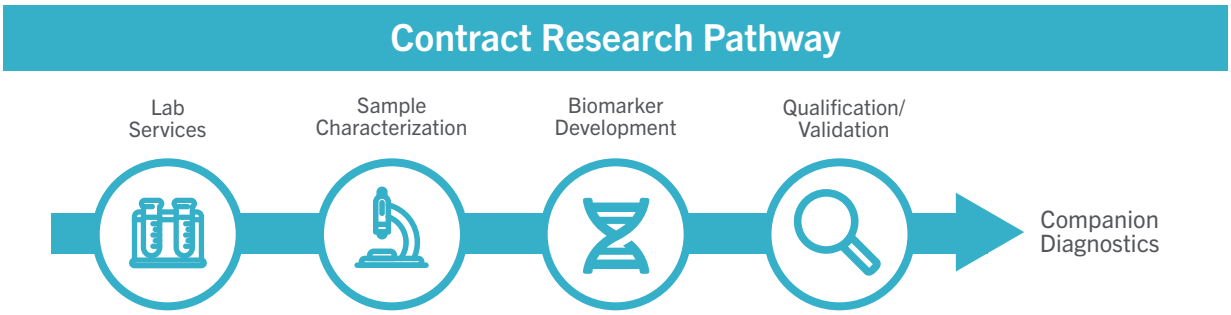

Figure 3: Contract Research Pathway

Since every individual is genetically distinct, the adage "one treatment for one disease" is no longer applicable in the new age of precision medicine. Today, the ability to identify a patient or groups of patients who may or may not benefit from a therapy is a key component in personalizing the management of clinical disease and outcomes. Drug selection and dosage may be customized according to individual biological characteristics, genetic alterations, ethnicity, gender, and results of diagnostic testing. The building blocks for this customization process starts with diagnostic biomarkers which provide the individualized ability to monitor therapeutic treatment success and failure of particular drugs, or even more broadly classes of drugs and therapeutics.

Contract research can assist with the design, management, and coordination of all aspects of the diagnostics development process from concept through regulatory approval by providing independent and unbiased guidance to both academic and commercial researchers based on the sponsor's goals and

objectives. As a single outsourcing partner, a CRO delivers a flexible process that is adaptable to changing needs, priorities, and schedules acting as either an augmentation of or replacement for in-house resources.

New molecular technologies, particularly next generation sequencing (NGS), has become the preferred methodology for novel biomarker discovery and drug target identification efforts. NGS provides a wealth of genomic data that has led to a greater understanding of underlying genomic alterations, mutations, and biological pathways that explain disease mechanisms and allow for precise targeting for new drug development making the technology integral to the development of precision medicine. Such analysis is becoming more accessible, as both NGS costs come down and computing power increases.

In addition to molecular laboratory services, genetic and other "-omics" characterization capabilities, digital imaging, site management, and other value-added services; contract research services enable the traditional biobanking business structure to flex in the direction of conducting third-party translational medicine, biomarker and assay development, validation and testing services for its customers on an out-sourced basis.

Biobanking brokers act as an intermediary between hospitals, clinics, and laboratories (where samples are originally collected and preserved) and their clients (researchers). Brokers source the samples requested by their clients and charge a fee for this service.

DEAL INSIGHT

OVERVIEW

Transposagen Biopharmaceuticals was acquired by Lonza America, giving Lonza exclusive rights to Transposagen's proprietary gene integration technology.

SIGNIFICANCE

Transposagen is a leader in gene editing and integration technologies and services with applications in research & drug discovery, and bioproduction of therapeutic proteins and cells. Transposagen's unique genome engineering capabilities allow for the creation of nearly any genetic modification in any genome. The company's gene integration assets enhanced Lonza's service and product offering for cell-line development and bioproduction.

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Case Study: Traditional Biobanking Broker Platform

STRATEGY DEVELOPMENT: CAPABILITIES ANALYSIS, ADD-ON CONSIDERATIONS

The construct of a unique platform recognizing and anticipating customer need allows for the greatest number and variety of exit opportunities, maximizes what already exists, and supplies customer with what they want and need. The following capabilities should be carefully evaluated in order to identify the optimal platform and position it for the greatest value opportunity.

DATA MANAGEMENT

Market trends point to the importance of robust, longitudinal data sets associated with characterized biospecimens. The ability to generate data from sample processing and/or to collect, store, curate, and/or process specimens is required to create these specialty data sets. Less sophisticated brokers in this regard will only be leveraged by clients as a tool or platform for the efficient inventorying and tracking of biospecimens. In this case, the management team's technical abilities and skills should be assessed to determine if they are capable of developing a more robust data collection and data exchange platform.

PHYSICAL HANDLING

The physical processing of specimens enables brokers to provide the high-value data and quality control (QC) demanded by the market, building a solid biobanking platform. Labs can act as a central processing facility, providing a much-needed quality control component, along with the ability to ensure proper labeling, tracking, etc. At the same time, labs can provide the additional characterization data of samples that are needed in order to reduce the number of rejects and "disorganized" sample sets from customers.

IMAGING

Imaging laboratory services can offer a highly valuable add-on service for contracted development and characterization activities. Imaging capabilities provide a differentiated service offering that could be positioned to create significant data generation capabilities for a future data model as well as better characterization and other services for the contract services model. Add-ons of imaging laboratory capabilities can provide a more complete service offering in the contract service segment in the future.

SPECIMEN SOURCING

The uniqueness, strength, and longevity of a platform's specimen network are vital considerations. The close cooperation and relationships established with these source providers acted as both a barrier to entry as well as a means of securing the supply chain. The mix of commercial, academic, and hospital sources impacts both competitive differentiation and risk profile. Reliance on too few sources, or only one type of source (commercial, commonly) presents significant supply chain risk, as a gap in supply leads to an immediate loss of revenue until new suppliers can be identified. This risk can be mitigated by building out a platform's network of contracted suppliers, securing them through acquisition, or both. Suppliers may find acquisition attractive, as many either lack the interest in or have few internal financial resources to build-out specimen

management systems and characterize samples in-house according to industry needs, thereby lacking industry-standard quality control, logistics, and validation capabilities. With this synergistic view, the expansion and diversification of a biobank's specimen supplier base can be effectively secured.

PATHWAY SELECTION: RATIONALE FOR CONTRACT RESEARCH

For a traditional biobanking platform, the opportunities to establish a network of biospecimen providers; expand the services surrounding procurement of samples for pharma, biotech, and diagnostic customers; and enhance customer service associated with technical and scientific consulting lend themselves to greater growth along the contract services pathway rather than the data pathway. In order for the platform to move into a more substantial contract services role, it is often necessary to add capabilities that promote independent development of customer projects that facilitate outsourcing, such as laboratory services, niche characterization capabilities, quality control, testing, and validation.

GROWTH STRATEGY: PROSPECTIVE COLLECTIONS MODEL

The growing scarcity of inventoried samples with patient data and proper consent has the potential to be resolved through prospective sample collection techniques borrowed from clinical research's site management organization (SMO) model.

The concept of establishing a prospective study where protocols, consent requirements, patient annotation, and sample characterization requirements are detailed prior to collection efforts, allows for the establishment of patient sample collection sites where near "real-time" samples can be collected that meet the highly specified requirements of the sponsor. By moving into a site management collections model for prospective studies, traditional biobanks can extend their reach and capture a larger swath of the value chain while maintaining the traditional infrastructure and capabilities set of a contract research biobanking entity.

Much of the market does not participate in prospective studies due to the cost and increased lead times required to receive samples, difficulty finding the quantity and quality of samples needed for development programs, and unmet need for more specific samples. The latter is becoming a differentiating factor among procurement vendors who have laboratory characterization services and in-house ability to better qualify samples prior to shipment. There exists a bureaucratic disconnect between researchers and their procurement vendors and ultimately the often-unattainable demands being placed on the biospecimen procurement industry. Researchers are demanding higher quality samples with specific characteristics complete with patient data and the requisite consent, while the procurement vendors are seeking to fulfill these internal requests at the lowest-cost price points available thereby creating their own systemic quality issues and high rejection rates by their own researchers.

As researchers continue to demand uniquely annotated samples for their precision medicine work and as rejection rates (as high as 33% in many cases) continue to increase, there will be a move towards higher

cost samples that are properly characterized for the end user along with the data and consent necessary for the ultimate use of the specimens. This drive for specificity will increase the value of properly characterized samples to the point where intentional prospective studies are required in order to best address the needs of researchers and development activities. Although a future-minded model, a prospective collections SMO model could be a logical, highly innovative, and differentiated outsourced service, yet a model fully understood by biobanking customers thanks to the clinical research market in which they also participate.

Figure 4: Prospective Collections Model

CONCLUSION

Biobanking is at the confluence of multiple healthcare trends, including high-value services like precision medicine and genomic services. Technological advancements have allowed molecular sequencing of biospecimens to become economically feasible, leading to extremely detailed and characterized biospecimens. There is also strong demand for the data being derived from biospecimens from both the pharmaceutical and diagnostic development industries, especially when linked with patient clinical data.

Foundational to the development of the precision medicine continuum, biobanking needs to become far more agile, first finding a way to intelligently identify the research community's need for specific biospecimens from particular patients and secondly collecting and delivering in an on demand model the exact specimens and data needed to advance precision research projects.

Crosstree sees significant potential within the biobanking industry and believes there is substantial opportunity for future growth due to recent technological advances and increased biospecimen demand within multiple healthcare markets, including disease management, epidemiology, and pharmaceutical, diagnostic, and biomarker development. We believe that the industry will continue to demand high-volume, low-value commodity samples for testing and validation but will also markedly increase its appetite for high-value, highly characterized samples from hard-to-find population groups and individuals which will drive value for those providers with the assets and tools in place for sourcing, collecting, processing, and characterizing such samples all at volumes and in an environment of exceptional quality control.

About Crosstree

As one of the leading investment banks in pharma services, Crosstree combines data, financial analysis, and an in-depth industry knowledge with real-world execution experience. Crosstree's consultants, advisors and bankers work with a world-class network of industry experts, executives, and investors in order to help formulate and execute the most accretive transactions possible for our clients. No other advisor has a deeper understanding of how the confluence of industry trends, market conditions, and growth opportunities will shape a company's value and strategic outcomes in the pharma services space.

Crosstree's deep expertise in pharma services, diagnostics and tools, and digital health provides an unprecedented advantage to prospective strategic partners in today's market. Because Crosstree works with such a comprehensive understanding of the pharma services industry, we can synthesize a company's capabilities, financial data, and market position to communicate a compelling value creation strategy or proposition to buyers, sellers, and other strategic partners.

Our Strategic Services team provides actionable plans and pragmatic guidance to create and realize greater value for our clients. By combining proprietary research, expert financial analysis, and industry knowledge with real-world execution expertise, Crosstree helps companies plan, evaluate, and execute viable in-organic growth strategies to achieve successful outcomes downstream.

In February 2021 Crosstree published its inaugural Innovations in Pharmaceutical Development™, a first-of-its-kind compendium of the industry's most innovative companies; a go-to resource of what is coming 2021 and beyond. Unlike other directories, this publication organizes the Pharma Services industry using Crosstree's proprietary and granular taxonomy, which helps define the industry in an easily understandable and concise way.

FIND OUT MORE

To learn more about Crosstree's Investment Banking and Strategic Services capabilities and life science expertise, visit CrosstreeCapital.com.

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4 An Asterand Bioscience executive stated the company speculatively increased their NSCLC specimen inventory to keep up with perceived future demand. The demand did not materialize and left Asterand with large amounts of undesirable biospecimens.