CHARTING DISRUPTION

GLOBAL X by Mirae Asset

OUTLOOK FOR 2024 AND BEYOND

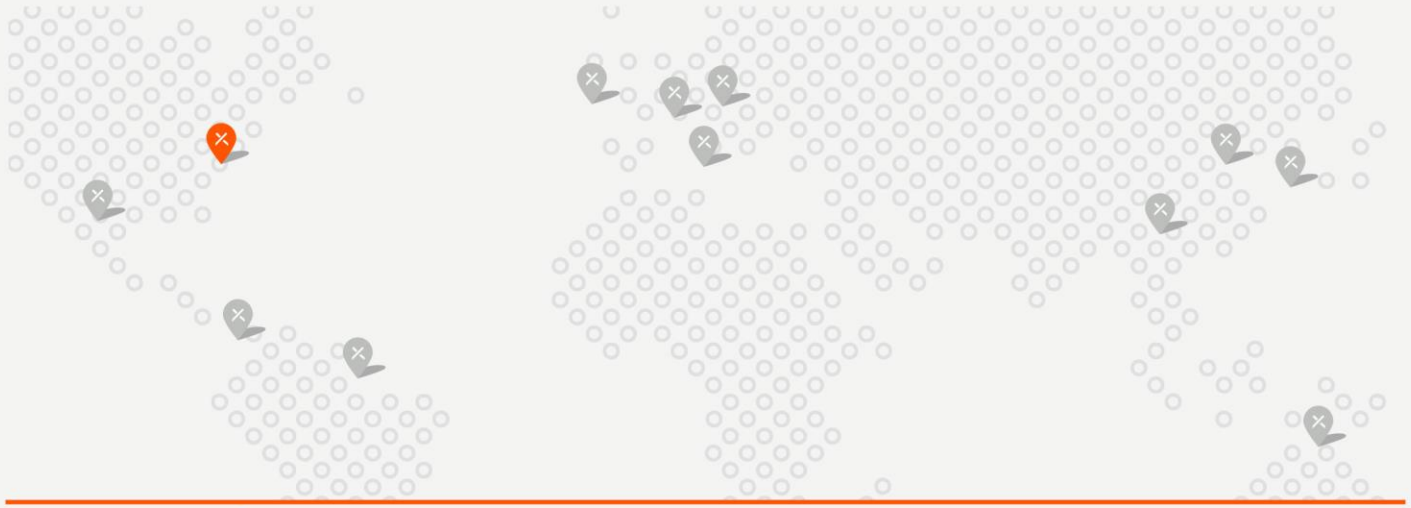
2024 EDITION

GLOBAL X
by Mirae Asset

Beyond Ordinary ETFs®

For more than a decade, our mission has been empowering investors with unexplored and intelligent solutions.

Headquartered in New York, with Global X ETFs listed throughout Europe, Asia, Latin America, and Australia.



$46bn in AUM across more than 200 ETF strategies[1]

Primary Listings by Office

United States
107 ETF Listings

Europe
34 UCITS ETF &
5 Crypto ETP Listings

Australia
35 ETF Listings

Latin America
32 ETF Listings
in Brazil & Colombia

Hong Kong
27 ETF Listings

Japan
36 ETF Listings

MIRAE ASSET
Building on principles

Global X ETFs is a fully-owned subsidiary of Mirae Asset Financial Group, a global industry leader with 55 offices and over 12,000 employees worldwide. Founded in 1997 as one of Asia's pioneering fund management companies, the Group now oversees **$565bn in client assets** across a portfolio that includes real estate, insurance, private equity, and venture capital.[2]

[1]As of October 31, 2023 [2]As of June 30, 2023

Charting Disruption 2024

Our future constantly develops and changes right in front of us. Yet much of the potential disruption seems unimaginable—until it happens.

Our flagship research project, Charting Disruption, aims to shed a quantifiable light on what the future may hold. It's where we explore the interplay between innovation and emerging technological as well as behavioral trends that can shape financial markets and their performance.

In charting potential disruption, we think it's helpful to zoom out to get a more complete view of where technology was and how far it's come. The advances in just the last 25 years alone prove momentous and the momentum of this trend of innovation continues.

It wasn't that long ago, for example, that people found it challenging to envision a world linked through smartphones and the internet. Before too long, most people won't be able to remember life without them.

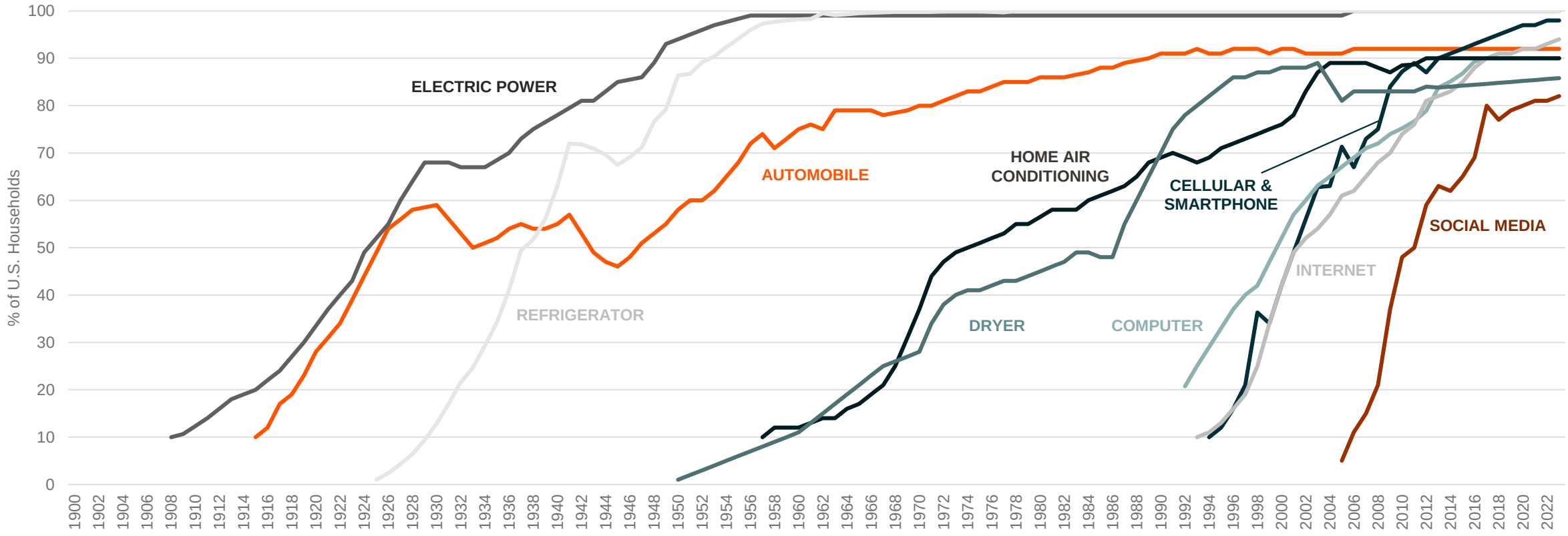
To explore the depth of changes like these, we partnered with handpicked experts in fields such as Artificial Intelligence, Digital Assets, CleanTech, Autonomous Vehicles, Genomics & Biotech, Battery Technology, and Food Innovation.

In what follows, we present unique forecasts, datasets, and analyses that reveal what we expect to disrupt our world in 2024 and beyond.

We hope you enjoy and gain a better understanding of what's possible.

Zooming Out for a Comprehensive View of Disruption

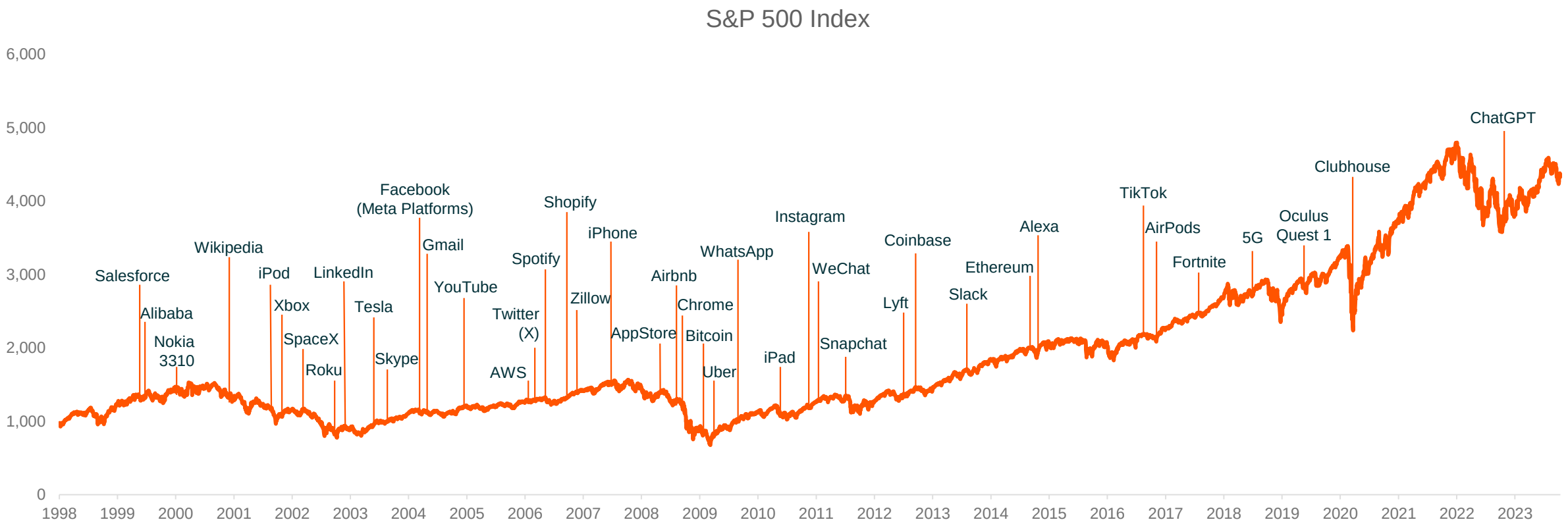
We may often underestimate how much the world can change within a lifetime. Recognizing past dramatic shifts can help us envision a vastly different world in the years or decades ahead.



Sources: Our World in Data. (2019, July 27). Share of United States Households Using Specific Technologies.

Things That Didn't Exist 25 Years Ago

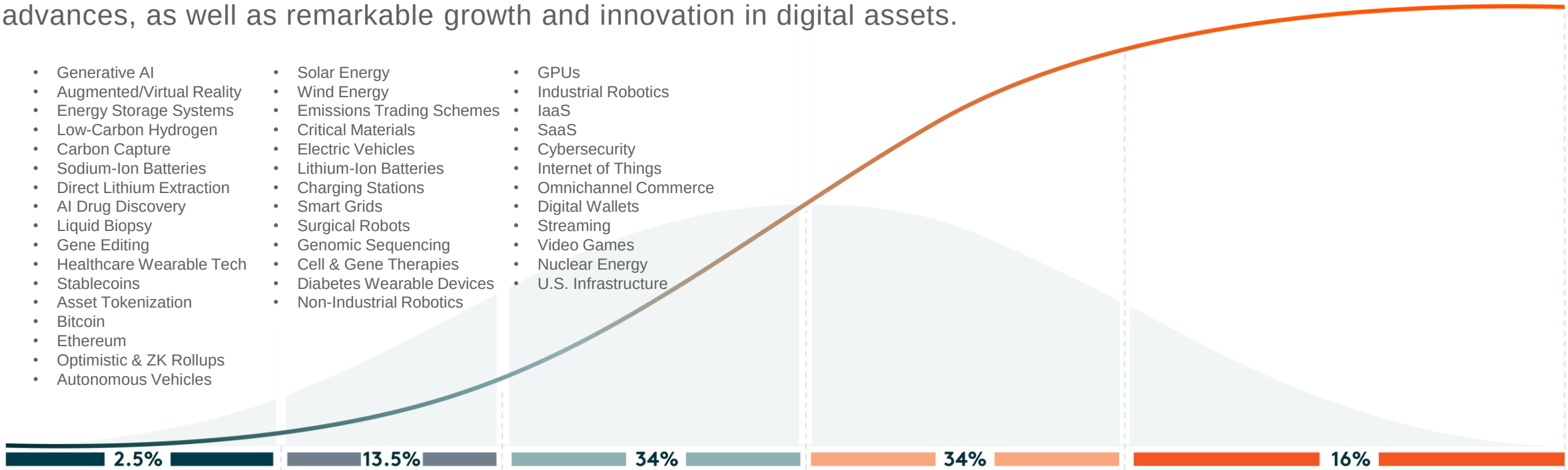
Throughout market cycles, innovation has not stopped. What's familiar to us today – social media, mobile payments, or e-commerce – was unimaginable to our ancestors a few generations ago.



Source: Bloomberg, L.P. (n.d.). [S&P 500 Index] [Data set]. Retrieved on October 13, 2023 from Global X ETFs Bloomberg terminal.

The Unimaginable Today Will Be Familiar Tomorrow

Anticipate a future marked by groundbreaking technologies, greener solutions to global issues, pioneering medical advances, as well as remarkable growth and innovation in digital assets.



INNOVATORS
Adoption starts slowly, as only a small group of Innovators take a chance on a new technology before it is proven or widely accepted.

EARLY ADOPTERS
Early Adopters accelerate and evangelize via word-of-mouth. This is often the tipping point, as Early Adopters convince others that a particular technology is worthwhile.

EARLY MAJORITY
Early Majority, we reach the part of the Adoption S-curve where the slope is the steepest, and hence the rate of adoption is at its fastest. In this phase, sales tends to explode.

LATE MAJORITY
Adoption continues growing at a solid pace as the Late Majority are convinced to participate, and the technology appears seemingly everywhere.

LAGGARDS
Finally, holdouts, begrudgingly acquiesce and accept/adopt a technology.

PHASES OF ADOPTION

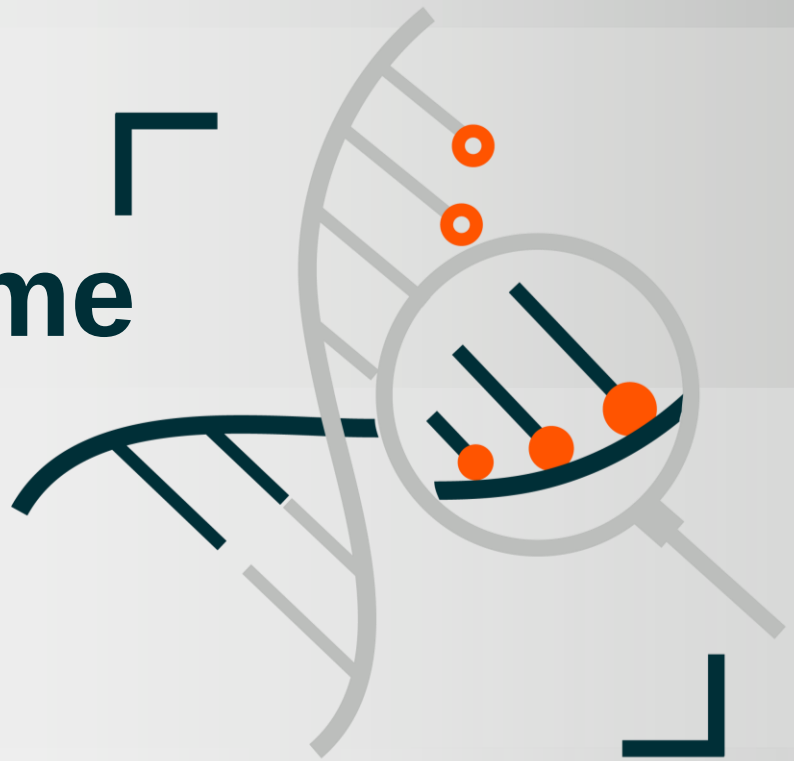
Displayed for illustrative purposes. Curve shape not indicative of mathematical transformation.

Charting Disruption 2024

Medical Breakthroughs

Medical Breakthroughs

Decoding the Human Genome



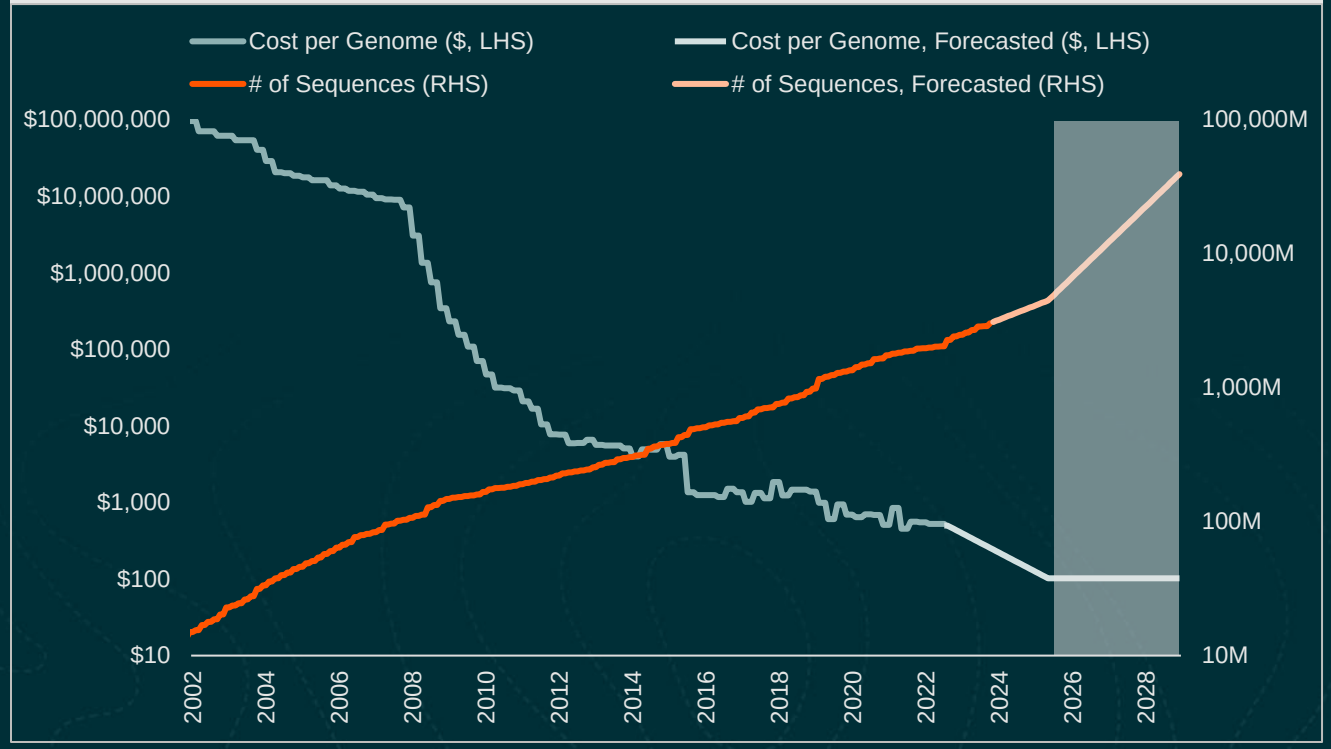
Secrets of Our Genetic Blueprint

Technological advancements have provided a stronger understanding of human biology than ever before, though questions remain regarding predispositions and links to illnesses. A new class of technological applications, however, provides a comprehensive toolkit for genomic diagnostics and life saving treatments. This allows for a clearer picture of how to improve human health and quality of life.

Reaching the Inflection Point for Genomic Adoption

Genomic sequencing technology has been used since the 1990s, though its potential for accessibility, diagnostics, and new customized treatments is just beginning to be tapped.

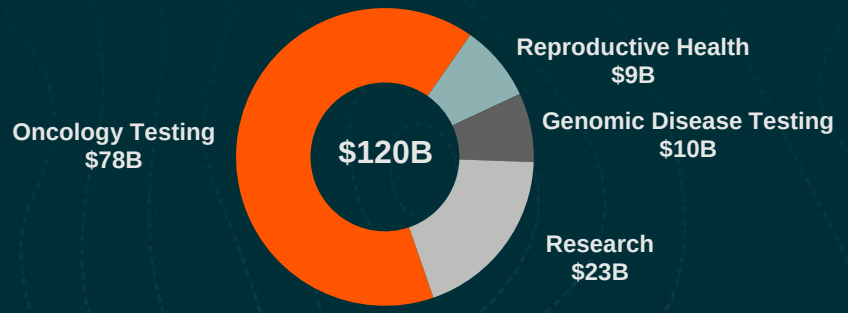
Sequencing Adoption to Accelerate as Cost Continues to Decline



The Sequencing Industry Is Poised for Rapid Expansion

- For genomic sequencing to reach its full potential, it requires tens of millions of individuals' sequencing to enable a comprehensive and unbiased study of the human genome. To date, 0.07% of the world's population has had their genome sequenced.[1]
- At $100 per genome sequence, the adoption of genomic technology is expected to accelerate, unlocking the industry's promise.[2] At a constant rate of decline, the milestone price of $100 per genome is expected by 2025.[3]
- Currently, the sequencing industry is only 7% penetrated, a figure expected to reach 14% by 2027.[4]

Genomic Sequencing Addressable Market, 2027



Sources: Text: 1. Illumina, 2023; 2. Nature, 2020; 3. Global X ETFs analysis of: National Human Genome Research Institute, n.d.; National Institute of Health, n.d.; 4. Illumina, 2023; Charts: Left: National Human Genome Research Institute, n.d.; National Institute of Health, n.d.; Right: Illumina, 2023

Genomics: Expanding Field Now Encompassing Multiple Technologies

Dr. Kieren Patel

Multi-omic analyses allow for an increasingly precise understanding of human biology, enabling improved diagnostic and therapeutic options.

Each –omic technology is a piece of the puzzle, contributing key information about biological and disease mechanisms.

	Genomics	Epigenomics	Transcriptomics	Proteomics
Study Of	DNA: Contains a person's unique genetic code and supplies the genetic instructions for life.	Modifications: Information not stored in the genome that can have a global impact on how DNA is (mis)regulated.	RNA: Carries forward DNA information to make proteins.	Proteins: Do most of the work in cells. Are required for the structure, function, and regulation of tissues and organs.
Informs	What could happen.	What is directionally happening.	What is directionally happening.	What is happening right now.
Market Size	$120 Billion[1]	$39 Billion[2]	$20 Billion[3]	$75 Billion[4]
By the Numbers	20,000 Genes[5]	100,000 Epigenomic Events[6]	100,000 Transcriptions[7]	1,000,000 Proteoforms[8]
Primarily Used To Analyze	Whole Genome: Analyzes the whole genome to discover novel genomic variants and identify previously unknown variants for future studies. Whole Exosome: Analyzes structures released by cells that are critical for cell-to-cell communication.	Chromosome Profiling: Analyzes "hot spots" where transcription activity is high and related cell functions. Methylated DNA Markers: Analyzes modifications to DNA that regulate transcription and correlate with disease.	Single-Cell Whole Transcriptome: Analyzes all transcripts in a cell to discover cell types, behaviors, and cell-cell interactions. Gene Expression Panels: Identifies which genes are active or inactive and impact on transcription processes.	Mass Spectrometry: Can detect and measure specific proteins, including post translational modifications. High/Low Plex Protein Detection: Can detect and measure the levels of multiple proteins simultaneously.
Useful For	Non-Invasive Prenatal Testing [NIPT] Tumor and Liquid Cancer Biopsies	Cancer Liquid Biopsy Biological Age Assessments	Immune Cell Profiling Reflex Pathways in Cancer Cells	Immunohistochemistry (IHC) Drug Discovery

Sources: Text: 1. Illumina, 2023; 2. Grand View Research, 2022a; 3. Grand View Research, 2022b; 4. The Analytical, Life Science & Diagnostics Association, 2021; 5. National Institute of Health, n.d.; 6. Nature, 2021; 7. National Institute of Health, n.d.; 8. Ibid.

Multi-omics Technologies: Converging Product Lineup Facilitating Growth

Dr. Kieren Patel

Ongoing efforts to improve data integration and system interoperability will play a key role in the multi-omic industry's growth prospects.

	Genomics	Transcriptomics	Proteomics
Thermo Fisher Scientific	Short-Read Sequencing	RNA Sequencing, Gene Expression Sequencing	Mass Spectrometry
Danaher Corporation			Mass Spectrometry, Immunoassays, Antibodies
NanoString Technologies		Spatial Biology	
Agilent Technologies			Mass Spectrometry
BGI Genomics	Short-Read Sequencing	RNA Sequencing	Mass Spectrometry
Illumina	Short-Read Sequencing, Long-Read Sequencing	RNA Sequencing	
Bio-Techne			Immunoassays, Antibodies
10X Genomics		Gene Expression Sequencing	Spatial Biology
Olink Holding			High-Plex
Oxford Nanopore	Long-Read Sequencing	RNA Sequencing, Gene Expression Sequencing	
Pacific Biosciences	Short-Read Sequencing, Long-Read Sequencing	RNA Sequencing	

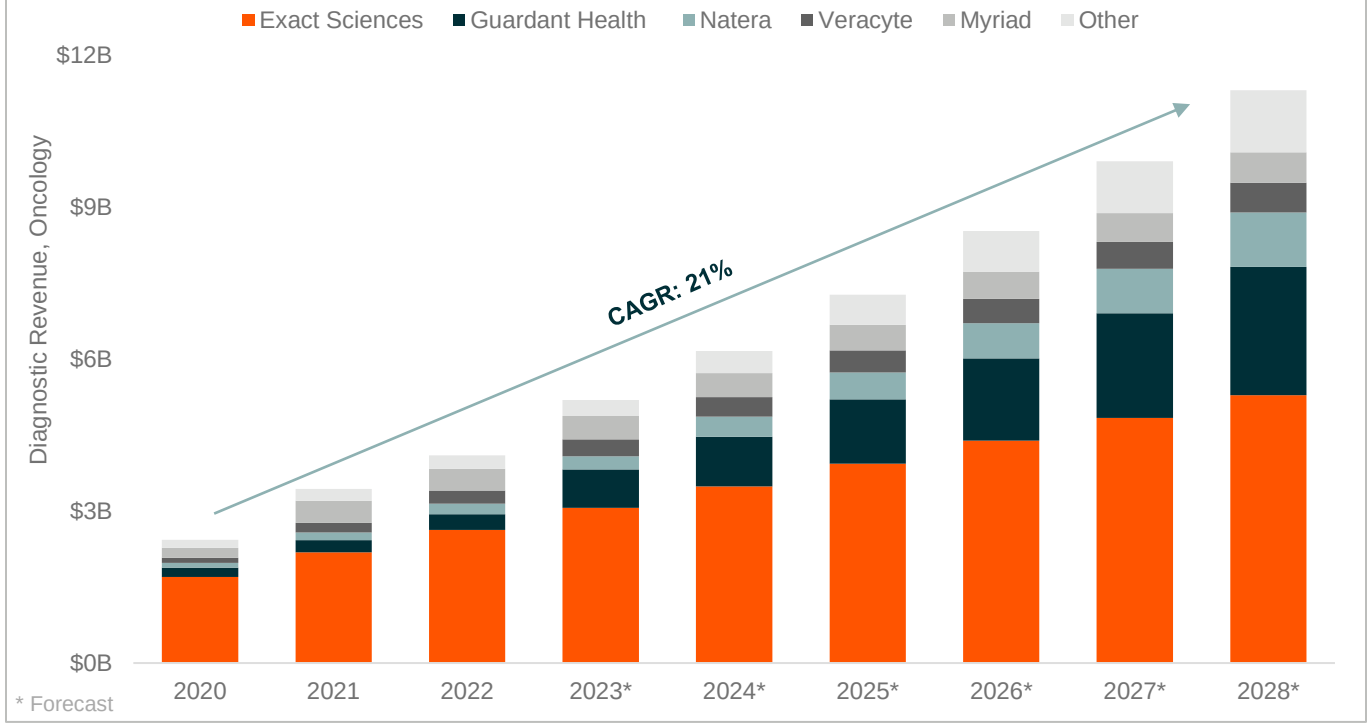
Note: Firms sorted by market capitalization as of November 15, 2023.

Sources: Thermo Fisher Scientifics, n.d.; Danaher Corporation, n.d.; NanoString, n.d.; Agilent Technologies, n.d.; BGI Genomics, n.d.; Illumina, n.d.; Bio-Techne, n.d.; Qiagen, n.d.; 10X Genomics, n.d.; Olink Holding, n.d.; Oxford Nanopore, n.d.; Pacific Biosciences, n.d.

New Diagnostic Opportunities Prompted by Multi-omic Capabilities

Multi-omic technologies have greatly enhanced physicians' diagnostic capabilities and now inform every step of patient care routine health checks to recurrence monitoring.

Oncology Diagnostics: Gaining Speed



Increasing Utility of Diagnostic Tests

The role of diagnostic aids has increased in importance, given that they now inform physicians across the entire care continuum.

- Health Check: Routine test for presence of disease-specific biomarkers in asymptomatic individuals.
- Diagnostic Aid: Informs diagnosis in suspected cases, such as patients with underlying symptoms.
- Therapy Guidance: Helps identify if a patient has a specific biomarker that is targeted by a commercially available drug. Helps predict response, and thus determines if the patient should receive the treatment.
- Intervention Outcome: Measures presence of the illness during treatments. Helps determine patient response to treatment.
- Recurrence Monitoring: Measures presence of illness during remission to monitor any potential recurrence of the disease.

Oncology Sector Has Validated Diagnostic Promise

The most mature segment is the oncology testing sector with a $78 billion market opportunity.[1]

Sources: Text: 1. Illumina, 2023; Chart: Evaluate Pharma, n.d.

New Diagnostic Opportunities: Neurological Disorders Present Highest Unmet Need

Neurological disorders are notoriously difficult to diagnose, though new blood-based and plasma-based tests offer a more accurate and cost-effective alternative to traditional methods.

Therapeutic Innovation Emphasizes Need for Improved Diagnostics

The Alzheimer's space has been gaining attention following the Food and Drug Administration's approval of Eisai's Leqembi and the expected approval of Eli Lilly's Donanemab by year-end.[1] Spurred by exciting developments like these, the Alzheimer's treatment category is expected to grow to $11.7 billion by 2028 from $747 million in 2022.[2]

The adoption of these novel treatments, however, relies on clinicians being able to identify which patients are most suitable for treatment. This problem has spurred innovation to improve the diagnostic capabilities to identify and categorize Alzheimer's patients.

Non-Invasive Multi-omic Tests Offer a Solution

Diagnosing Alzheimer's traditionally relies on expensive PET scans or measuring biomarkers in spinal fluid, collected via a lumbar puncture. These methods can be difficult in practice and struggle to identify early stages of the disease. Capacity issues are also notable, with only about 2,000 PET centers in the United States.[3]

New blood-based and plasma-based alternatives offer a more scalable, less invasive, alternative with the goal of identifying Alzheimer's presence even before a patient is symptomatic. These alternatives can serve an $8 billion market.[4]

	PET Scan	CSF Test	Blood or Plasma-Based Tests
Definition	Positron emission tomograph (PET) scans show how organs and tissues are working.	Cerebrospinal fluid (CSF) carries waste out of the brain, potentially including proteins that point to Alzheimer's.	DNA and protein material in the blood can point to Alzheimer's.
Average Cost	$5,000[5]	$1,000[6]	$400[7]
Capacity	Low	Medium	High
Precision	Medium	High	Medium

Sources: Text: 1. STAT News, 2023; 2. Evaluate Pharma, n.d.; 3. STAT News, 2023; 4. Quanterix, 2023; 5. University of California, 2023; 6. Ibid; 7. Scientific American, 2023

Pharmaceutical & Diagnostic Conversion Accelerating Genomic Adoption

Dr. Kieren Patel

Growing efforts from pharmaceutical firms to partner with or acquire diagnostics firms will help drive adoption of genomic technologies and further refine diagnostic capabilities.

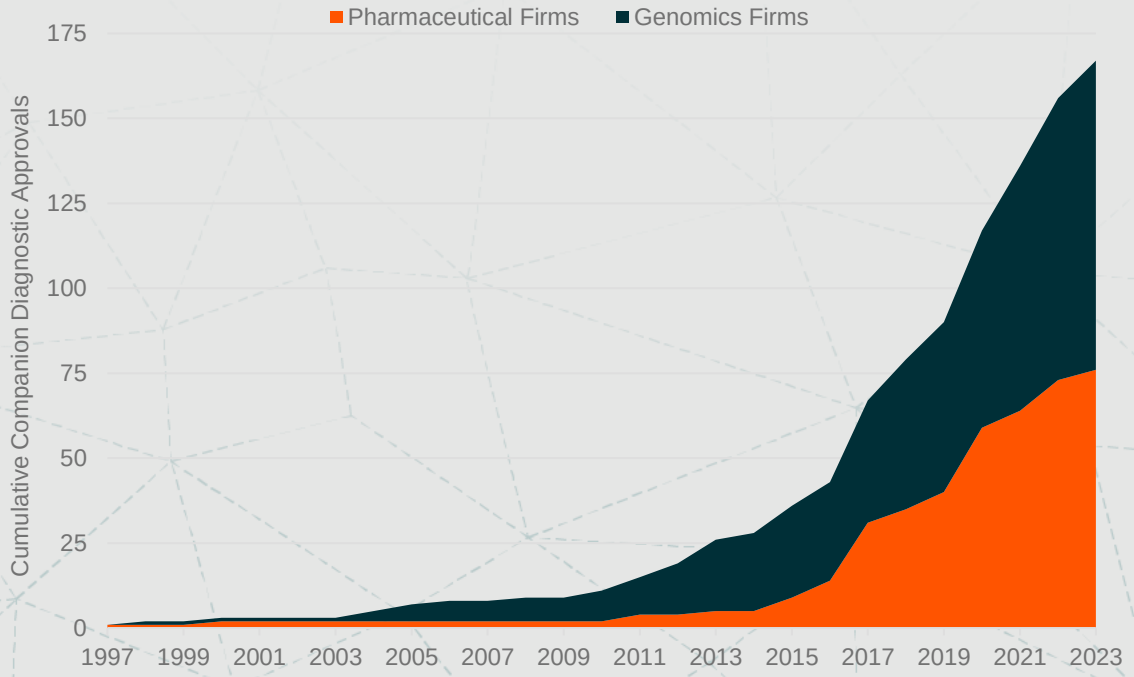
Genomic Profiling Increasingly Informs Therapeutic Intervention

- Companion diagnostics (CDx) tests are used to help match patients to a specific therapy or drug by identifying possible driving factors for the illness. These tests look for possible gene changes or biomarkers in the patient's sample that commercially available drugs target. The tests can also shed light on potential side effects and measure how well the treatment is working.
- These tests play an increasingly important role in the success of investigational treatments and the widespread adoption of approved therapies. As a result, pharmaceutical and biotechnology firms continue to prioritize partnerships and acquisitions to strengthen diagnostic capabilities.

Successful Diagnostic Factors Inform Therapeutic Intervention

- Prioritizing Scalable Diagnostics: Diagnostic results should be robust, repeatable, and clear with simple positive/negative readouts. Workflows should be simple enough to be easy and cost effective for doctors to incorporate. This ensures broad adoption and clinician support.
- Emphasis on Actionable Insights: Excessive reports that are time-consuming and difficult to interpret will have limited adoption, given the room for misinterpretation. Measuring the data that matter allows doctors to tailor patient care accordingly and avoid the noise that adds to the complexity and cost of care.

Pharma Companies Expanding Role in Diagnostics

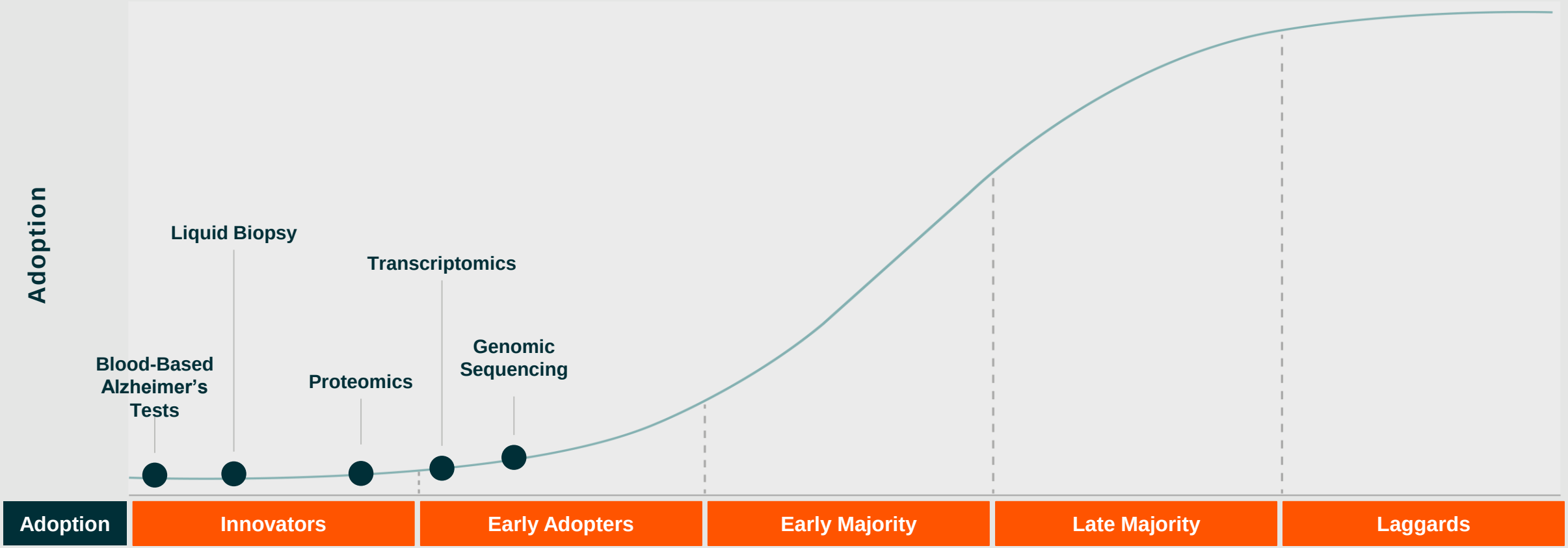


Notes: 2023 approvals as of October 6, 2023. Roche is only pharmaceutical firm in above.

Source: Food and Drug Administration, n.d.

Decoding the Human Genome: S-Shaped Curve of Adoption

We expect $17 billion in revenue for the global sequencing industry by 2027, doubling the 2023 total.[1]



Note: For illustrative purposes only.
Source: Text: 1. Illumina, 2023

Medical Breakthroughs

Therapeutics

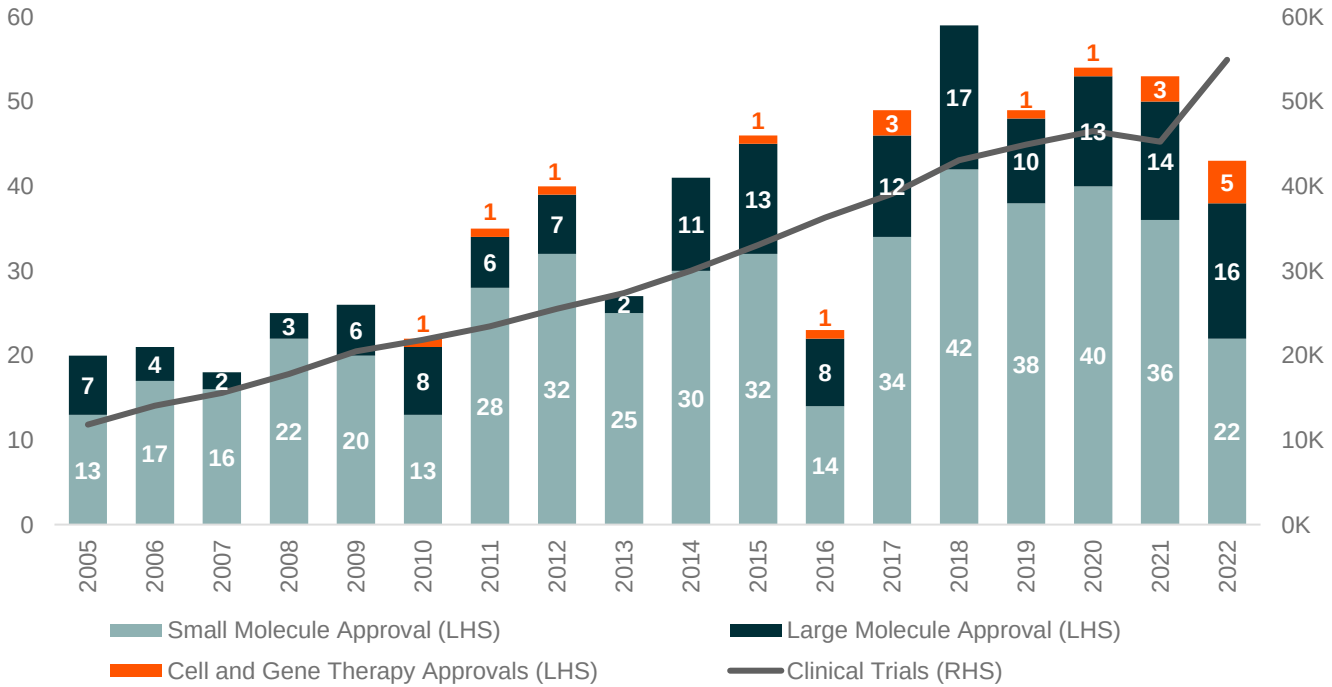
Shaping Personalized Medicine

Genomic technologies have opened the door for a new era of drug discovery. Such advancements are revolutionizing disease management and illness prevention, resulting in superior patient outcomes. Newer genomic treatments, like gene therapies and genomic editing, offer near-cures for highly cumbersome illnesses.

Therapeutic Development: A New Era of Drug Discovery Is Underway

Validation and adoption of genomic technologies have accelerated development of highly targeted treatments and regulatory approvals. New drug categories, such as cell and gene therapies, seek to further improve drug efficacy.

Increasingly Complex Treatments Offer New Efficacy Standards



Small Molecule Drugs consist of small, simple chemical structures and are usually administered orally.

Large Molecule Drugs (aka Biologics) are made from living cells, tissues, and viruses. They are administered via injections or infusions.

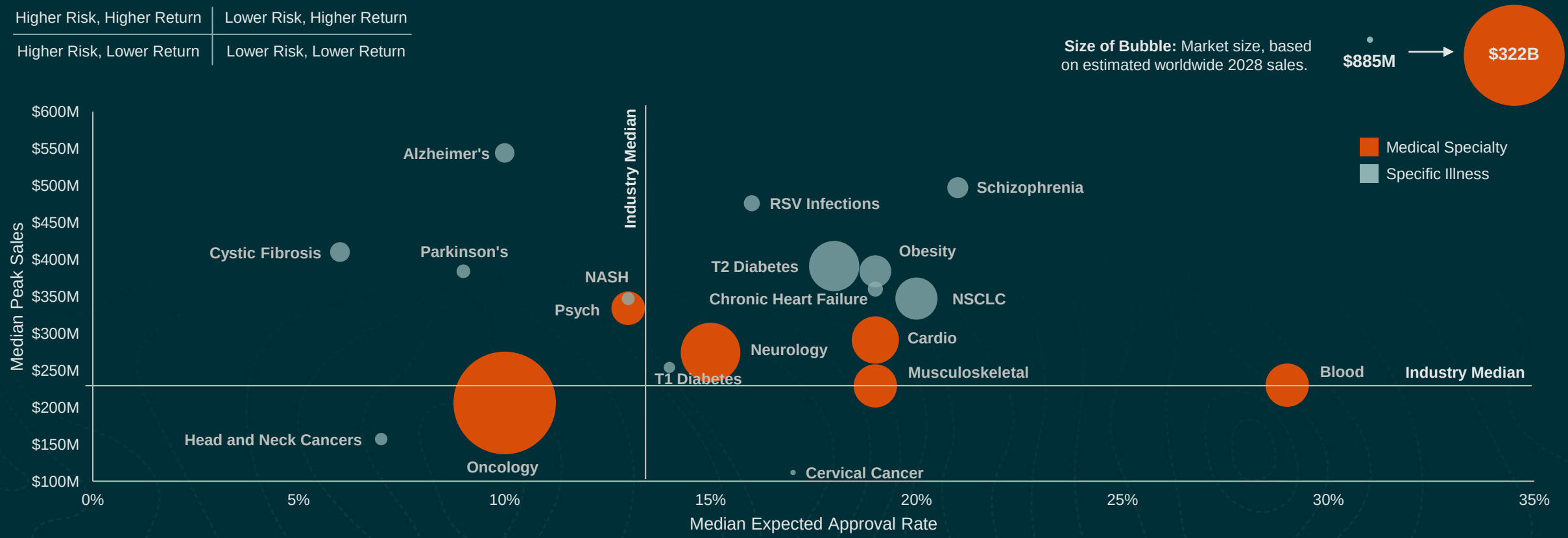
Cell and Gene Therapies rely on living cells and genetic alterations to repair, replace, or restore damaged tissue and treat illnesses. This is a relatively new treatment category and is traditionally administered via infusions.

Historically, the medical community has been limited in how it can address diseases. With an increased understanding of illnesses and new therapeutic technologies, the medical community now has additional opportunities for improved treatments across virtually all disease categories.

Sources: Food and Drug Administration, n.d.a; Food and Drug Administration, n.d.b; World Health Organization, 2023

Therapeutic Innovation Evident Across a Wide Spectrum of Illnesses

The prioritization of therapeutic development is influenced by unmet medical need, size of the patient population affected, historical success in treating the illness, and the competitive landscape.

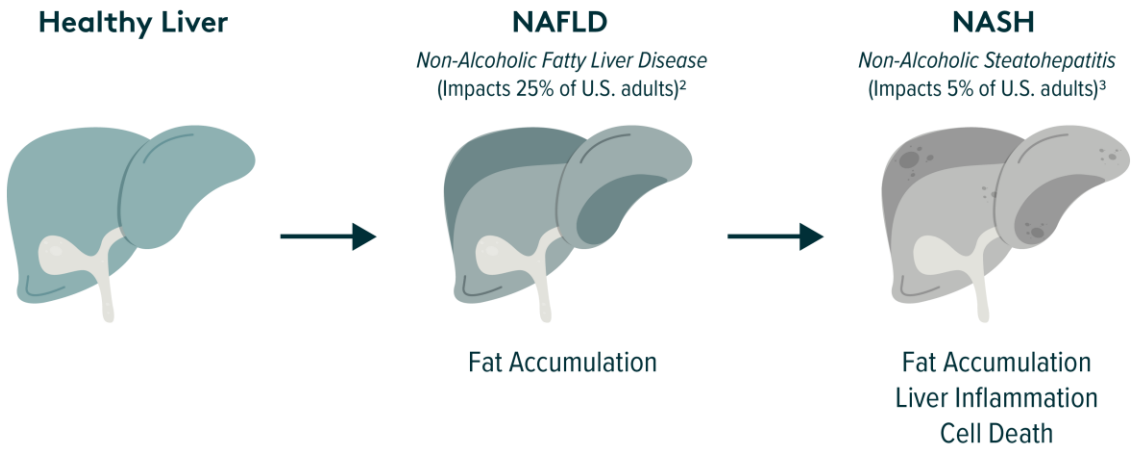


Source: Evaluate Pharma, n.d.

Case Study: Non-Alcoholic Fatty Liver Disease (NAFLD)

NAFLD is a high-risk, high-return category for therapeutic development given the lack of available treatments and scale of affected patients. The annual cost of managing NAFLD in the United States is $103 billion.[1]

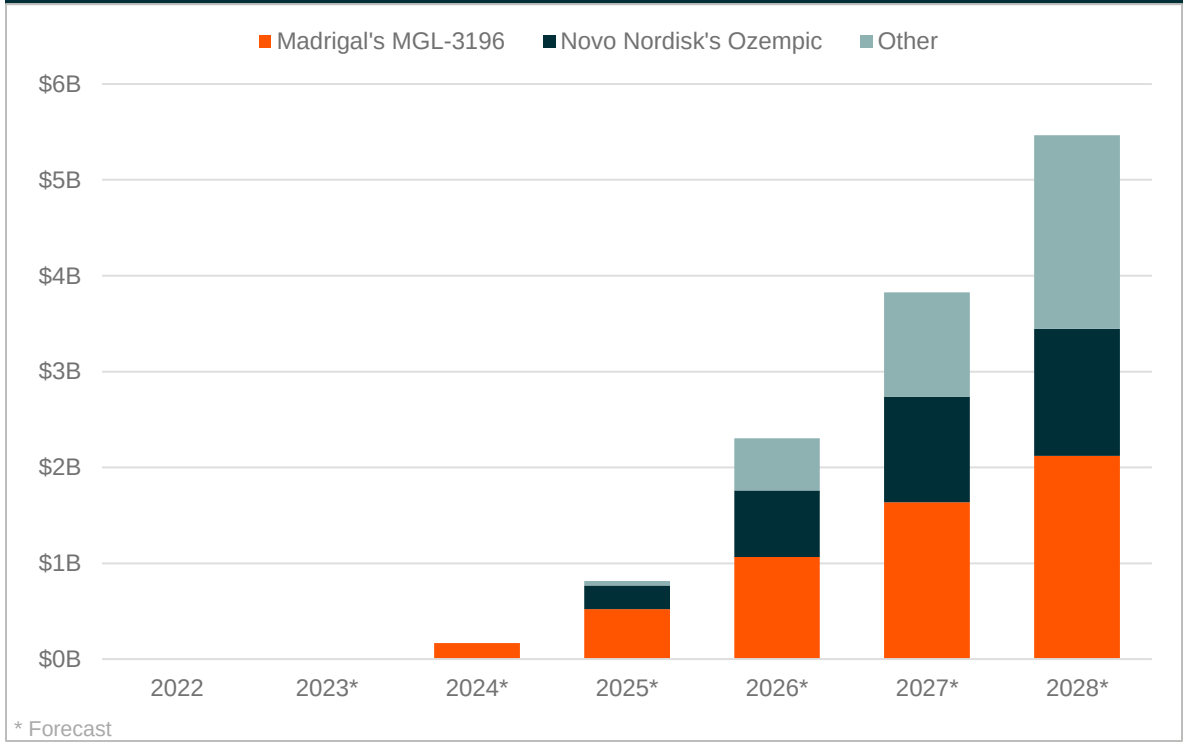
NAFLD: Growing Market for Diabetes Drug Treatments



NAFLD and NASH currently have no approved treatments. As cases continue to largely go untreated, NASH prevalence is projected to increase 63% between 2015 and 2030.[4]

Given overlap in risk factors between diabetes and liver disease, diabetic treatment Ozempic is expected to be the second highest grossing treatment for NAFLD and NASH by 2028.[5,6] Up to 75% of people who are overweight and 90% of individuals with extreme obesity have NAFLD.[7]

Expected Market Winners for NAFLD and NASH



Note: NAFLD is also recently referred to as metabolic dysfunction-associated steatotic liver disease (MASLD). NASH is also recently referred to as metabolic dysfunction-associated steatohepatitis (MASH).

Sources: Text: 1. National Institute of Health, 2016; 2. American Liver Foundation, 2023-Aug; 3. Ibid; 4. American Liver Foundation, 2023-Sep; 5. Evaluate Pharma, n.d.b; 6. Evaluate Pharma, n.d.a; 7. National Institute of Health, 2019. Chart: Evaluate Pharma, n.d.a; Evaluate Pharma, n.d.b

Preventative Healthcare: Treating Obesity, a Starting Point for Better Health

FDA-approved diabetes drugs have become household names for their success in achieving weight loss in obese patients. Now the healthcare industry seeks to replicate success in cardiac and metabolic illnesses.

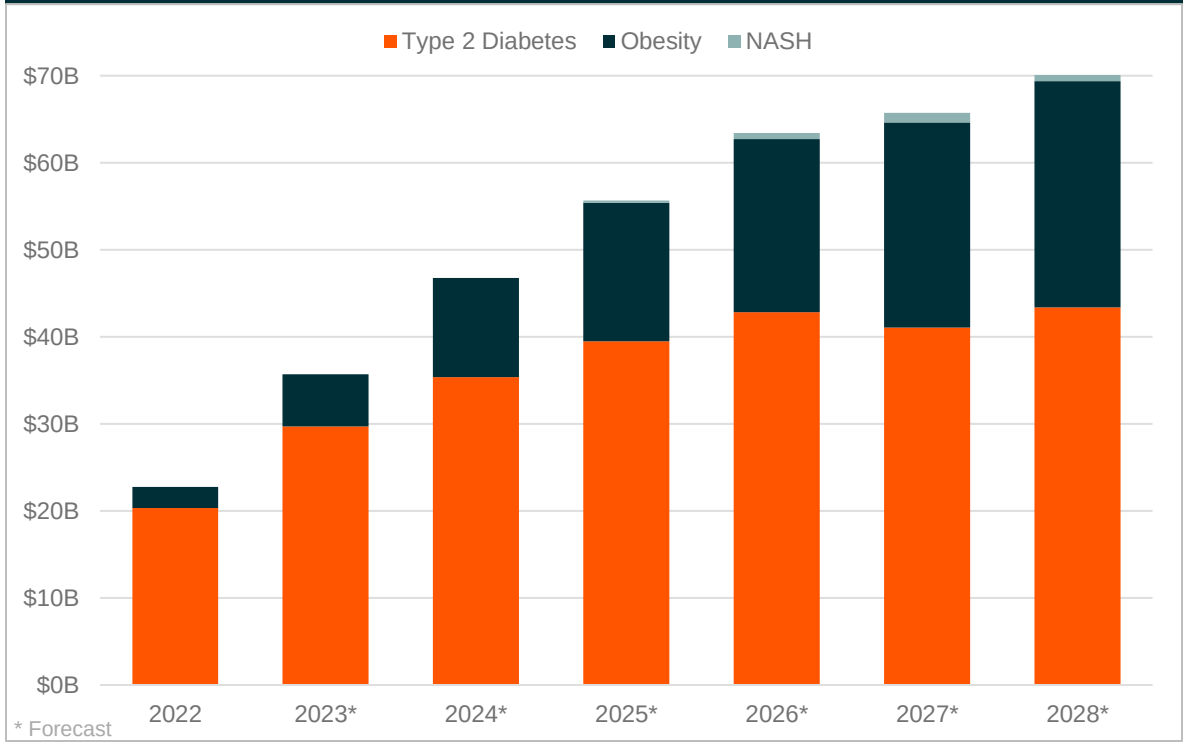
Obesity Is a Primary Risk Factor in Multiple Diseases

The obesity market is expected to be worth over $100 billion by the end of the decade, up from $2.8 billion today.[1,2] Global obesity rates have nearly tripled since 1975, increasing prevalence rates for related disorders.[3]

	Increased Risk	Annual Cost in United States
Type 2 Diabetes (T2D)	Obesity accounts for 80–85% of the risk of developing T2D.[4]	$380 billion[5]
Cardiovascular Disease	Obesity accounts for up to 78% of hypertension cases.[6]	$320 billion[7]
Liver Disorders	Up to 90% of obese individuals have NAFLD.[8]	$103 billion[9]

Glucagon-like peptide-1 (GLP-1) treatments, like Ozempic and Mounjaro, were developed for type 2 diabetes. As they also show the ability to curb hunger, their potential use for obesity and obesity-driven illnesses is a promising development. Patients undergoing GLP-1 treatments have experienced weight loss of up to 22.5% of their body weight, rivaling weight loss from gastric bypass and sleeve gastrectomy surgeries.[10]

GLP-1 Market: Growing Utility Across Multiple Illnesses



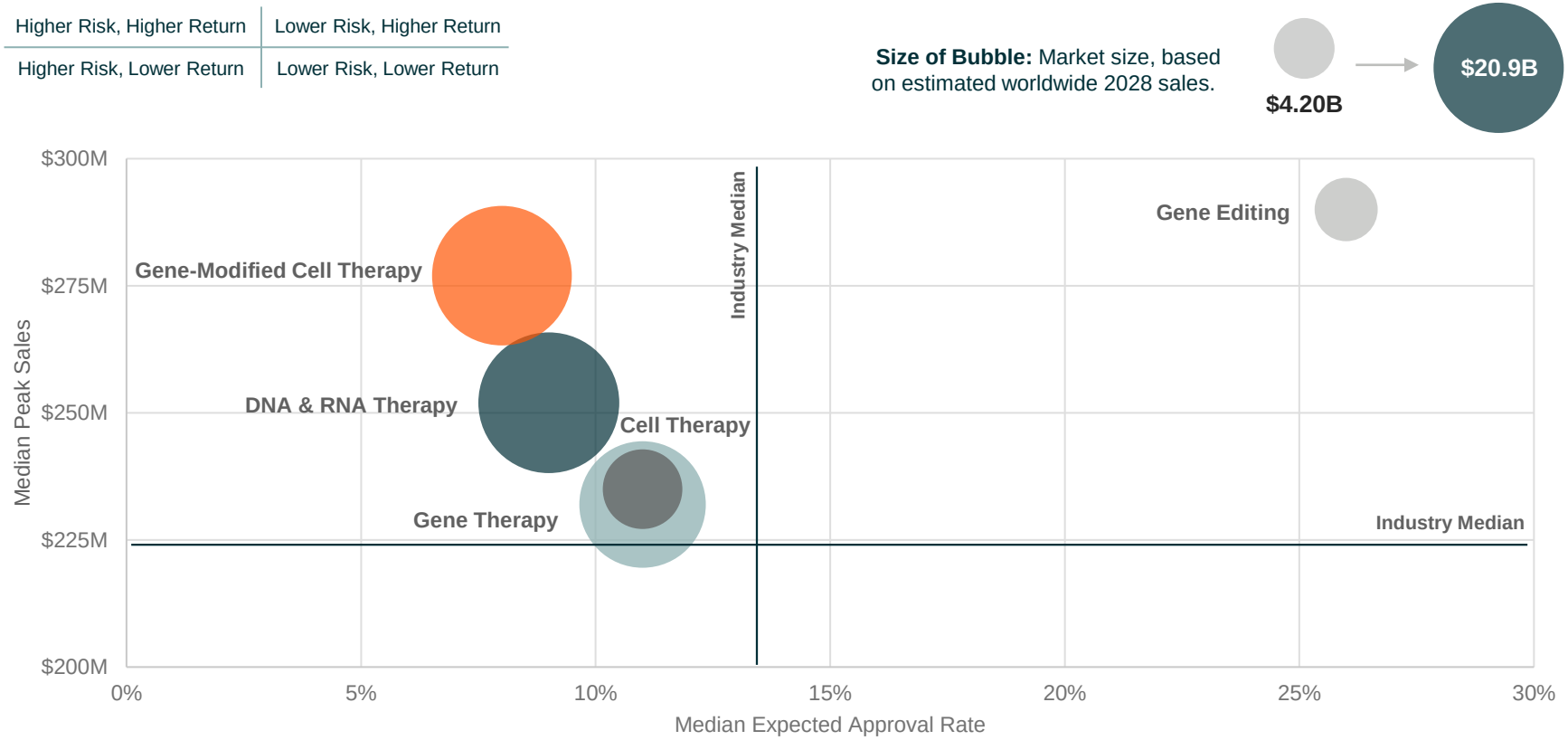
Sources: Text: 1. Barron's, 2023; 2. Evaluate Pharma, n.d.; 3. World Health Organization, 2021; 4. Diabetes U.K., 2022; 5. International Diabetes Federation, 2021; 6. National Institute of Health, 2020; 7. American Heart Association, 2021; 8. National Institute of Health, 2019; 9. National Institute of Health, 2016; 10. Eli Lilly, 2022; Chart: Evaluate Pharma, n.d.a; Evaluate Pharma, n.d.b

An Arsenal of Investigational Technologies to Combat Illnesses

The pharmaceutical industry now has numerous technologies to address, and ultimately cure, common diseases.

Novel Technologies Give Hope

- **Gene Editing:** Editing parts of the genome by removing, adding, or altering sections of DNA.
- **Cell Therapy:** Transplanting healthy human cells to replace or repair damaged tissue and/or cells.
- **Gene Therapy:** Replacing a defective or missing gene in a patient's cells with a healthy version of that gene.
- **DNA & RNA Therapy:** Providing instructions to the body's RNA for making proteins or turning genes on and off.
- **Gene-Modified Cell Therapy:** Transplanting genetically modified cells to fight disease.

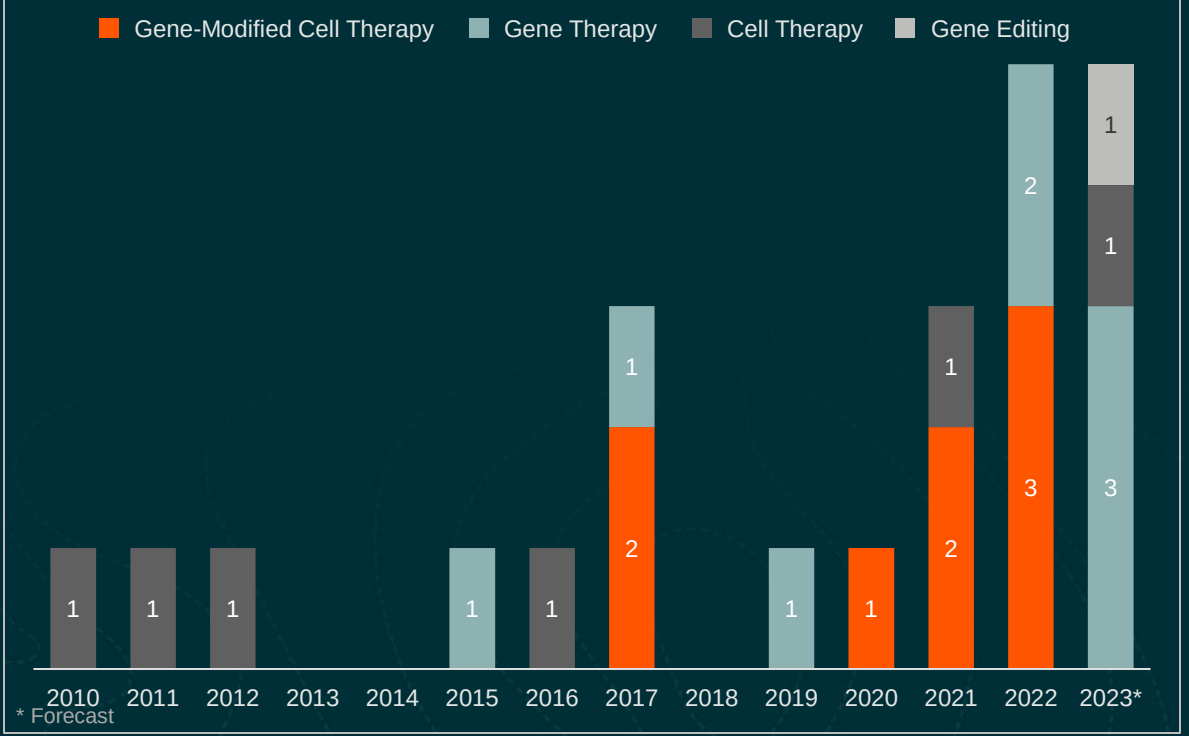


Source: Evaluate Pharma, 2023

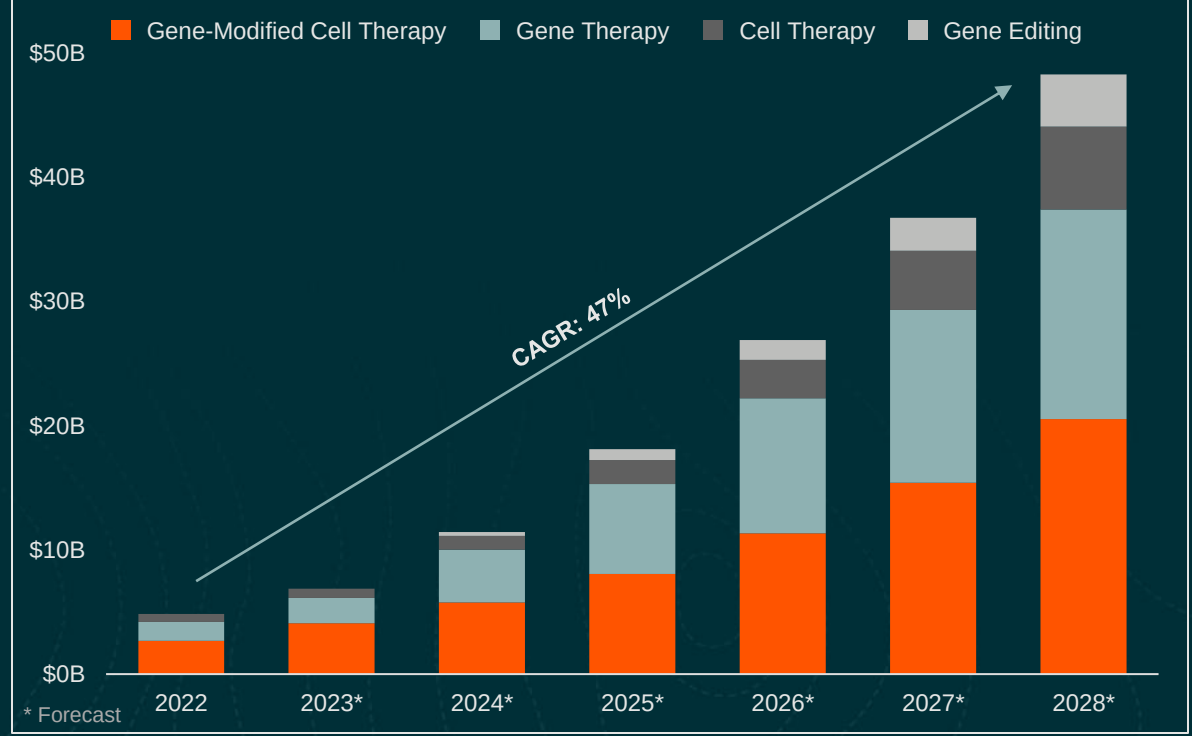
Genomic Medicines: Gaining Momentum

We believe 2023 will mark a breakout year in the genomic medicines space and the beginning of the gene editing market, which is expected to be worth nearly $4.2 billion by 2028.[1]

Approvals Ramping Up: Confirming Genomic



Genomic Medicines: Validation of Sector Driving Growth



Sources: Text: 1. Evaluate Pharma, n.d.; Charts: Left: Food and Drug Administration, n.d.; Right: Evaluate Pharma, n.d.a; Evaluate Pharma, n.d.b; Evaluate Pharma, n.d.c; Evaluate Pharma, n.d.d

Genomic Medicines: Price to Value Analysis

New therapeutic categories offer one-time treatment alternatives for cumbersome illnesses, changing drug pricing strategies. Though treatments seem more expensive at face value, new methods offer a longer-term economic benefit.

Therapy	Indication	E.U. Approval	E.U. Pricing	U.S. Approval	U.S. Pricing
Bluebird's Zynteglo	Thalassemia	Jun 2019	Withdrawn	Aug 2022	$2,800,000
Novartis' Zolgensma	SMA	May 2020	€1,900,000	May 2019	$2,125,000
Bluebird's Skysona	Cerebral ALD	Jul 2021	Withdrawn	Sep 2022	$3,000,000
BioMarin's Roctavian	Hemophilia A	Aug 2022	€1,500,000	Jun 2023	$2,500,000

Note: SMA = Spinal Muscular Atrophy; ALD = Adrenoleukodystrophy

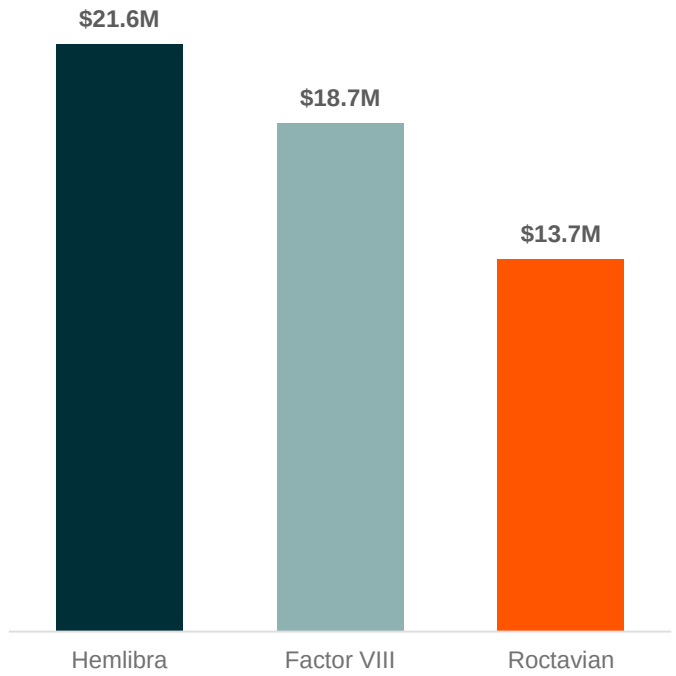
Are the High Prices Justified?

Hemophilia A is a genetic disorder caused by missing or defective Factor VIII, an important clotting protein. This disorder can result in spontaneous bleeding or disproportionate bleeding following an injury.

- Gene Therapy Advantage: Roctavian is a one-time gene therapy that reduces bleeding rates by 85%.[1] Though the dose cost is significantly higher, the infrequency of administration compared to alternative treatments awards Roctavian significant lifetime cost-of-care savings up to $7.9 million.[2]
- Shortfalls of Traditional Treatment: Hemlibra is a once weekly injection that can result in up to $482,000 in annual costs.[3] In contrast, Factor VIII, administered via an infusion as frequently as every day, results in an estimated $265,000 annual cost.[4]

Given the curative intent of gene therapies, a different pricing framework is needed. For example, some firms created outcome-based policies. Bluebird will offer up to an 80% refund of the price of its thalassemia gene therapy, Zynteglo, if the patient does not see a sustained response up to 2 years after administration.[5]

Lifetime Cost of Care: Hemophilia A

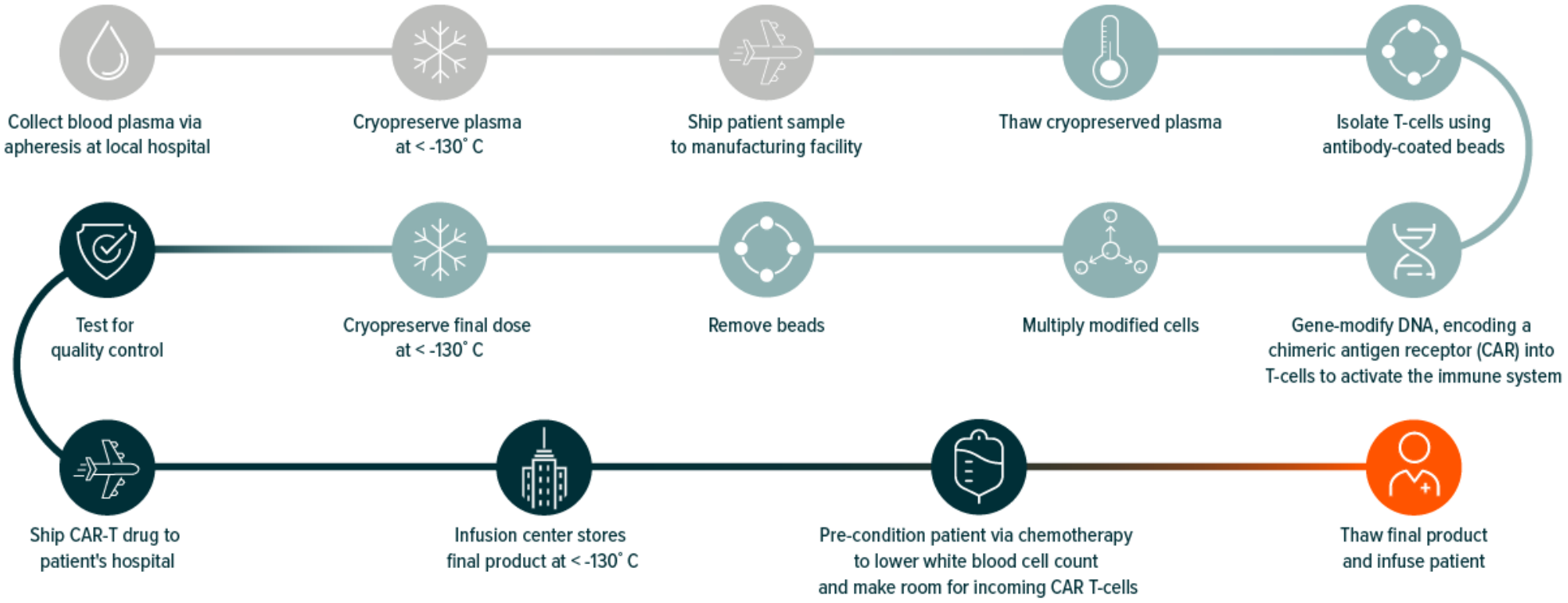


Sources: Text: 1. European Medicines Agency, 2022; 2. National Institute of Health, 2021-May; 3. Fierce Healthcare, 2018; 4. National Institute of Health, 2021-Mar; 5. Bloomberg Intelligence, 2023; Charts: Left: Bloomberg Intelligence, 2023; Right: National Institute of Health, 2021

Genomic Medicines: High Prices Driven by Cumbersome Manufacturing Guidelines

Manufacturing genomic medicines is incredibly complex. Manufacturing can take 2–3 weeks for cell therapies and up to 3 months for gene therapies, with input costs ranging from $100,000 to $300,000 per dose.[1,2,3]

Manufacturing Process for CAR-T Gene-Modified Cell Therapy

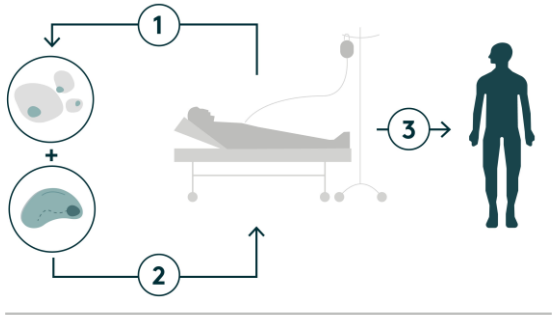


Sources: Text: 1. University of Pittsburgh Medical Center, n.d.; 2. Bluebird Bio, 2023; 3. Genetic Engineering & Biotechnology News, 2023

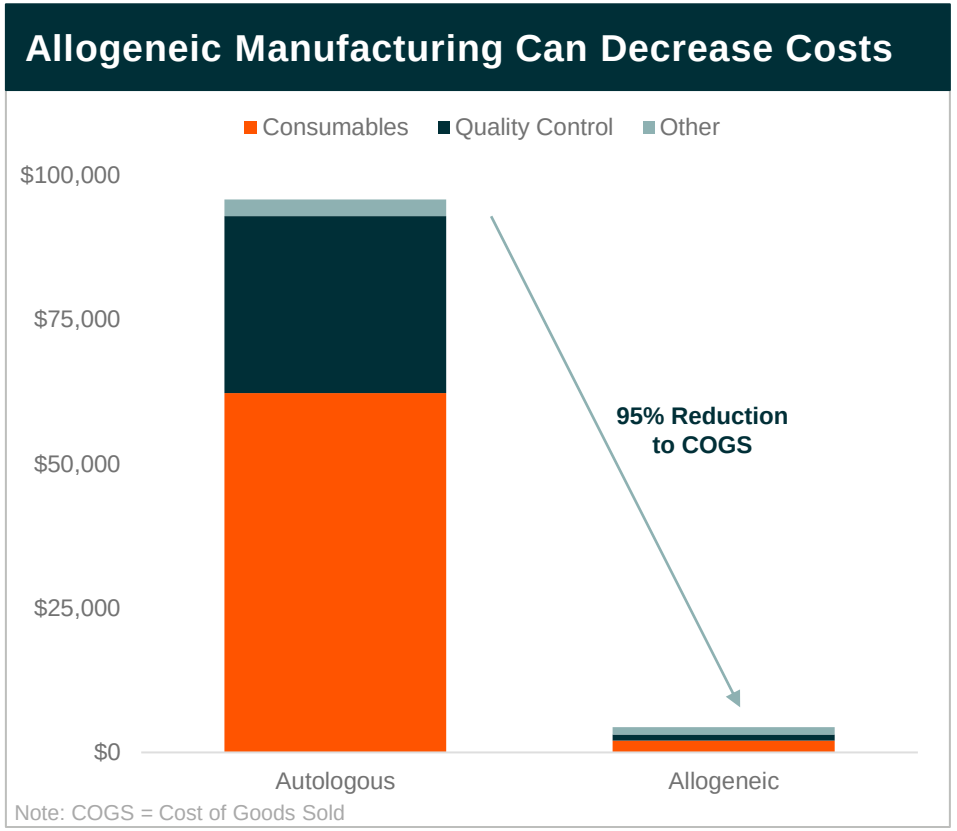
Wide-Scale Availability of Cell and Gene Therapies Depends on Manufacturing Improvements

Investigational methods like allogeneic manufacturing seek to improve manufacturing costs, turnaround times, and supply, which can help drive changes in reimbursement coverage and develop industry best practices.

Autologous Manufacturing:
The patient's own cells are extracted, edited, and then returned to the patient to combat an illness.



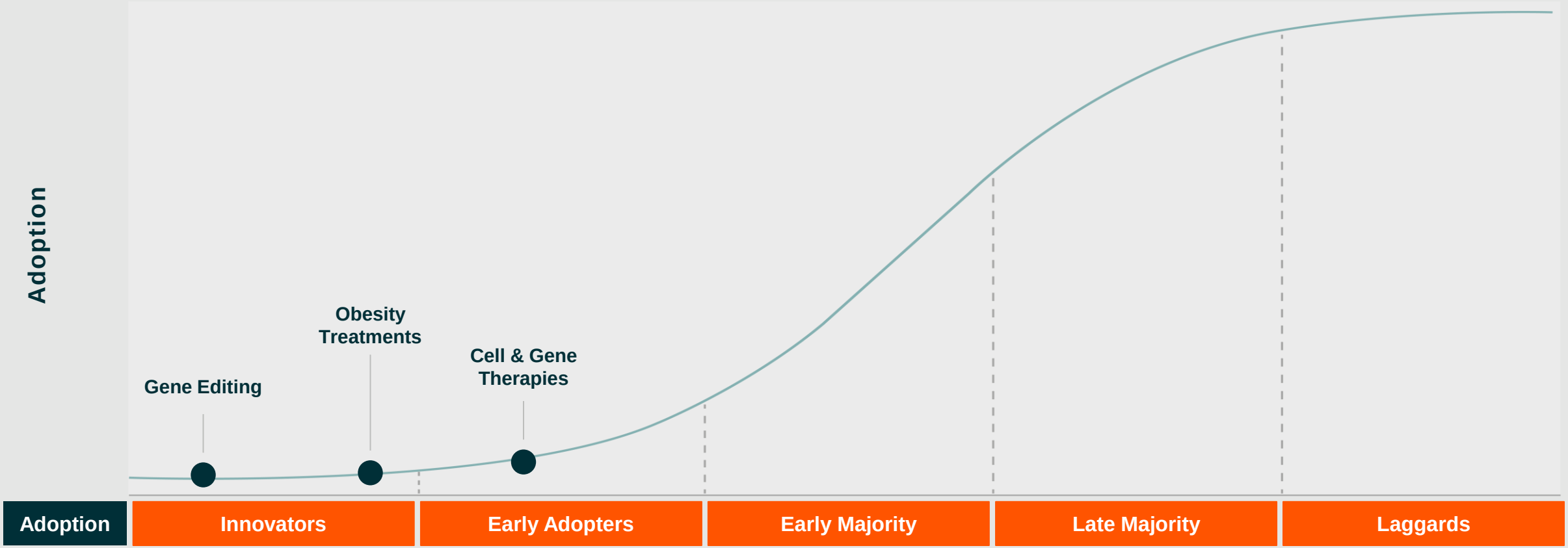
Allogeneic Manufacturing:
Donated cells are edited and delivered to the patient to combat an illness. This method is more scalable and cost effective.



Source: International Society for Cell & Gene Therapy, 2019

Therapeutics: S-Shaped Curve of Adoption

We expect genomic medicines to comprise 6% of the $1.24 trillion pharmaceutical market in 2028, up from 1% of the $895 billion market in 2022.[1]



Note: For illustrative purposes only.

Sources: Text: 1. Evaluate Pharma, n.d.a; Evaluate Pharma, n.d.b; Evaluate Pharma, n.d.c; Evaluate Pharma, n.d.d; Evaluate Pharma, n.d.e; Evaluate Pharma, n.d.f

Medical Breakthroughs

Digitizing Medicine

AI, Surgical Robots & More

The only thing more complex than human biology may be the systems used to facilitate patient care. Friction and inefficiencies abound. Against this backdrop, digital health is primed as a solution. By leveraging digital health technologies, such as artificial intelligence (AI) and wearable sensors, we expect improved patient outcomes and greater access to life-saving genomic treatments. With healthcare spending now an estimated 11% of global GDP, we believe there are considerable opportunities in the digital health space to render longstanding inefficiencies in healthcare a thing of the past.[1]

Sources: Text: 1. World Health Organization (WHO), 2022

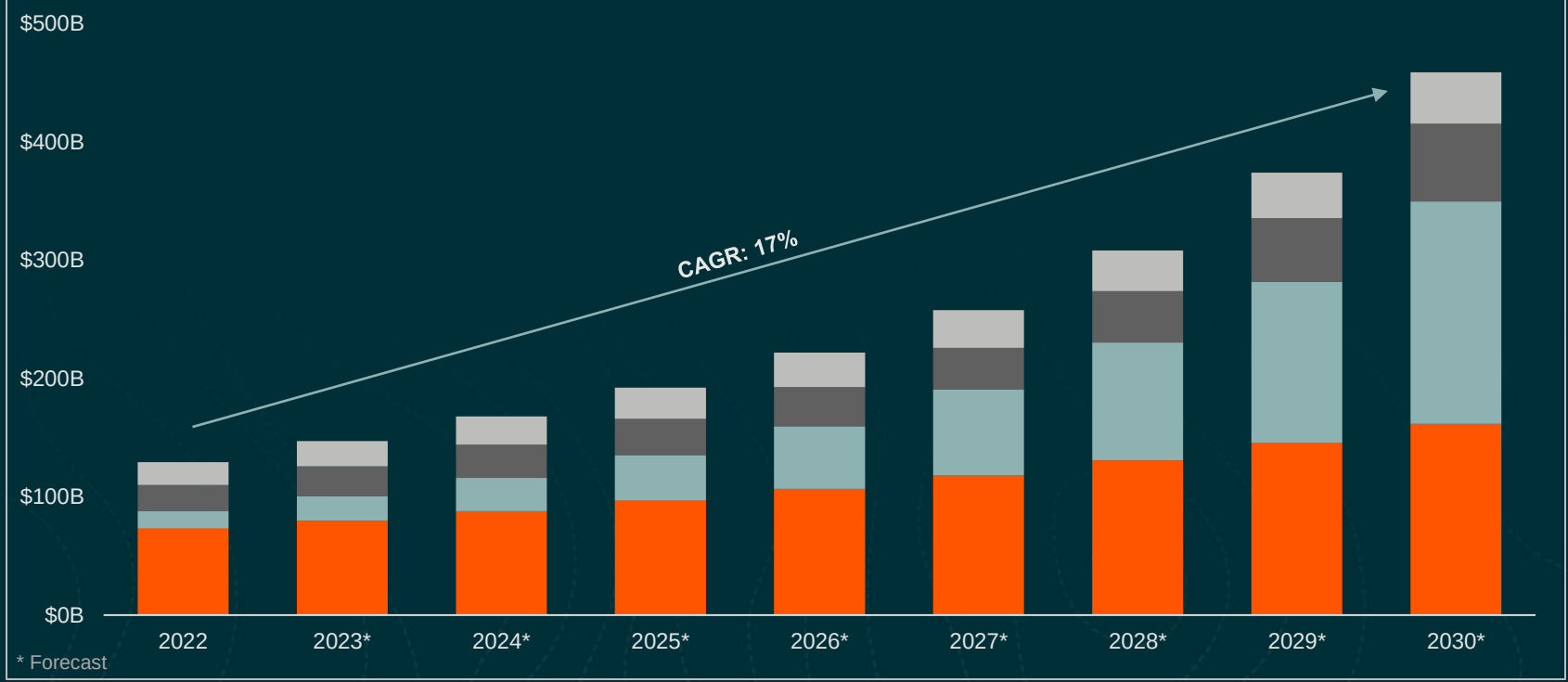
Digital Health: Growing Market Driven by Inefficiencies in Patient Care

The digital health market is still in its infancy, and we expect continued industry consolidation as well as interoperability of digital health segments to help increase ease of use and accelerate patient and physician adoption.

A New Technological Toolkit

- **Administrative Digitization:** Software to streamline and automate medical processes. **10% CAGR**
- **Healthcare Analytics:** Platforms for statistical and computational analysis of medical data. **37% CAGR**
- **Telemedicine:** Healthcare that remotely connects patients with medical professionals. **15% CAGR**
- **Wearable Sensors:** Devices that automatically transmit data to patients and their physicians. **11% CAGR**

Digital Health Market Opportunity: Ample Room to Grow



Sources: Data Bridge Market Research, 2023; Evaluate Pharma, n.d.a; Evaluate Pharma, n.d.b; Evaluate Pharma, n.d.c; Insight Partners, 2023; Precedence Research, 2022-Aug; Precedence Research, 2022-Oct; Precedence Research, 2023; Statista Market Insights, 2023

AI in Healthcare Promises to Enhance the Industry's Reach

AI has the potential to save the United States as much as 10% of annual healthcare spending.[1]

DATA SOURCES		OUTPUT		IMPACT AT MATURITY
Genomic Sequencing Clinical Trials Prescriptions Insurance Claims Pharmacies Electronic Medical Records Apps & Wearables	Artificial Intelligence	Drug Discovery & Development	Drug Design Clinical Trial Operations	$70 billion global annual savings.[2,3]
		Patient Care Guidance	Medical Diagnosis Treatment Guidance Health Monitoring & Wearables AI-Assisted Surgical Robots	30-40% improvement to medical outcomes.[4]
		Health Operations	Visit Documentation Patient Education & Communication Insurance Authorization Medical Supply Chain	$900 billion global annual savings.[5,6]

Sources: Text: 1. National Bureau of Economic Research, 2023; 2. Evaluate Pharma, 2022; 3. Morgan Stanley, 2022; 4. Frost & Sullivan, 2016; 5. National Bureau of Economic Research, 2023; 6. WHO, n.d.

AI in Healthcare Operations: The Missing Link to Transformative Digitization

Healthcare has made great strides in digitizing operations, but it lacks automation. AI can streamline processes, like data input, into electronic databases and help the industry glean more insights from the data it generates.

Healthcare Needs Automation

An estimated 80% of U.S. healthcare documents are still sent via snail mail and fax.[1] More documents are digital, but processes remain inefficient.

A recent study revealed that doctors spend 73% of their time on administrative tasks and only 27% of their time actually with patients.[2]

Unsurprisingly, 78% of physicians report burnout and fatigue related to health IT systems.[3]

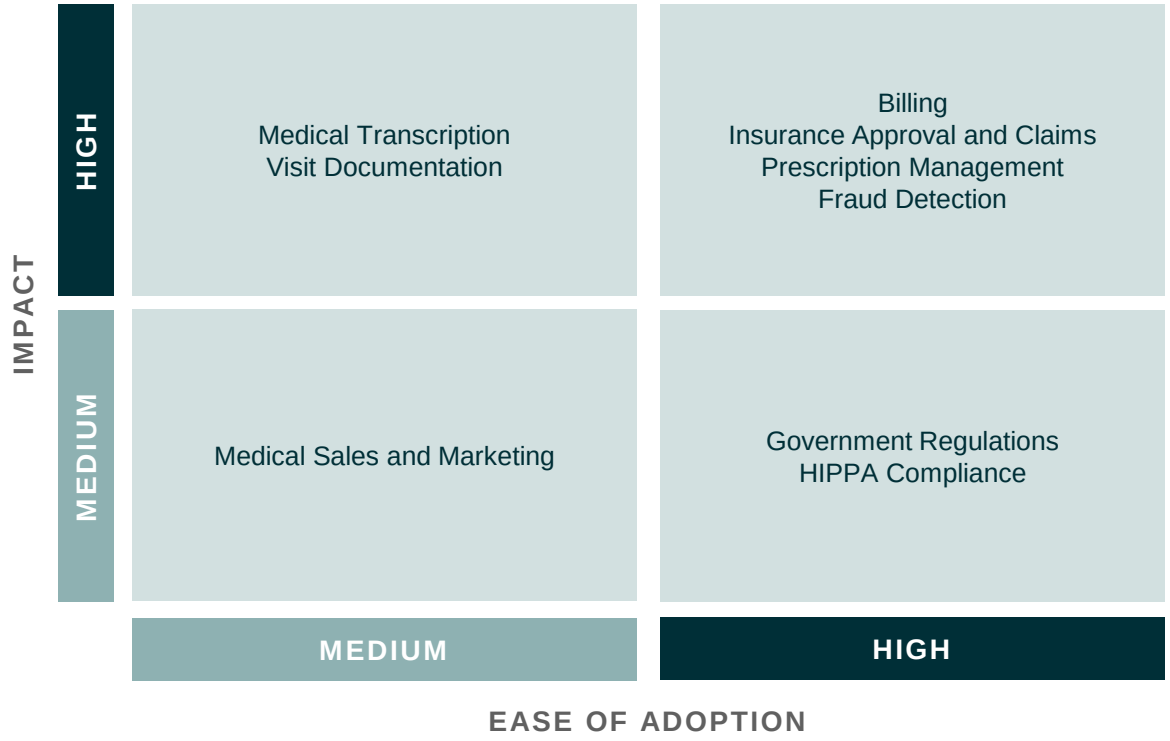
AI Brings Cost Savings Potential to the Healthcare Ecosystem

Private insurance firms could save 7–9% of costs, resulting in $80–110 billion annual savings.[4]

Physician groups could save 3–8% of costs, resulting in $20–60 billion savings.[5]

Hospitals could save 4–11% of costs, resulting in $60–120 billion annual savings.[6]

AI Implementation in Healthcare Operations

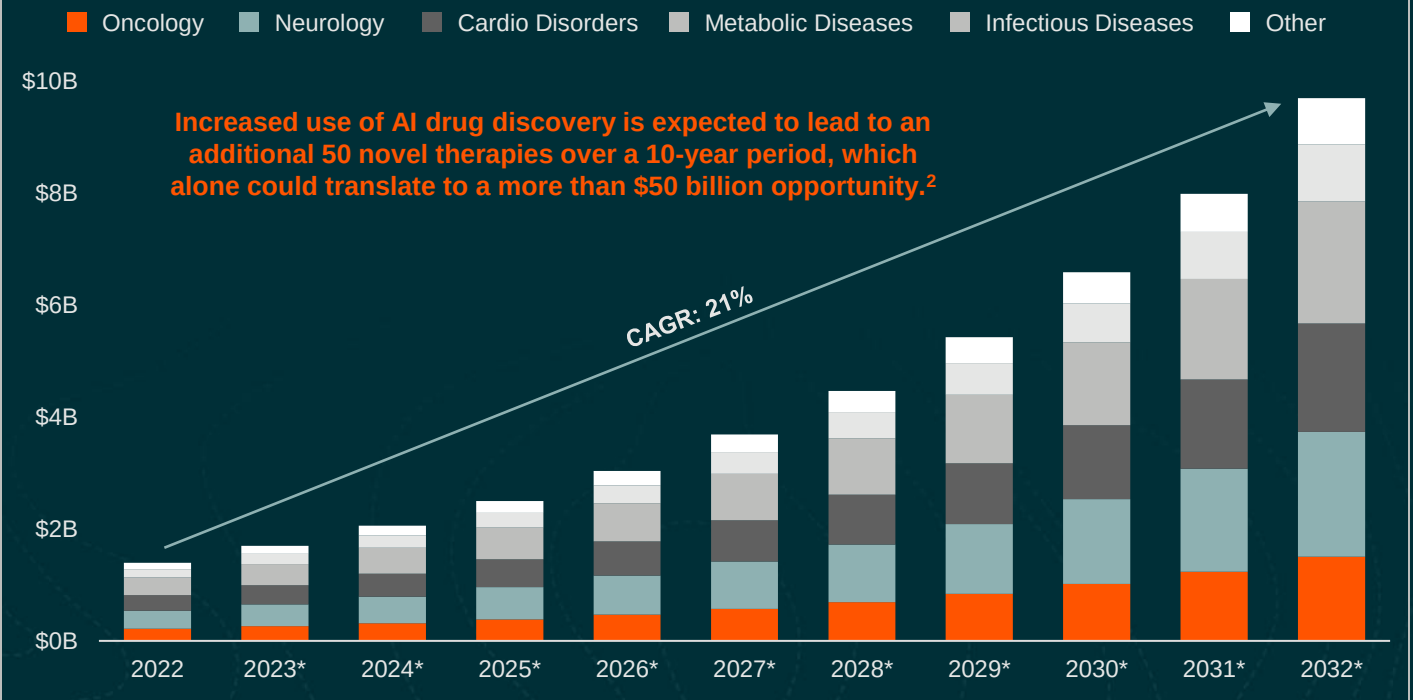


Sources: Text: 1. Doximity, 2023; 2. Gist Healthcare, 2018; 3. Doximity, 2023; 4. National Bureau of Economic Research, 2023; 5. Ibid; 6. Ibid.

AI in Drug Discovery: Supercharging Decades of Computer-Aided Drug Design

Computer simulation software has been used to develop investigational drugs since the 1990s.[1] Today's AI-enabled models propose a new standard for drug discovery that offers improved drug efficacy and decreased costs.

AI Drug Discovery Software Market: The Tip of the Iceberg



AI Improves Unit Economics for Drug Development

Despite technological advancements, developing a new medicine still takes 10–15 years and cost an average of $1.3 billion.[3, 4] Complicating matters, 90% of investigational drugs fail when tested in humans due to having no effect or too many side effects.[5]

By running millions of scenarios, AI software could reduce the cost of preclinical drug development by 20-40% as well as accelerate design and validation of drug candidates by as much as 15 times.[6, 7]

Benefits to AI-Enabled Drug Discovery

Better Molecule Construction: AI software predicts the 3D structure of target proteins, drug-protein interactions, and activity in new therapies.

Maximized Investigational Efforts: AI software helps design multi-target drug molecules and predict drug repurposing to maximize a treatment's reach.

Enhanced Patient Identification: AI software predicts toxicity and efficacy of the treatment via genomic profiling.

Sources: Text: 1. National Institute of Health 2009; 2. Morgan Stanley, 2022; 3. PhRMA 2021; 4. Journal of the American Medical Association, 2020; 5. National institute of Health, 2019; 6. Morgan Stanley, 2022; 7. Margaretta Colangelo, 2019; Chart: Grand View Research, 2022; Precedence Research, 2022

AI in Drug Development: Modernizing In-Human Clinical Trials

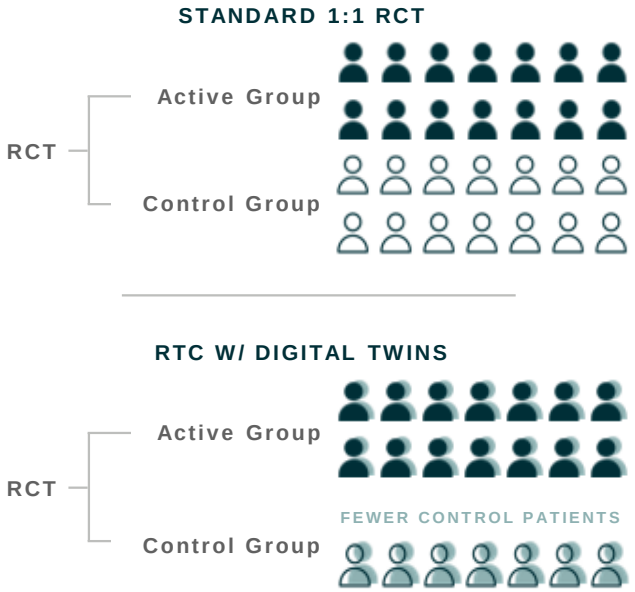
Clinical trials are notoriously difficult to design and operate. AI offers a scalable solution for some of the biggest stumbling blocks in the drug development process while reducing operating costs.

Where Current Trial Protocols Go Wrong and How AI Can Help

	Impact	AI's Solution
Poor Design	The causes of a negative trial outcome can be difficult to discern. Unknown flaws in trial design or trial execution can mask the true efficacy of a drug and next steps for researchers.	AI can identify patterns that humans can't, helping determine if, for example, a drug is only a good fit for a specific subsect of patients. Digital twins can also help identify potential flaws in a trial's design.
Ineffective Recruitment	An estimated 86% of trials miss their enrollment deadlines, due in part to 85% of patients being unaware that they could participate.[1] Nearly a third of phase III trials fail due to enrollment difficulties.[2]	AI can proactively identify patients best suited for clinical trials, while digital twins can simulate dosing regimens and patient progressions, reducing the number of participating patients.
Insufficient Data	A rubric is used to evaluate drug efficacy, but many trials rely on surrogate endpoints, including most cancer trials.[3] In these cases, the trial measures drug effectiveness by using a specific data point that might result in clinical improvement, though does not guarantee it.	AI-powered wearables can help measure drug efficacy and monitor patients during clinical trials. Increased integration with electronic patient-recorded data and telemedicine are expected to make AI models more powerful.

The Digital Twin Advantage

Researchers can monitor patients in real-time while simulating clinical outcomes in a randomized clinical trials (RCT).

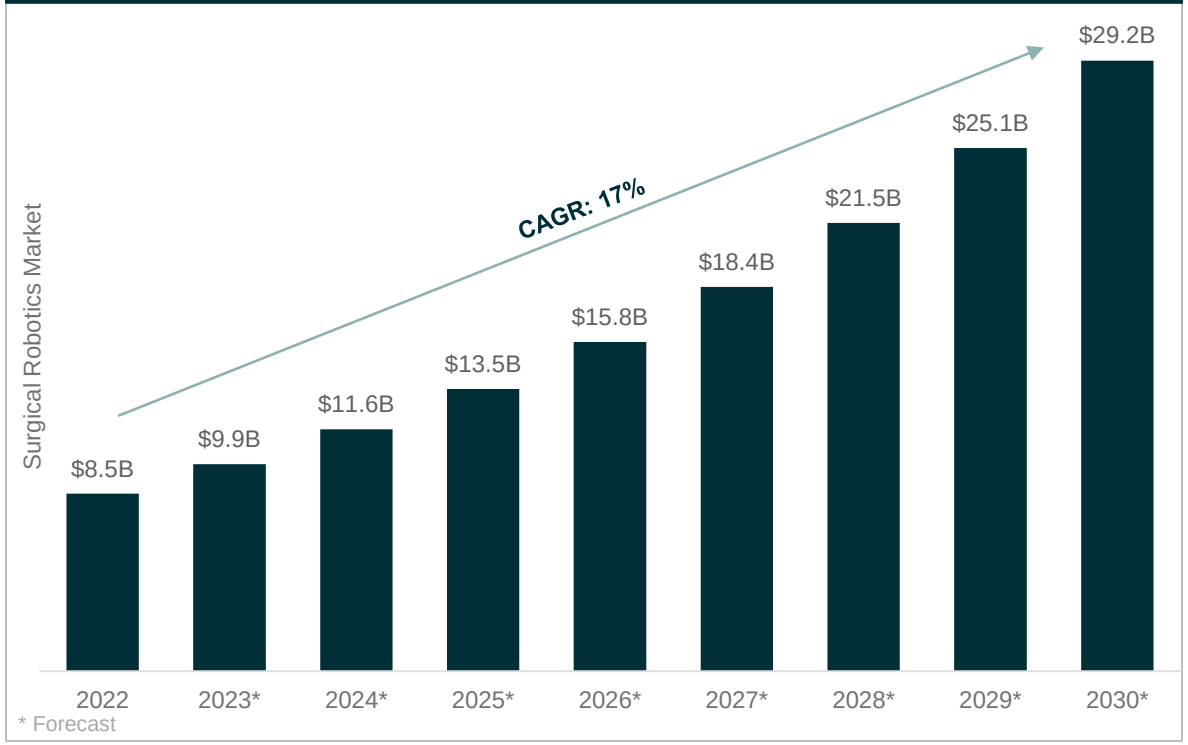


Sources: Text: 1. Clinpal, n.d.; 2. Ibid; 3. Clinical Trials Arena, 2021

Surgical Robots: Harnessing Innovative Hardware and Applying AI to Improve Patient Outcomes

Robot-assisted surgeries have a growing track record of success with patients. Key benefits include shorter hospital stays, smaller surgical scars, lower risk of infection, and less pain during recovery.[1]

Surgical Robots: Ripe for Growth as Adoption Spikes

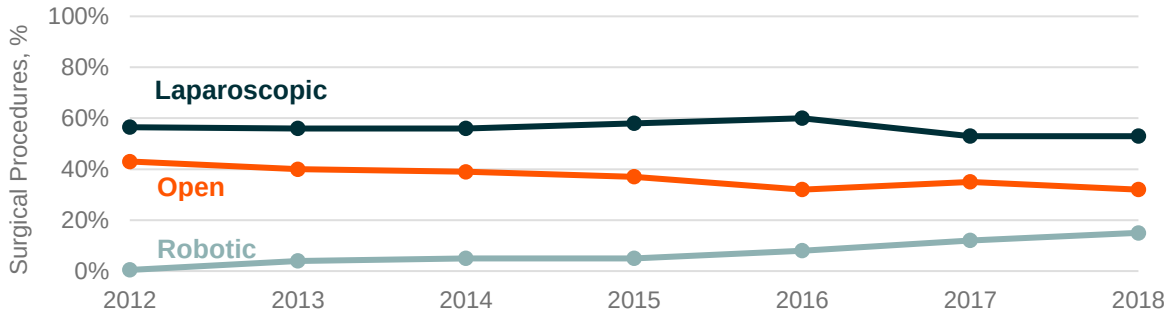


< 5% of Surgeries Are Robot-Assisted – That's Changing[2]

- Surgical robots have been around for over 20 years, but with new technology they now help with more complex surgeries, including general, orthopedic, and spinal procedures.
- An estimated 78% of U.S. surgeons are interested in embracing surgical robots due to their improved capabilities.[3]
- New sales models, such as equipment leasing contracts, are expected to help accelerate adoption and stabilize revenue for robotic surgery firms.

Case Study: Surgical Robot Adoption Trends

A hospital study shows less-invasive procedures rise following surgical robot purchase.



Sources: Text: 1. Cleveland Clinic, n.d.; 2. Medtronic, 2023; 3. Bain & Company, 2023. Charts: Left: Markets and Markets, 2023; Right: Journal of the American Medical Association, 2020

Surgical Robots: An Evolving Category with a Growing Product Lineup

We expect firms to focus on adapting their existing robotic software and hardware to service a greater proportion of procedures in the general surgery category rather than develop vertical-specific robots.

	General Surgery	Orthopedic Surgery	Spinal Surgery	Lung Biopsy
Intuitive Surgical	da Vinci			Ion
Asensus Surgical	Senhance			
Medtronic	Hugo*		Mazor	
Johnson & Johnson	Ottava	Velys		Monarch
Stryker		Mako		
Zimmer Biomet		Rosa		
Globus Medical			ExcelsiusGPS	
Vicarious Surgical	Beta 2			

Notes: Medtronic's Hugo is commercially available in Europe, Canada, and Japan. A Launch in the United States is expected in 2024.[1] Legend: Commercially Available, In Development

General surgery is the most mature category, with Intuitive Surgical a leading player. **Over 13 million procedures have been performed with Intuitive's da Vinci platform**, which has over 8,000 placements globally.[2] Launches in the next few years from Medtronic and Johnson & Johnson, as well as a next-generation da Vinci platform, are expected to increase robotic surgery adoption.[3] Newer entrants, like Vicarious Surgical, want to raise the bar via augmented intelligence and more cost-effective manufacturing, which could lead to platforms with **capital costs 5–10 times lower** than existing robots.[4]

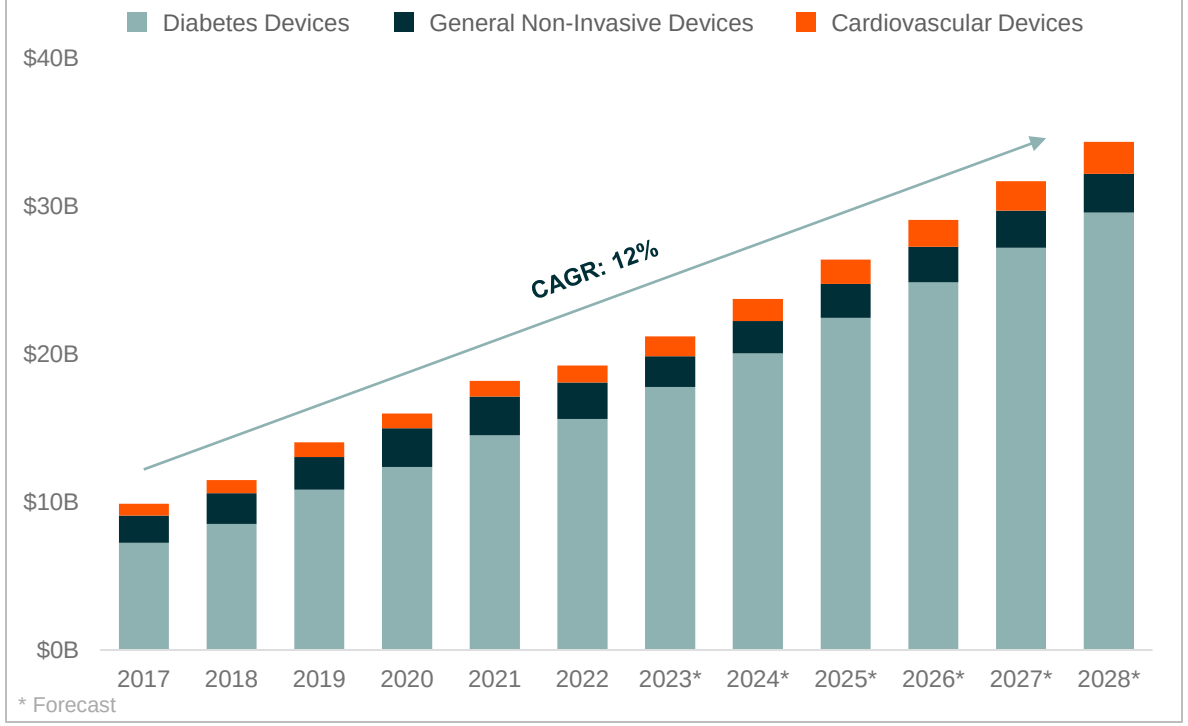
Recent developments in lung biopsy also point to increased conversion between diagnostic and surgical intervention, helping to engrain surgical robotics across the healthcare continuum.

Sources: Text: 1. Fierce Biotech, 2022; 2. Intuitive Surgical, 2023; 3. Intuitive Surgical, 2023; 4. Medtech Drive, 2021; Chart: Intuitive Surgical, 2023; Asensus Surgical, n.d.; Medtronic, n.d.a.; Medtronic, n.d.b.; Johnson & Johnson, n.d.; Stryker, n.d.; Zimmer Biomet, n.d.; Globus Medical, n.d.; Vicarious Surgical, 2022

Wearable Technology: Diabetes Devices Created the Blueprint for Other Health Categories

Given significant success in diabetic monitoring, the wearables industry now looks to bring this type of technology to other health categories, notably cardiovascular care.

Monitoring Wearable Devices: Only Getting Started



* Forecast

Cardiovascular Monitoring: Growing Patient Demand

Innovation in cardiovascular diagnosis and monitoring has accelerated in recent years given the large patient population. Nearly half of U.S. adults, for example, have some type of cardiovascular disease.[1] To address this population, new devices have come to market for:

- **Arrhythmia Diagnosis and Monitoring**
  - An estimated 11 million individuals in the United States have arrhythmias, and an average of 160,000 deaths each year are associated with atrial fibrillation (Afib).[2]
  - Wearables like iRhythm Technologies' ZIO can detect 99% of arrhythmias via small, patches.[3] Incumbent devices only detect 47% of arrhythmias, on average.[4]
- **Blood Pressure Monitoring**
  - In the United States, approximately 120 million individuals have hypertension, yet only 1 in 4 adults with high blood pressure have their condition under control.[5] Caring for patients with hypertension costs the United States about $131 billion each year.[6]
  - Continuous blood pressure (BP) monitors can measure BP levels as often as every 15 minutes, providing vital information for physicians to develop treatment plans.

As the cardiovascular device segment continues to mature, we expect increased consolidation of monitoring capabilities in a single device, which should help accelerate adoption and drive reimbursement coverage.

Sources: Text: 1. American Heart Association, 2019; 2. iRhythm Technologies, 2023; 3. American Journal of Cardiology, 2013.; 4. Ibid; 5. Centers for Disease Control and Prevention, 2023; 6. Ibid. Chart: Evaluate Pharma, n.d.a; Evaluate Pharma, n.d.b; Evaluate Pharma, n.d.c

Wearable Technology: Neurology Devices Are the Next Frontier

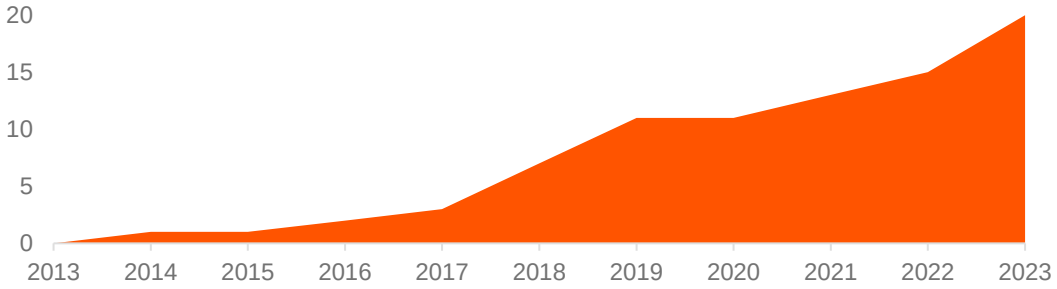
Leveraging adoption of diabetes and cardiovascular devices, we expect neurological wearables to drive the next wave of technological innovation in the healthcare industry.

Wearable Technology Bridges Gaps in Current Neurological Care

Neurological disorders are notoriously difficult to diagnose, monitor, and treat. Wearable sensors can have broad reaching potential across many conditions.

- Sleep: Wearable sleep trackers can help diagnose and monitor sleep disorders, like sleep apnea and insomnia, in the comfort of a patient's home.
- Head Trauma: Sensors can detect impacts and measure the force and direction of injuries, helping determine severity of the trauma and inform patient care.
- Epilepsy: Monitors can help identify seizure triggers, track the effectiveness of medication, as well as warn patients and loved ones of impending seizures.

Cumulative FDA Approvals of Neurology AI-Enabled Devices



Note: 2023 Approvals as of October 19, 2023.

Wearables Particularly Useful for Age-Related Diseases

We view self-sustaining monitoring and therapeutic systems as the future of patient care, though it is particularly beneficial for elderly patients. In a recent Global X ETFs survey, we found that individuals are even more likely to encourage elderly loved ones to utilize wearable technology where available.

Would you utilize a wearable sensor for a chronic illness, if appropriate?

% of Respondents

Would you encourage an elderly loved one to utilize a wearable sensor that could automatically transmit health vitals to their physician and alert emergency services, if needed?

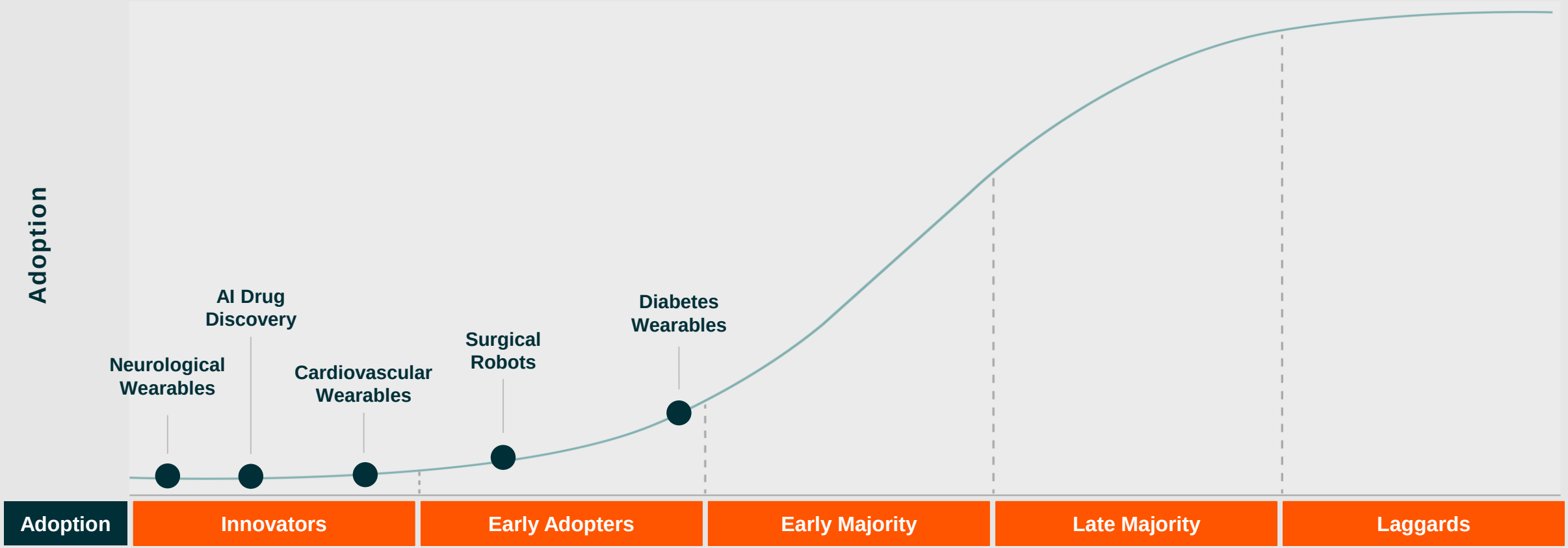
% of Respondents

Note: Number of respondents = 1,032.

Sources: Charts Left: Food and Drug Administration, 2022; Right: De, 2023

Digitizing Medicine: S-Shaped Adoption Curve

We expect the digital health industry to reach $459 billion by 2030, representing 17% compound annual growth.[1]



Note: For illustrative purposes only.

Sources: Text: 1, Data Bridge Market Research, 2023; Evaluate Pharma, n.d.a; Evaluate Pharma, n.d.b; Evaluate Pharma, n.d.c; Insight Partners, 2023; Precedence Research, 2022-Aug; Precedence Research, 2022-Oct; Precedence Research, 2023; Statista Market Insights, 2023

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Appendix: Decoding the Human Genome

Appendix: Sources – Decoding the Human Genome

Reaching the Inflection Point for Genomics Adoption

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- National Human Genome Research Institute. (n.d.). DNA Sequencing Costs: Data. Accessed on November 15, 2023.
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New Diagnostic Opportunities Prompted by Multi-omic Capabilities

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New Diagnostic Opportunities: Neurological Disorders Experience Highest Unmet Need

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New Diagnostic Opportunities: Neurological Disorders Experience Highest Unmet Need (continued)

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S-Shaped Adoption Curve – Decoding the Human Genome

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Appendix: Therapeutics

Appendix: Sources – Therapeutics

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Genomic Medicines: Gaining Momentum

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Appendix: Sources – Therapeutics

Genomic Medicines: Gaining Momentum (continued)

Charts

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