

# Why Invest In Genomic Revolution?

As of September 30, 2024

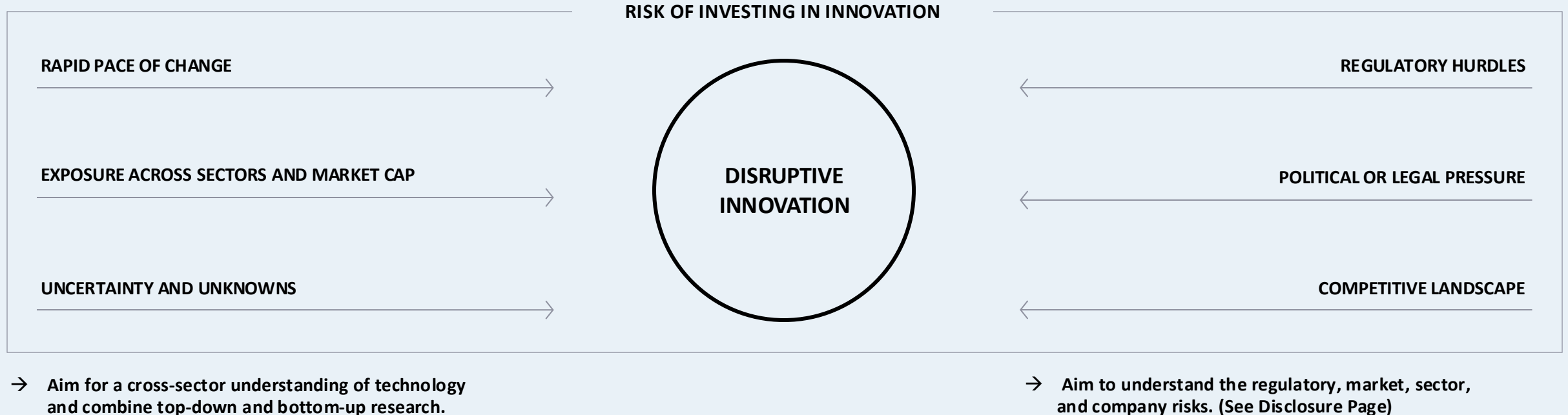




# Risks of Investing in Innovation

Please note: Companies that ARK believes are capitalizing on disruptive innovation and developing technologies to displace older technologies or create new markets may not in fact do so. ARK aims to educate investors and seeks to size the potential investment opportunity, noting that risks and uncertainties may impact our projections and research models. Investors should use the content presented for informational purposes only, and be aware of market risk, disruptive innovation risk, regulatory risk, and risks related to certain innovation areas.

Please read risk disclosure carefully.





# Definitions, Risk & Disclosure Associated with Multiomics

**Health Care Sector Risk.** The health care sector may be affected by government regulations and government health care programs, restrictions on government reimbursement for medical expenses, increases or decreases in the cost of medical products and services and product liability claims, among other factors. Many health care companies are: (i) heavily dependent on patent protection and intellectual property rights and the expiration of a patent may adversely affect their profitability; (ii) subject to extensive litigation based on product liability and similar claims; and (iii) subject to competitive forces that may make it difficult to raise prices and, in fact, may result in price discounting. Many health care products and services may be subject to regulatory approvals. The process of obtaining such approvals may be long and costly, and delays or failure to receive such approvals may negatively impact the business of such companies. Additional or more stringent laws and regulations enacted in the future could have a material adverse effect on such companies in the health care sector. In addition, issuers in the health care sector include issuers having their principal activities in the biotechnology industry, medical laboratories and research, drug laboratories and research and drug manufacturers, which have the additional risks described below.

**Biotechnology Company Risk.** A biotechnology company's valuation can often be based largely on the potential or actual performance of a limited number of products and can accordingly be greatly affected if one of its products proves, among other things, unsafe, ineffective or unprofitable. Biotechnology companies are subject to regulation by, and the restrictions of, the U.S. Food and Drug Administration, the U.S. Environmental Protection Agency, state and local governments, and foreign regulatory authorities.

**Pharmaceutical Company Risk.** Companies in the pharmaceutical industry can be significantly affected by, among other things, government approval of products and services, government regulation and reimbursement rates, product liability claims, patent expirations and protection and intense competition.

Definitions:

**Deoxyribonucleic acid (DNA)** is a polymer composed of two polynucleotide chains that coil around each other to form a double helix carrying genetic instructions for the development, functioning, growth and reproduction of all known organisms and many viruses. **Ribonucleic acid (RNA)** is a polymeric molecule essential in various biological roles in coding, decoding, regulation and expression of genes. **The phenotype** is the set of observable characteristics or traits of an organism. The term covers the organism's morphology or physical form and structure, its developmental processes, its biochemical and physiological properties, its behavior, and the products of behavior. Protein quantification is necessary to understand the total protein content in a sample or in a formulated product.

**A double-strand DNA break (DSB)** occurs or arises when both strands of the DNA duplex are severed, often as the result of ionizing radiation. **Zinc finger nucleases (ZFNs)** are a class of engineered DNA-binding proteins that facilitate targeted editing of the genome by creating double-strand breaks in DNA at user-specified locations.

**Transcription Activator-Like Effector Nuclease (TALENs)** are chimeric proteins that contain two functional domains: a DNA-recognition transcription activator-like effector (TALE) and a nuclease domain. They work for gene editing by recognizing a specific sequence, which the user can design, and introducing a double-stranded break with an overhang. **Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)** is gene editing is a genetic engineering technique in molecular biology by which the genomes of living organisms may be modified. It is based on a simplified version of the bacterial CRISPR-Cas9 antiviral defense system. **Cas9 Enzyme (Cas)** is a protein which plays a vital role in the immunological defense of certain bacteria against DNA viruses.

**Base editing** is a novel technology that has the potential to generate gene knockouts or to correct certain errors or mutations in the DNA of intact cells. Prime editing is a gene editing method that can perform targeted small insertions, deletions, and base swapping in a precise way.

**Antisense Oligonucleotide (ASO)** is a single-stranded, synthetic RNA (or DNA) sequence. ASOs are designed to selectively bind via complementary base-pairing to messenger RNA (mRNA) and are the basis for one type of RNA-based therapeutics being explored to treat cancer and genetic disorders.

**Multi-omics** aims to combine two or more omics data sets to aid in data analysis, visualization and interpretation to determine the mechanism of a biological process. Proteomics is the large-scale study of proteins. **Epigenetics** is the study of how your behaviors and environment can cause changes that affect the way your genes work. Unlike genetic changes, epigenetic changes are reversible and do not change your DNA sequence, but they can change how your body reads a DNA sequence. A variant is any change in the DNA sequence of a cell. Variants may be caused by mistakes during cell division, or they may be caused by exposure to DNA-damaging agents in the environment.

**Primary Sequence** is the linear sequence of amino acids in a protein or of nucleotides in a nucleic acid. **Phasing** involves separating maternally and paternally inherited copies of each chromosome into haplotypes to get a complete picture of genetic variation.

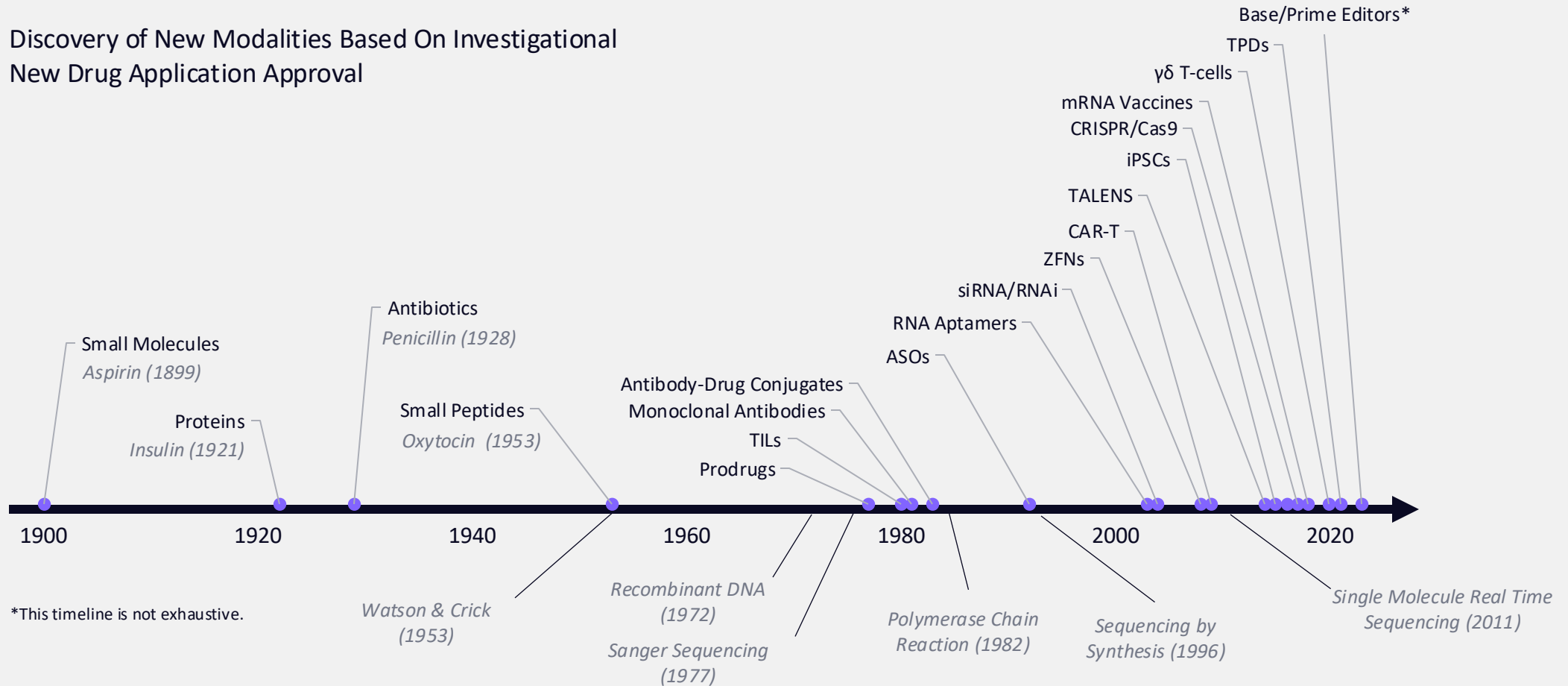
**Posttranslational modifications (PTMs)** are covalent processing events that change the properties of a protein by proteolytic cleavage and adding a modifying group, such as acetyl, phosphoryl, glycosyl and methyl, to one or more amino acids.

**Proteoforms** are the different forms of a protein produced from the genome with a variety of sequence variations, splice isoforms, and post-translational modifications. Proteoform captures the disparate sources of biological variation which alter primary sequence and composition at the whole-protein level. Gene isoforms are mRNAs that are produced from the same locus but are different in their transcription start sites, protein coding DNA sequences and/or untranslated regions, potentially altering gene function.

# New Therapeutic Modalities Are Proliferating

During the last thirty years, the number of therapeutic modalities with entirely new mechanisms of action has proliferated. Not only have they expanded the number of treatable diseases, but they have also improved efficacy and safety. In 2023, more than 25% of clinical trials were harnessing new therapeutic modalities.

## Discovery of New Modalities Based On Investigational New Drug Application Approval



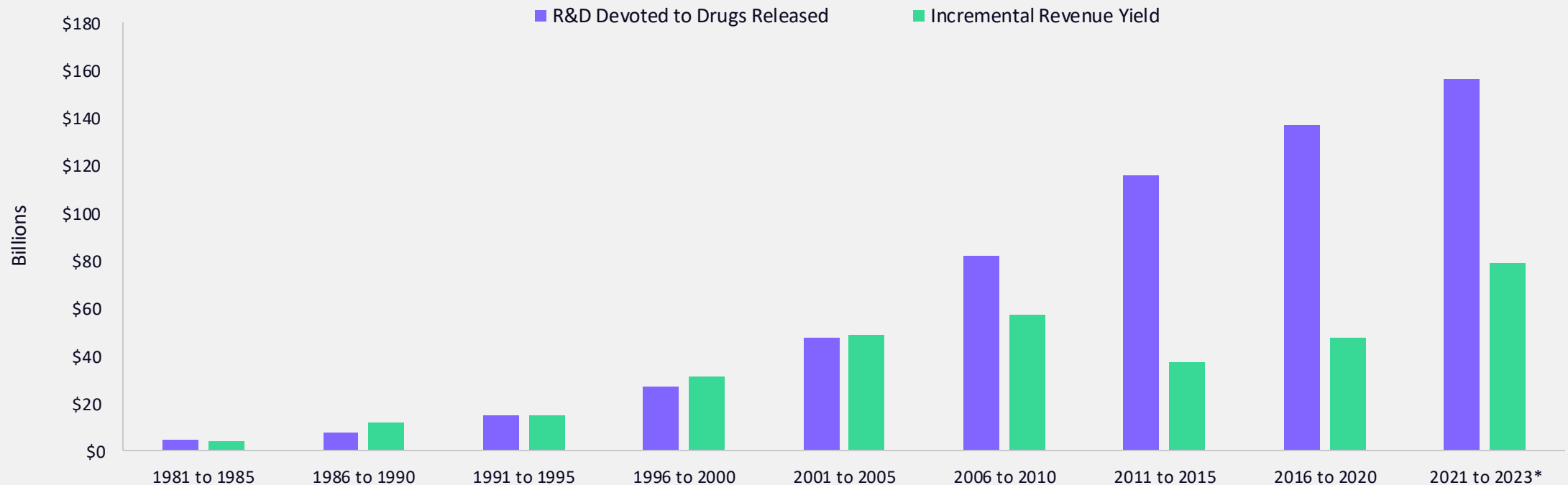
Sources: ARK Investment Management LLC, 2024. This ARK analysis is based on a range of external sources, including Biomedtracker, which may be provided upon request. Forecasts are inherently limited and cannot be relied upon. For informational purposes only and should not be considered investment advice or a recommendation to buy, sell, or hold any particular security. Past performance is not indicative of future results.



# Precision Therapies Could Reverse The Downtrend In Returns On Research And Development (R&D)

Given regulatory bottlenecks and legacy drug discovery methods, the return on therapeutic R&D has been falling for nearly 25 years. According to our research, novel therapeutic modalities and R&D methods, coupled with regulatory approval of “precision” therapies, could reverse the downward trend in return on investment in the pharmaceutical industry.

Average Annual R&D And Incremental Revenue Attributable To Drugs Released



\*Shorter time frame. Data impacted due to COVID.

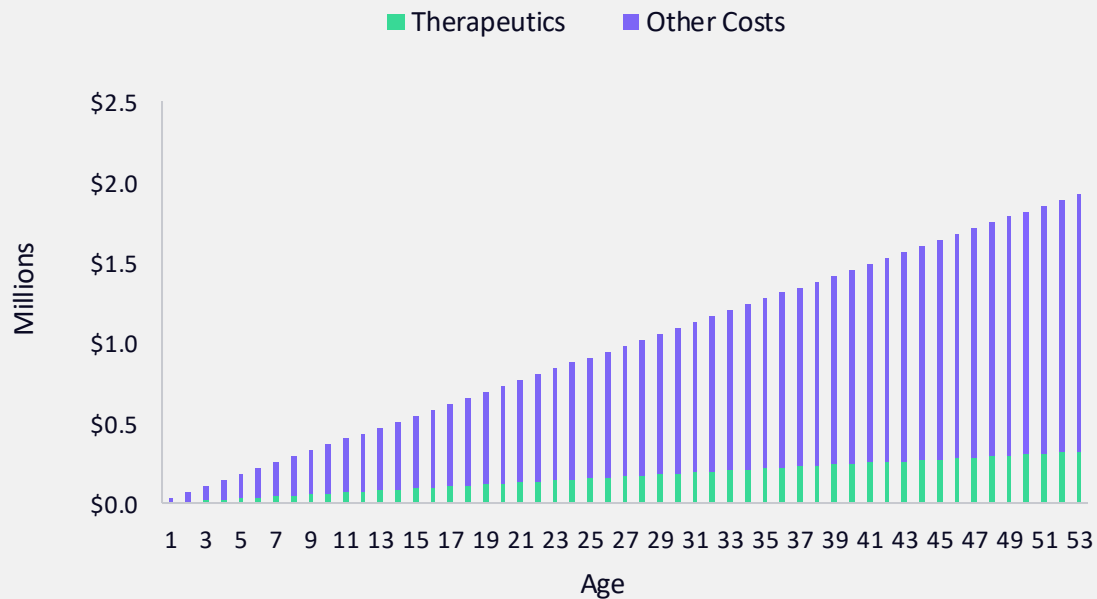
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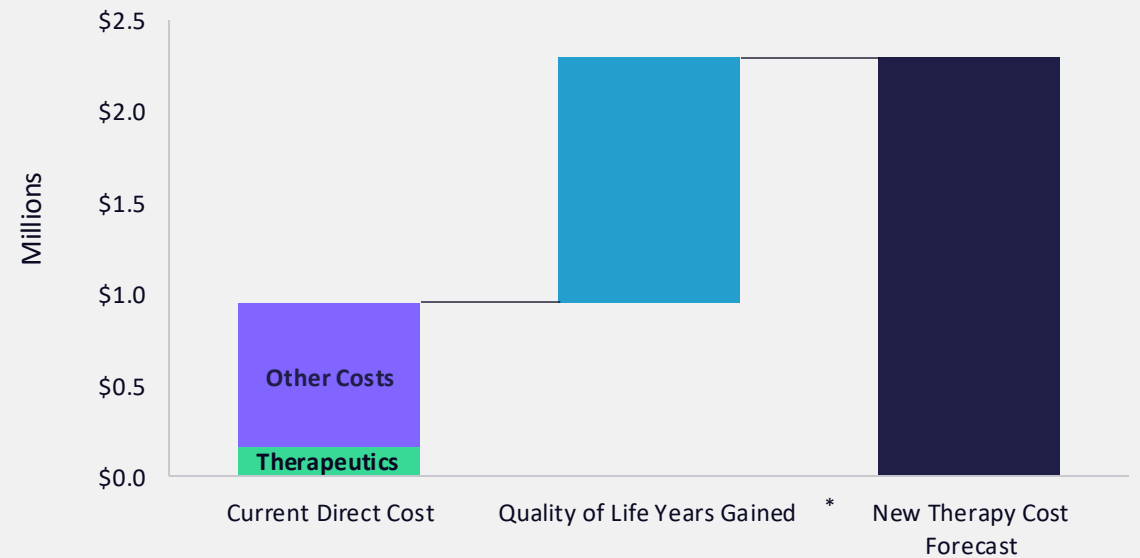
# The Value Of Curing Rare Diseases Like Sickle Cell Anemia Is High

Among precision therapies, gene editing medicines like CRISPR-Cas9 have the potential to cure rare genetic diseases such as Sickle Cell Disease (SCD). SCD is an inherited red blood cell disorder that affects more than 100,000 people in the US and 20 million people globally, primarily in Africa. Today, therapeutics account for ~16% of the total spent on treating SCD disease in the US, but they have done little more than manage symptoms, as the life expectancy of SCD patients is only 56% that of the general population.

### SCD Healthcare Costs Over Average Patient Lifetime



### Reasonable Cost For Sickle Cell Disease Cure



\*Quality of Life Years Gained = Health Utility \* Duration  
For Health Utility, 0 means dead and 1 means full health

Data are as of December of 2023.

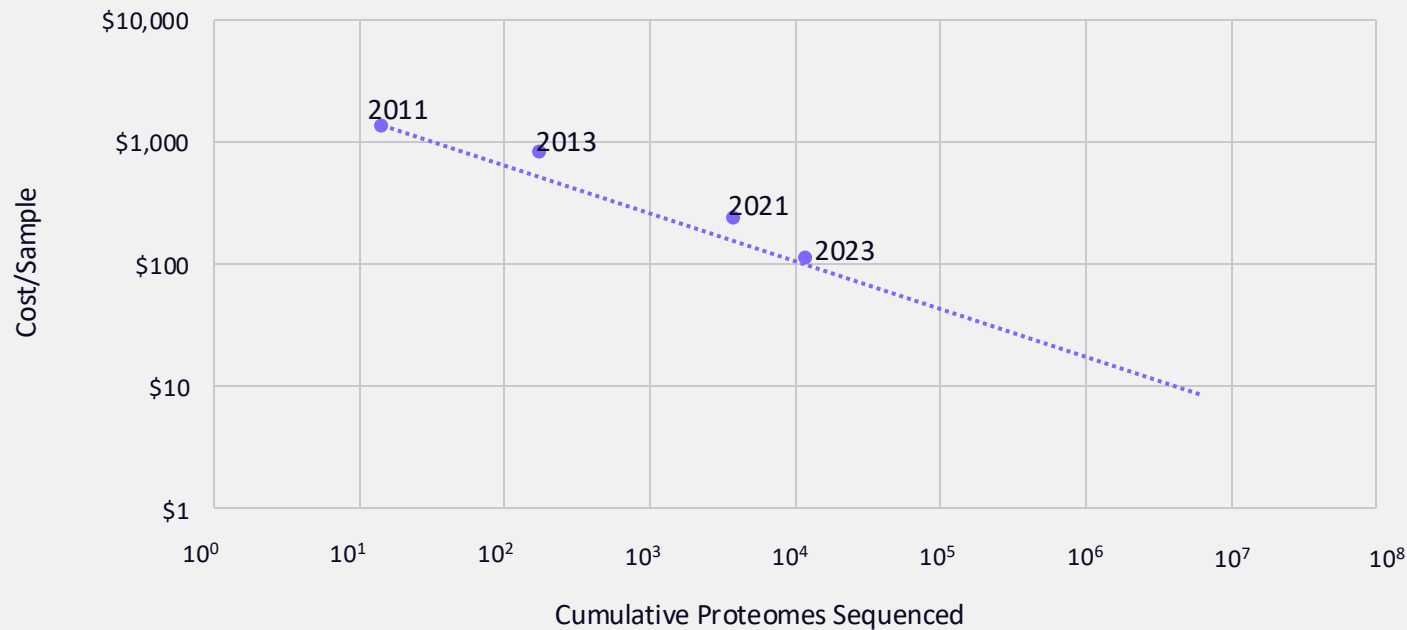
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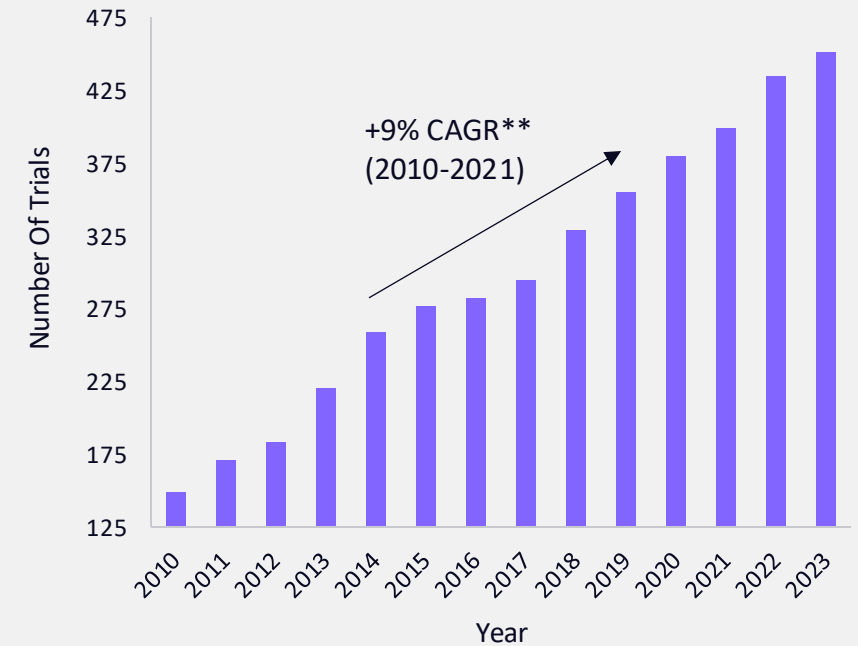
# Wright's Law\* Has Predicted The Cost Decline Of Proteomics

As the number of proteomes analyzed by mass spectrometry has increased, costs have dropped dramatically, unlocking new possibilities in medical research and diagnostics. Our research suggests that for untargeted proteomics using mass spectrometry, the cost per sample is declining 23% at an annual rate, or ~11% for each cumulative doubling in the number of proteomes sequenced. Proteomic discoveries are paving the way for the identification of novel biomarkers, enabling the earlier detection and treatment for unique cancer subtypes.

### Wright's Law Has Predicted The Cost Decline For Untargeted Proteomics



### US Trials With Patient Biomarkers

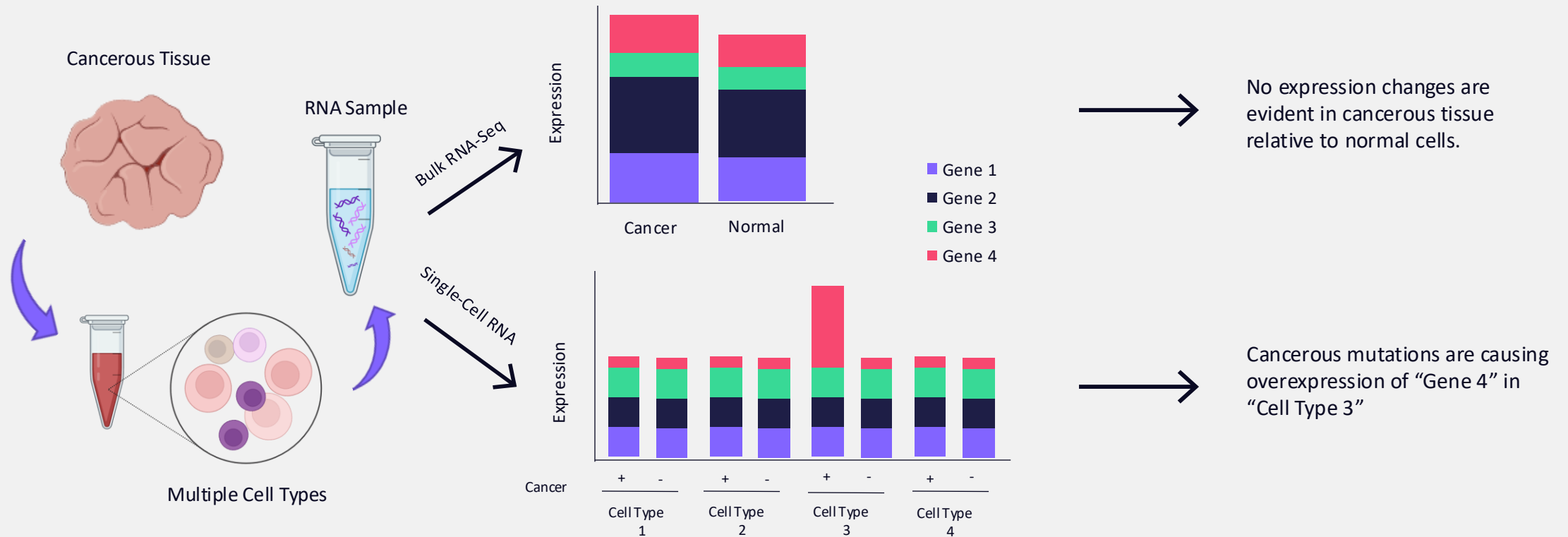


\*Wright's Law states that for every cumulative doubling of units produced, costs will fall by a constant percentage. Sources: ARK Investment Management LLC, 2024, <https://www.ark-invest.com/wrights-law/>. \*\*CAGR stands for Compound Annual Growth Rate. This ARK analysis is based on a range of external sources, which may be provided upon request. Forecasts are inherently limited and cannot be relied upon. For informational purposes only and should not be considered investment advice or a recommendation to buy, sell, or hold any particular security. Past performance is not indicative of future results.



# Single-Cell RNA Sequencing Is Revolutionizing Our Understanding Of Cancer

While traditional gene expression analysis using RNA-seq can measure only the expression of genes in a mixture of different cell types, single-cell RNA-seq (scRNA-Seq) can delineate the expression of different cell types in a complex tissue sample. Theoretically, linking gene expression to specific cells increases the accuracy of measuring by 10x and cuts costs per gigabyte by 76%.





# Drug Development Costs Could Drop Precipitously

Advances in fundamental biology, artificial intelligence, automation, and trial design should lower preclinical drug development costs significantly. They enable methods that eliminate less-promising candidates early in the drug development process, prevent downstream misallocation of R&D capital, and create a larger chemical search space early in the discovery phase. During the next decade, companies leveraging these techniques fully could lower costs per approval by almost 50%, in part by more than doubling the odds of success for those drug candidates that do enter clinical trials.

## Efficiency Innovations

### Innovative Trial Design

- + Adaptive Clinical Trial Design
- + Precision Biomarkers
- + Decentralized/Virtual Trials

### Fundamental Biology

- + Single-Cell Biology
- + Proteomic Techniques
- + Virtual Compound Libraries
- + Biomarker Development
- + Humanized animal models

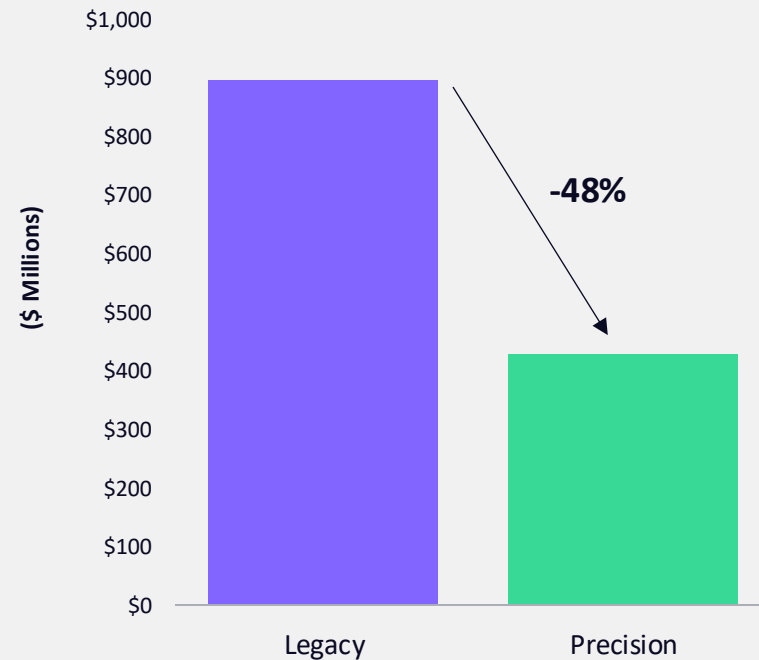
### Automation

- + Automated Liquid Handling
- + Automated Invivomics
- + Automated Microsynthesis
- + CRISPR "Perturb-Seq" Screens
- + Organ-on-a-chip Technology

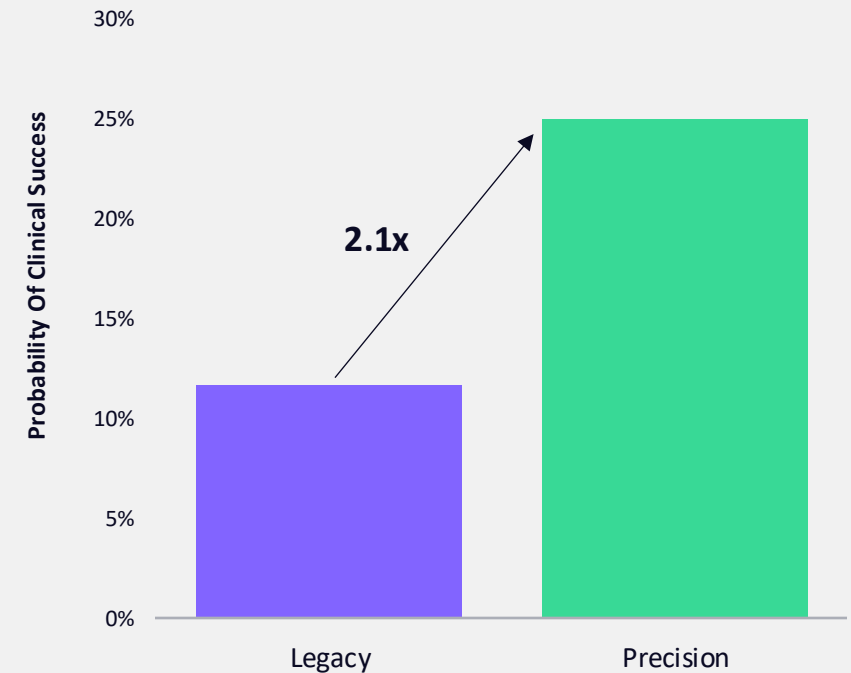
### Artificial Intelligence

- + AI-Enabled Pathway Analysis
- + AI-Enabled Toxicity Prediction
- + In-Silico Molecular Modeling
- + ML-Driven Compound Screens

## R&D Cost Per Drug Approval (Including Failures)



## Clinical Success Probability



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## 5 Reasons Investors Should Consider ARKG

- 1. Exposure To Innovation:** Aims for thematic multi-cap exposure to innovative elements including gene therapy bio-informatics, bio-inspired computing, molecular medicine, and pharmaceutical innovations.
- 2. Growth Potential:** Aims to capture long-term growth with low correlation of relative returns to traditional growth strategies and negative correlation to value strategies.
- 3. Tool For Diversification<sup>1</sup>:** Offers a tool for diversification due to little overlap with traditional indices. It can be a complement to traditional value/growth strategies.
- 4. Grounded In Research:** Combines top-down and bottom-up research in its portfolio management to identify innovative companies and convergence across markets.
- 5. Cost Effective:** Seeks to provide a lower cost alternative to mutual funds with true active management in an exchange traded fund (ETF) that invests in rapidly moving themes.

[1] Diversification does not assure a profit. The information herein is general in nature and should not be considered financial advice. An investor should consult a financial professional regarding the investor's specific situation.



# ARK Genomic Revolution ETF — ARKG

Genomic sequencing is changing the way biological information is collected, processed, and applied. ARKG is focused on the disruptive innovations that are increasing precision, restructuring health care, agriculture, pharmaceuticals, and enhancing the quality of life.

- Ticker: ARKG
- Fund AUM: \$1.33 Billion
- Typical Number of Holdings:: 30-55 U.S. Equities/U.S.-listed ADRs
- Expense Ratio: 0.75%

TOP 10 HOLDINGS	Weight (%)
TWIST BIOSCIENCE CORP	8.5%
CAREDX INC	7.0%
RECURSION PHARMACEUTICALS INC	6.3%
CRISPR THERAPEUTICS AG	6.2%
INTELLIA THERAPEUTICS INC	4.8%
ADAPTIVE BIOTECHNOLOGIES CORP	4.4%
VERACYTE INC	4.4%
10X GENOMICS INC	4.3%
IONIS PHARMACEUTICALS INC	4.1%
NURIX THERAPEUTICS INC	3.7%
	<b>53.7%</b>

MARKET CAPITALIZATION	(%)
Mega (\$100B+)	4.8%
Large (\$10 - \$100B)	9.8%
Medium (\$2 - \$10B)	41.6%
Small (\$300M - \$2B)	41.3%
Micro (\$50 - \$300M)	2.3%

PORTFOLIO COMPOSITION	(%)
Precision Therapies	39.2%
Multiomic Technologies	37.4%
Programmable Biology	11.2%
Neural Networks	6.8%
Next Gen Cloud	3.1%
Adaptive Robotics	1.6%

SECTORS	(%)
Health Care	99.0%
Information Technology	0.8%

*Holdings are subject to change and should not be considered as investment advice, or a recommendation to buy, sell or hold any particular security. It should not be assumed that an investment in the securities identified was or will be profitable.*

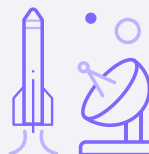
*Source: ARK Investment Management LLC; All data as of September 30, 2024.*



## Thematic Strategies Focused on Disruptive Innovation



**ARKK**  
ARK Innovation ETF



**ARKX**  
ARK Space Exploration & Innovation ETF



**ARKW**  
ARK Next Generation Internet ETF



**PRNT**  
The 3D Printing ETF



**ARKQ**  
ARK Autonomous Tech. & Robotics ETF



**IZRL**  
Israel Innovative Technology ETF



**ARKG**  
ARK Genomic Revolution ETF



**ARKF**  
ARK Fintech Innovation ETF



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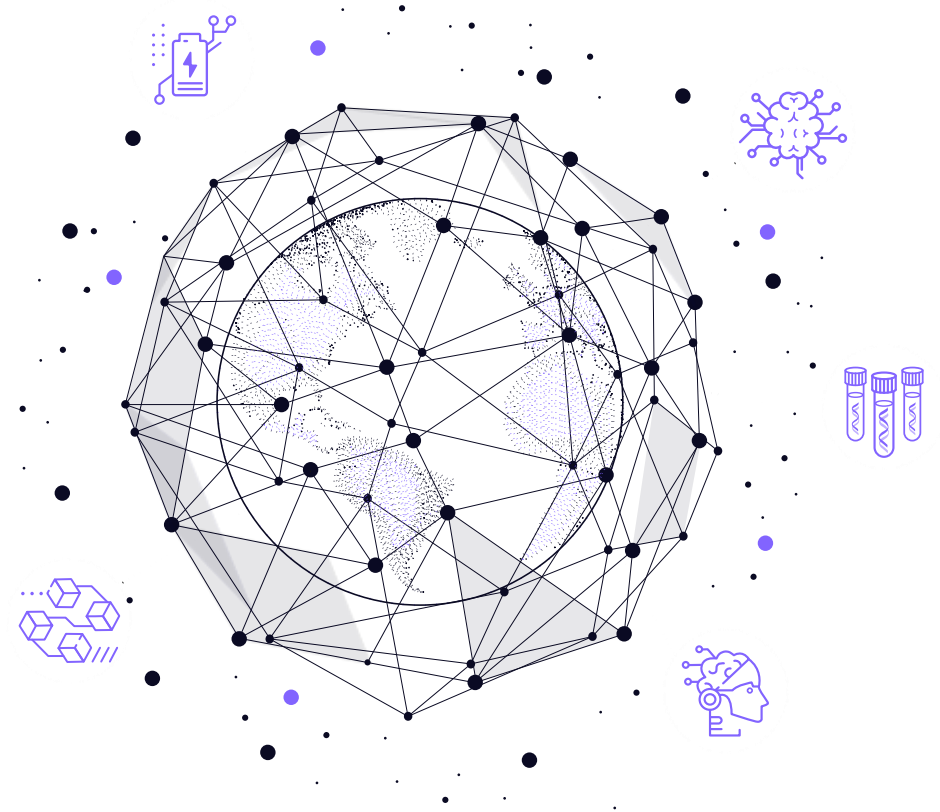
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Factsheet, prospectus, and latest performance reports are available for download on our website: [ark-funds.com/investor-material](https://ark-funds.com/investor-material)

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***Investors should carefully consider the investment objectives and risks as well as charges and expenses of an ARK ETF before investing. This and other information are contained in the ARK ETFs' prospectuses, which may be obtained by visiting [www.ark-funds.com](http://www.ark-funds.com). The prospectus should be read carefully before investing.***

***Investing in securities involves risk and there's no guarantee of principal.***

**Fund Risks:** The principal risks of investing in ARKG: **Equity Securities Risk.** The value of the equity securities the Fund holds may fall due to general market and economic conditions. **Foreign Securities Risk.** Investments in the securities of foreign issuers involve risks beyond those associated with investments in U.S. securities. **Health Care Sector Risk.** The health care sector may be adversely affected by government regulations and government health care programs, restrictions on government reimbursements for medical expenses, increases or decreases in the cost of medical products and services and product liability claims, among other factors. Many health care companies are heavily dependent on patent protection and intellectual property rights and the expiration of a patent may adversely affect their profitability. **Biotechnology Company Risk.** A biotechnology company's valuation can often be based largely on the potential or actual performance of a limited number of products and can accordingly be greatly affected if one of its products proves, among other things, unsafe, ineffective or unprofitable. Biotechnology companies are subject to regulation by, and the restrictions of, the U.S. Food and Drug Administration, the U.S. Environmental Protection Agency, state and local governments, and foreign regulatory authorities. **Pharmaceutical Company Risk.** Companies in the pharmaceutical industry can be significantly affected by, among other things, government approval of products and services, government regulation and reimbursement rates, product liability claims, patent expirations and protection and intense competition. Detailed information regarding the specific risks of ARKG can be found in the ETF's prospectus. Additional risks of investing in ARKG include Foreign Securities Risk, Information Technology Sector Risk, equity, market, management and non-diversification risks, as well as fluctuations in market value and NAV. **Disruptive Innovation Risk.** Companies that ARK believes are capitalizing on disruptive innovation and developing technologies to displace older technologies or create new markets may not in fact do so. Companies that initially develop a novel technology may not be able to capitalize on the technology. Companies that develop disruptive technologies may face political or legal attacks from competitors, industry groups or local and national governments. These companies may also be exposed to risks applicable to sectors other than the disruptive innovation theme for which they are chosen, and the securities issued by these companies may underperform the securities of other companies that are primarily focused on a particular theme.

The Adviser expects to invest at least 80% of the Fund's assets in Genomics Revolution Companies. However, certain of these companies do not currently derive a substantial portion of their current revenues from genomic-focused businesses and there is no assurance that any company will do so in the future, which may adversely affect the ability of the Fund to achieve its investment objective.

An investment in an ETF is subject to risks and you can lose money on your investment in an ETF. There can be no assurance that the ETF will achieve its investment objective. The ETF's portfolio is more volatile than broad market averages. Shares of ARKG are bought and sold at market price (not NAV) and are not individually redeemed from the ETF. ETF shares may only be redeemed directly with the ETF at NAV by Authorized Participants, in very large creation units. There can be no guarantee that an active trading market for ETF shares will develop or be maintained, or that their listing will continue or remain unchanged. Buying or selling ETF shares on an exchange may require the payment of brokerage commissions and frequent trading may incur brokerage costs that detract significantly from investment returns.

Portfolio holdings will change and should not be considered as investment advice or a recommendation to buy, sell or hold any particular security. Please visit [www.ark-funds.com](http://www.ark-funds.com) for the most current list of holdings for the ARK ETFs.

Percentages shown for each ARK ETF's Top Ten holdings are based on the ARK ETF's total investments. Portfolio Composition categories are determined by ARK Invest. Certain information was obtained from sources that ARK believes to be reliable; however, ARK does not guarantee the accuracy or completeness of any information obtained from any third party.

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