

A decorative trail of small, light blue particles curves across the top half of the slide, starting from the left and ending on the right. The background is a gradient from dark blue on the left to a lighter teal on the right.

# Corporate Presentation

March 2024

CODEXIS<sup>®</sup>

We engineer enzymes

# Forward Looking Statements

These slides contain forward-looking statements that involve risks and uncertainties. These statements relate to future events or our future financial or operational performance and involve known and unknown risks, uncertainties and other factors that could cause our actual results or levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” or the negative of these terms, and similar expressions and comparable terminology intended to identify forward-looking statements. In addition, forward-looking statements include all statements that are not historical facts including, but not limited to, the potential revenues and margins of Codexis’ Pharmaceutical Manufacturing business and our expectations that such business will return to growth in 2024, its future pipeline, future conversion rate, range of future peak revenue and the number of new commercial products that will be available within the next 4-6 years; potential details and features of the ECO Synthesis™ platform such as it being scalable and able to reduce waste, as well as having higher purity and better unit economics than existing methods, and whether it can obviate the need for massive early stage investment required for phosphoramidite chemistry; the level of future demand for RNAi therapeutics based on product candidates in development and estimated infrastructure investment required to meet such future demand; the future ECO Synthesis™ market opportunity, including statements regarding its potential annual demand, whether and to what extent Codexis is able to capture market share and Codexis’ potential revenue from such market opportunity; Codexis’ expectations for the build-out of its planned ECO Synthesis™ Innovation Lab; timing of the commercial launch of Codexis’ ecoRNA™ ligase program offering and its expected features and benefits; timing of news updates regarding the ECO Synthesis™ platform and Codexis’ achievement of key development, pre-commercial and commercial milestones; and Codexis’ generating positive cash flow around the end of 2026. These forward-looking statements represent our estimates and assumptions only as of the date hereof, and, except as required by law, Codexis undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

Actual results could differ materially from Codexis’ current expectations for a variety of reasons, including due to the factors set forth in Codexis’ most recently filed periodic report, including under the caption “Risk Factors,” and Codexis’ other current and periodic reports filed with the SEC. If any of these risks or uncertainties materialize, or if Codexis’ underlying assumptions prove to be incorrect, actual results or levels of activity, performance or achievement, or any of the foregoing forward-looking statements, may vary significantly from what Codexis projected.

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# Codexis: Catalyzing Innovation Through Engineered Enzymes

## Powerful Underlying Science & Deep Technical Expertise

20+ years leveraging proprietary CodeEvolver® directed evolution platform to engineer exquisite enzymes for small molecule production and life science applications

## Revenue Generating Pharma Manufacturing Business

Foundational biocatalysis business in small molecule manufacturing supports future innovation

## Potential Game-Changing Technology

Potential to disrupt multi-billion dollar market via enzymatic synthesis of RNAi with ECO Synthesis™ manufacturing platform

## Experienced Management Team & Strong Cash Position

Proven management team who can execute on high-value opportunities



Pro Forma Cash as of 12/31/23 = \$70 Million<sup>1</sup>

\$29M Net Proceeds from Strategic Debt Financing in Feb 2024

Path to Potential Positive Cash Flow Around End of 2026

<sup>2</sup> <sup>1</sup>Includes cash and cash equivalents of approximately \$65 million as of December 31, 2023, and a \$5 million upfront payment received in January 2024 in connection with the Company's acquisition agreement with Nestlé Health Science for CDX-7108

# Leverage Core Strength in Enzyme Engineering to Drive Maximum Value Creation Across Key Markets

## Foundational Business: Pharmaceutical Manufacturing

- Customized biocatalysts to support small molecule production
- ~\$40M base revenues, strong gross margins (~60%) and anticipated return to growth in 2024
- Leverage Pharma Manufacturing technical expertise and commercial reach to drive successful execution of the ECO Synthesis™ manufacturing platform opportunity

## Game-Changing Technology: ECO Synthesis™ Manufacturing Platform

- Platform in development to enable commercial-scale manufacture of RNAi therapeutics
- Positioned to play a key role to meet projected future wave of demand for RNAi therapeutics
- Expect to enter RNAi synthesis market with double-stranded ecoRNA™ ligase in 2024

## Partnered Programs Leveraging Codexis' Enzyme Engineering Expertise

- **Codex® HiCap RNA Polymerase:** global exclusive license to Aldevron



- **CDX-7108:** asset sale to Nestlé Health Science



- **Newly engineered dsDNA ligase:** global exclusive license to Roche

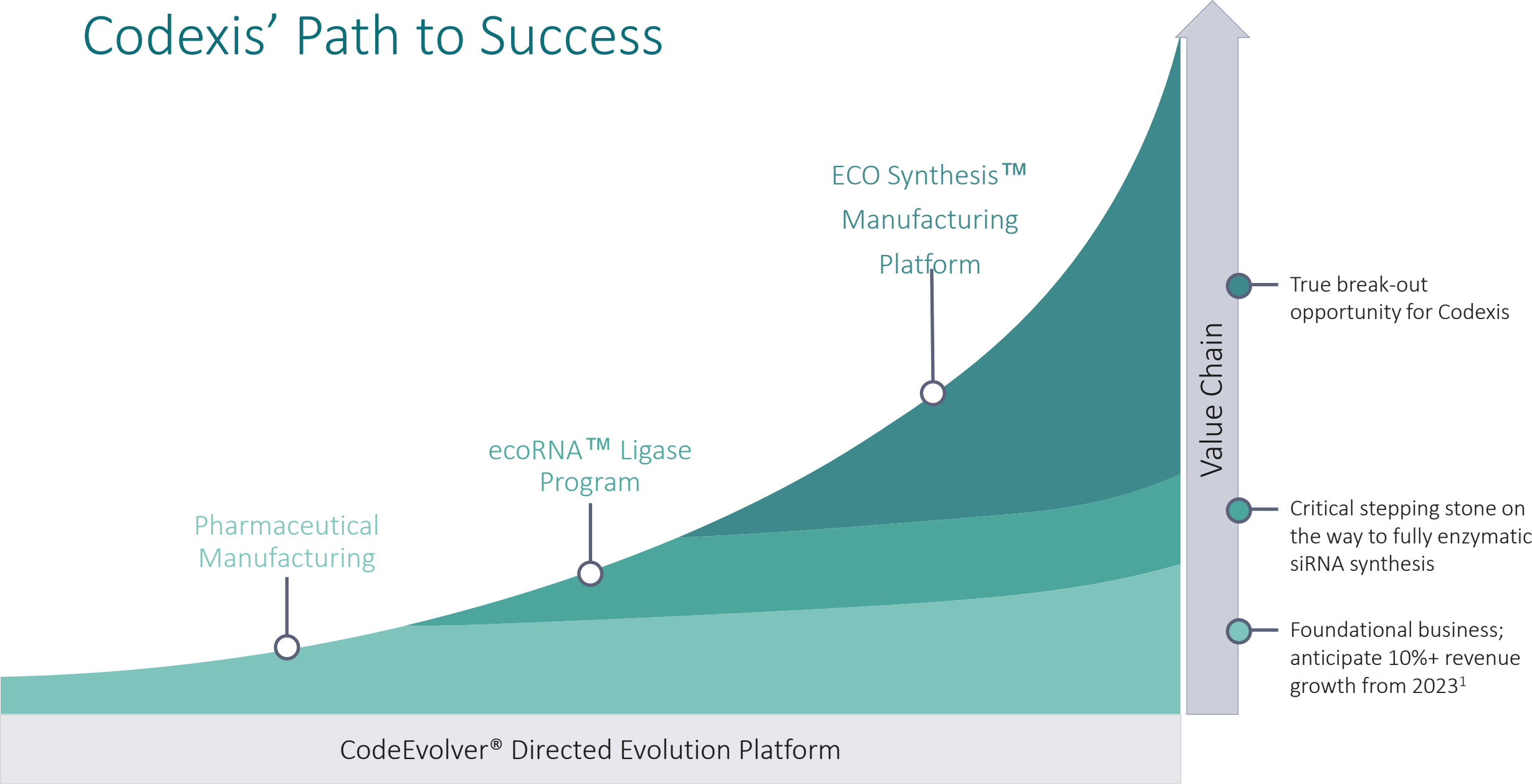


- **TnX transposase:** collaboration with seqWell



Foundational CodeEvolver® Directed Evolution Platform Serves as Backbone of Codexis and Drives Exquisite Enzyme Engineering Capabilities

# Codexis' Path to Success



<sup>1</sup>Excludes CDX-616 product revenue (related to PAXLOVID™)

# Pharmaceutical Manufacturing

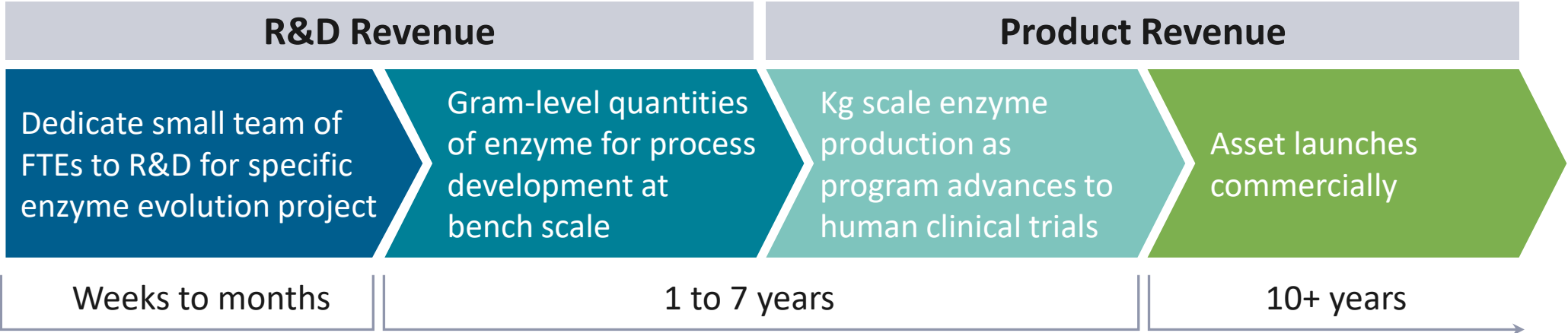
Evolved enzymes for biocatalysis  
of small molecule manufacturing

# Pharma Manufacturing: Two Paths to Revenue

Customer Engagement

Screening program identifies “off-the-shelf” enzyme for customer from existing kits and enzyme collections

Project requires additional enzyme evolution



# Pharma Manufacturing: Steady Pipeline to Drive Annual Growth

**GOAL:** maintain consistent volume of pipeline programs YOY to support ongoing product revenue growth

Fill pipeline with new programs



Existing development-stage programs will fund future growth



12 named programs currently in Phase 2 and 3 clinical trials use Codexis engineered enzymes



Expect conversion of ~40-50% of current Phase 2/3 pipeline to commercial products within 4-6 years

Currently selling custom engineered enzymes for 16 commercial drugs including multiple large disease indications

Anticipate increasingly diverse product mix to drive revenue as additional pipeline assets convert to commercial



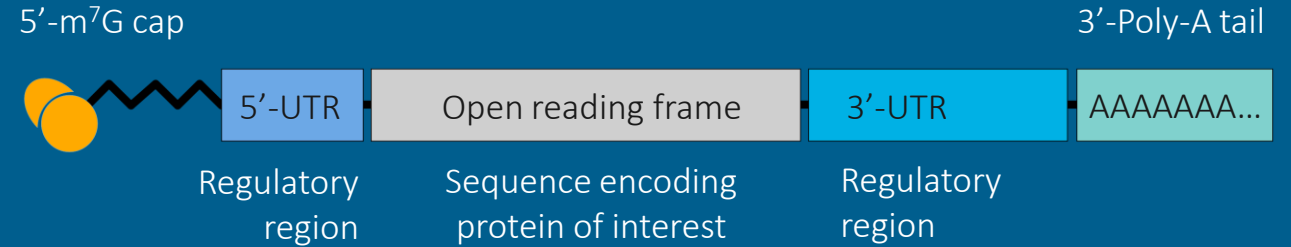
# ECO Synthesis™ Manufacturing Platform

Engineering the next generation of  
enzymes for oligonucleotide manufacturing

# Comparing & Contrasting mRNA and siRNA

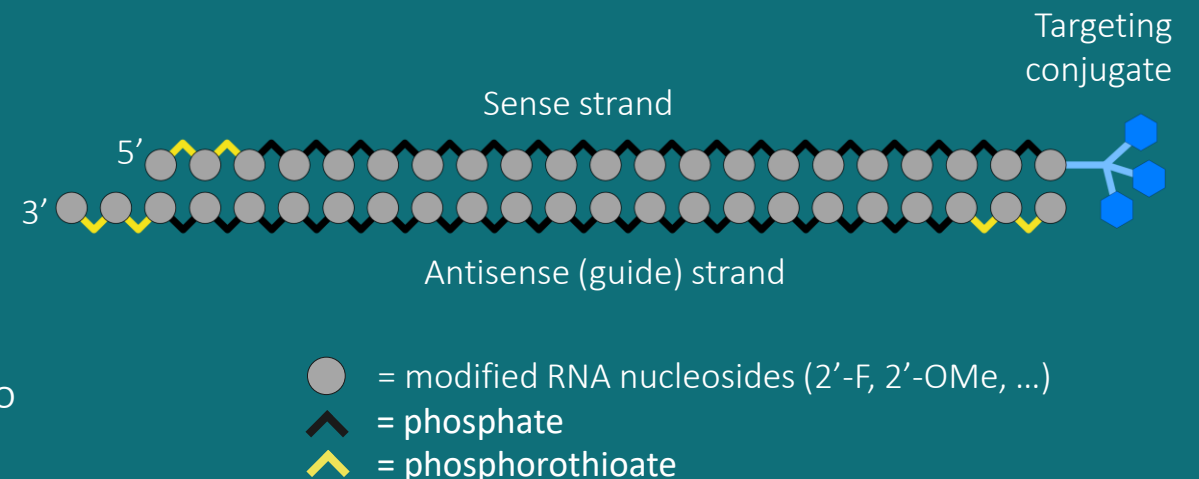
## mRNA

- Single stranded
- 2000+ nucleotides in length
- Composed of mostly native RNA building blocks
- Recent demand associated with mRNA vaccine and immuno-oncology products
- Codex<sup>®</sup> HiCap RNA Polymerase enables production of synthetic mRNA at high yield and purity



## siRNA

- Double stranded (complementary strands)
- 18-25 nucleotides in length
- Composed of modified RNA building blocks
- Anticipated wave of demand as additional siRNA therapeutics are developed and approved to address prevalent disease indications
- ECO Synthesis<sup>™</sup> manufacturing platform in development to enable commercial-scale, enzymatic synthesis of siRNA

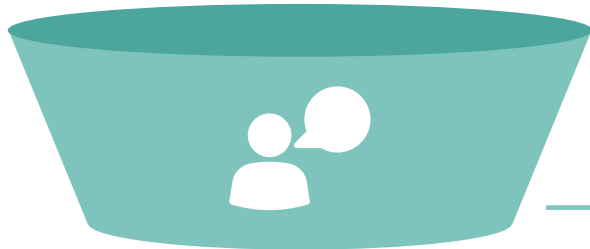


# ECO Synthesis™ Manufacturing Platform: Positioned to Deliver in RNAi Market

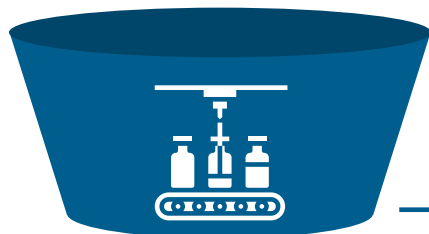
## RNAi Demand is Coming



Chemical synthesis (phosphoramidite chemistry) alone **will be challenged to meet projected future wave of demand for RNAi therapeutics**



Customers are asking us for a **scalable, sustainable enzymatic solution** to complement chemical synthesis



Codexis positioned to win based on **20-year history of enzyme engineering** and **directly relevant Pharmaceutical Manufacturing commercial expertise**

# RNAi Therapeutics: a Growing Modality

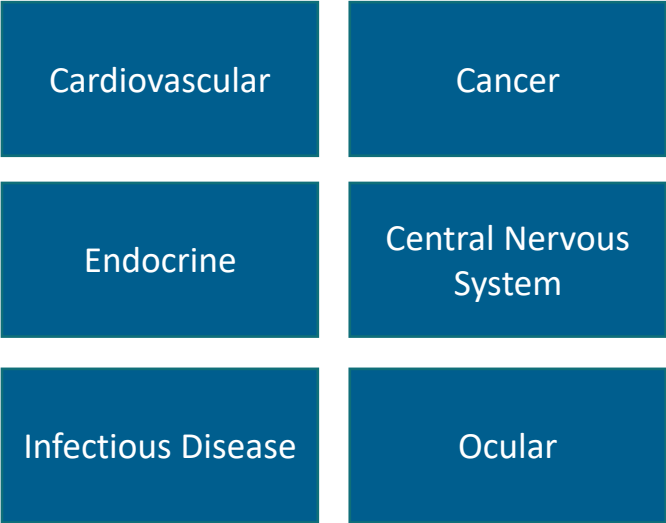
- Discovered 25 years ago, RNAi (RNA interference) is a natural defense against foreign RNA, such as viruses
- siRNAs are short, double-stranded oligonucleotides with an antisense strand designed to target an mRNA of interest
- siRNA can selectively target and silence genes related to disease through sequence-specific mRNA degradation; critical advantage over small molecule or antibody-based therapies is exquisite target specificity
- siRNA shows promise for the treatment of multiple cancers, viral infections, cardiovascular disease, neurodegenerative disorders and diabetes
- 6 currently approved siRNA therapies:
  - Patisiran (2018) – rare orphan indication
  - Givosiran (2019) – rare orphan indication
  - Lumasiran (2020) – rare orphan indication
  - Inclisiran (2021) – cardiovascular indication
  - Vutrisiran (2022) – rare orphan indication
  - Nedosiran (2023) – rare orphan indication



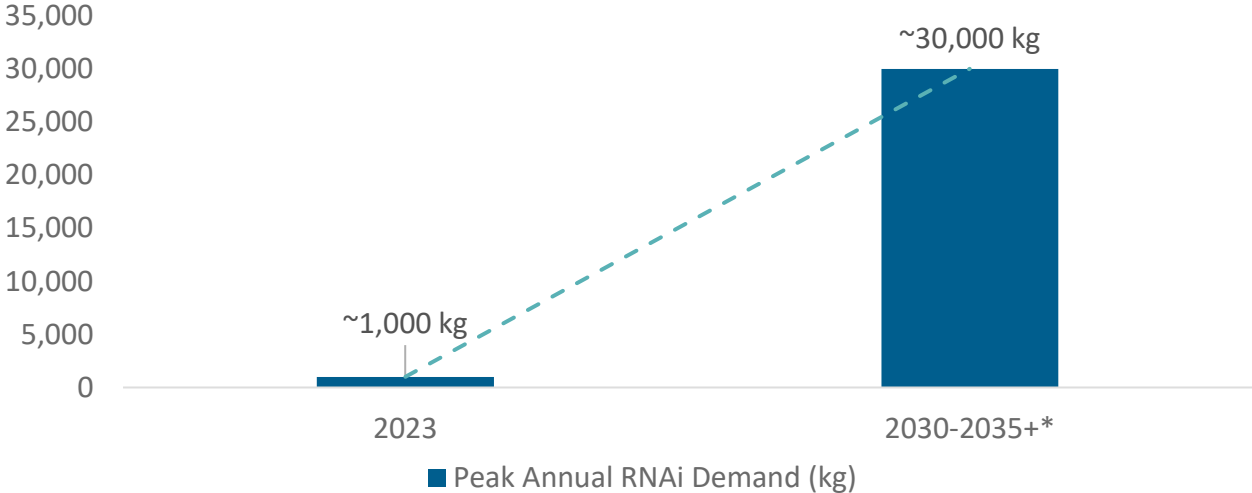
# RNAi Demand Growing Rapidly with Increasing Application in Large Patient Indications

- **>450 RNAi pipeline assets** in development today; 42 large indication assets currently in Phase 2 & 3 clinical trials
- Assuming approximately one-third of RNAi assets in development today gain approval by 2030, peak annual kgs of RNAi demand could grow to **~30K kg/year\***

## Key Disease Areas in Clinical Development



Worldwide RNAi Oligonucleotide Demand (kg)



\*Assumes 35% of assets currently in Phase 2/3 clinical trials are approved by 2030; assumed rate of approval is based on our estimates and data from Wong & Siah Biostatistics (2019)

# Traditional Chemical Synthesis Alone will be Challenged to Meet Anticipated Increase in RNAi Demand

Phosphoramidite chemistry: scale-constrained and challenged to meet coming RNAi demand

- Chemical synthesis is currently limited to **single-digit kilogram batch sizes**
- Requires **large volumes of solvent (acetonitrile)**; subject to supply constraints and price volatility
- Produces **millions of liters of costly, harmful chemical waste**
- Results in **low purity output** due to complex protection/deprotections
- Requires **significant capital investment** for high-cost raw materials, purification and waste disposal

## Infrastructure required to meet demand

- Agilent invested **\$725M** in facility expansion<sup>1</sup> to produce up to 1K kg of RNAi per year
- **\$10B to \$20B** infrastructure investment required to meet anticipated annual demand of ~30K kg by ~2030



# KOL Perspectives on Enzymatic Synthesis of RNAi Therapeutics

December 2023 Codexis KOL event included industry leader perspectives on the potential role of an enzymatic route of synthesis in commercial-scale siRNA production



“ I have long felt that **an enzymatic route of synthesis is a critical innovation** to reduce required infrastructure investments, mitigate high volumes of hazardous waste and ensure that drug developers can effectively address the coming demand of these medicines for patients.

- John Maraganore, PhD

Founder and Former Chief Executive Officer,  
Alnylam Pharmaceuticals  
Member of Codexis Strategic Advisory Board

“ Traditional chemical synthesis remains limited by scale per batch, expensive equipment, significant purification and waste disposal costs and a negative environmental impact. **A fully enzymatic approach has the potential to improve efficiencies across each of these areas.**

- David Butler, PhD

Chief Technology Officer,  
Hongene Biotech Corporation



# Our Solution: Codexis ECO Synthesis™ Manufacturing Platform for Large-Scale RNAi Therapeutics Production

ECO: Enzyme-Catalyzed Oligonucleotide *Synthesis*

## The Product:



## The Output:



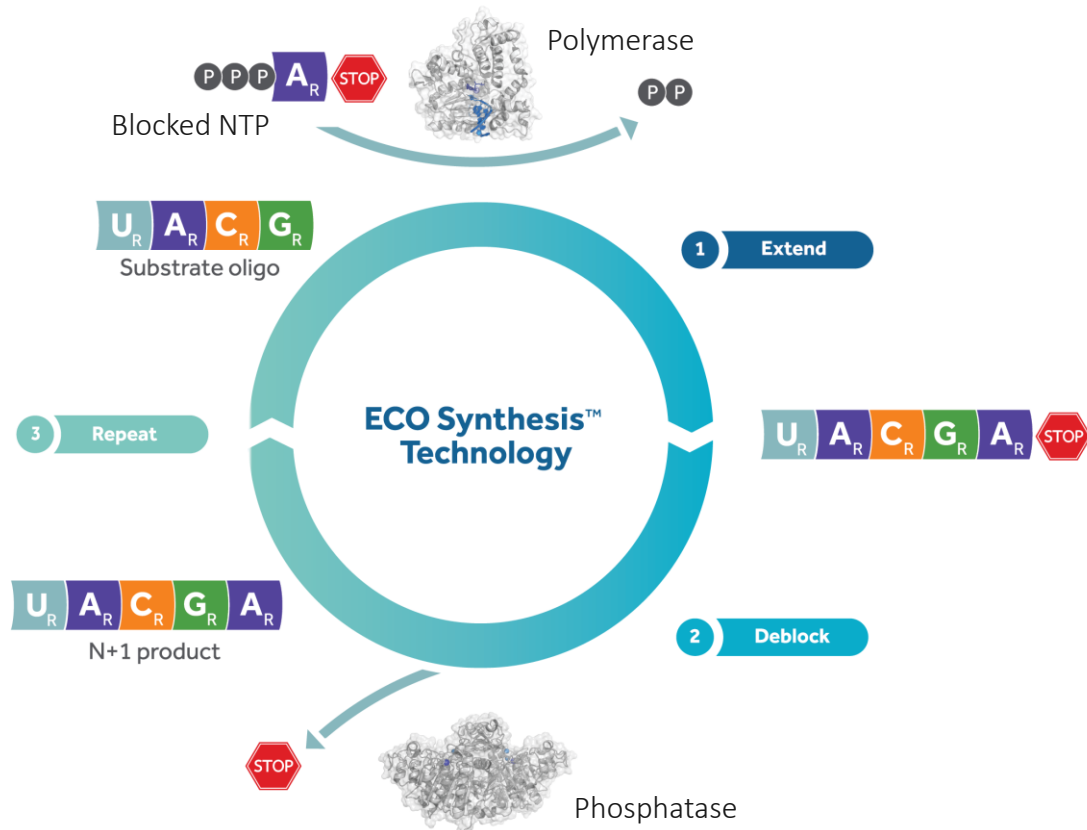
*siRNA synthesized at gram-scale with ECO Synthesis™ manufacturing platform*

## Current Status:

- In December 2023, CDXS achieved gram-scale synthesis with the ECO Synthesis™ manufacturing platform
- Enables a comprehensive assessment of the purity profile for siRNA produced with the ECO Synthesis™ manufacturing platform
- Allows us to start sharing data-driven insights with potential customers to facilitate early access conversations



# Technical Overview: ECO Synthesis™ Manufacturing Platform



Our ECO Synthesis™ manufacturing platform, which is in development, is *the first public disclosure of de novo enzymatic synthesis* of modified RNA over multiple cycles of nucleotide addition

## ECO Synthesis™ Manufacturing Platform

- Core technology requires a suite of enzymes, including:
  - Controlled addition of modified RNA bases (*TdT polymerase*)
  - Deblocking of 3' blocking group (*phosphatase*)
- Expanded technology is designed to include an enzymatically generated supply of 3' blocked NTP substrates (*4-6 enzymes*)

A First for Codexis: Developing a Complete Platform that Consists of Proprietary Enzymes and Processes

# Chemical Synthesis vs. ECO Synthesis™ Manufacturing Platform

## Phosphoramidite Chemistry

### Limited Scalability

- Best suited for bench top scale due to limited, single-digit kilogram batch sizes
- Capacity will be challenged to support future demand

### Toxic Solvent Use

- Requires large volumes of inorganic solvent (acetonitrile) with high disposal costs
- Likely future supply chain limitations & price volatility

### Low Purity

- Inefficient for longer RNAs
- Significant impurities from complex protection / deprotections

### High Cost

- High-cost infrastructure investment & raw materials
- High purification costs
- Expensive waste disposal



## ECO Synthesis™ Manufacturing Platform

### Scalable

- ✓ Enzymes and flow process
- ✓ Flow process enables 10s to 100s of kg/batch
- ✓ Closed-loop system – volumetric reagent efficiency

### Reduced Waste

- ✓ Aqueous reactions
- ✓ Significantly decreases chemical waste streams
- ✓ Path to enzymatically created monomers

### High Purity

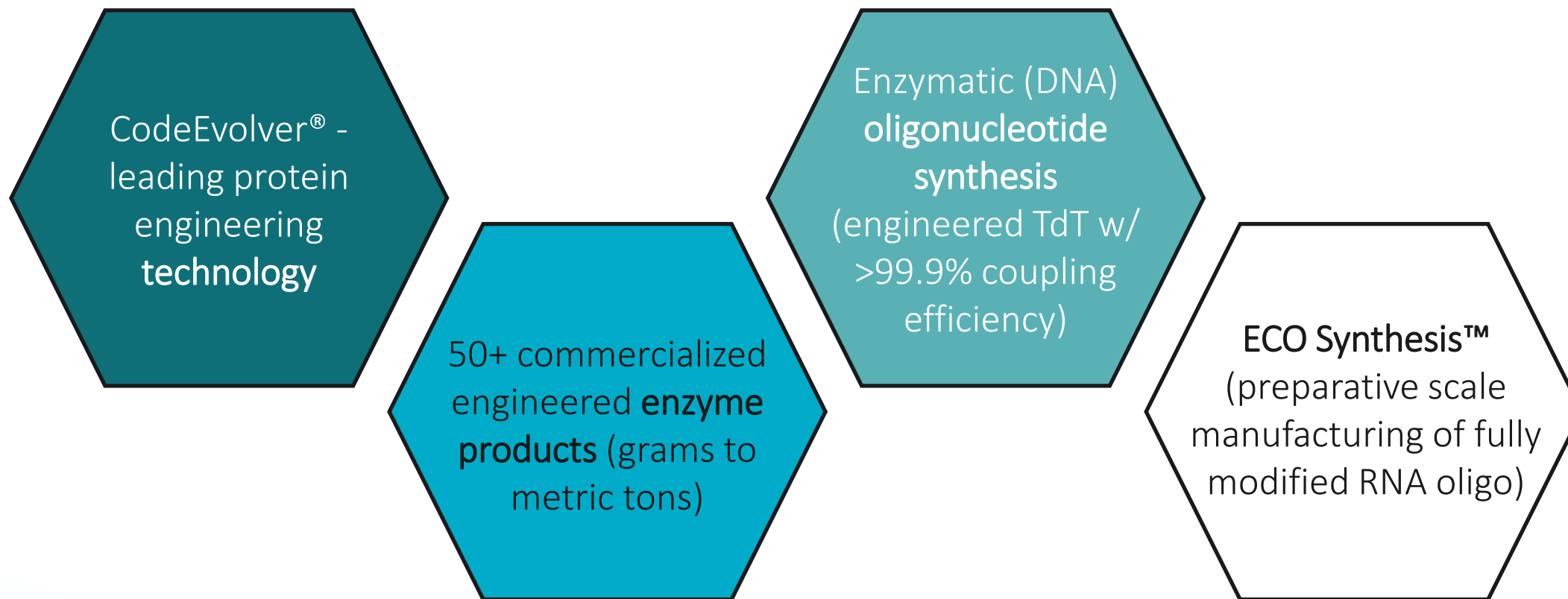
- ✓ Higher purity output reduces downstream purification needs

### Valuable Economics

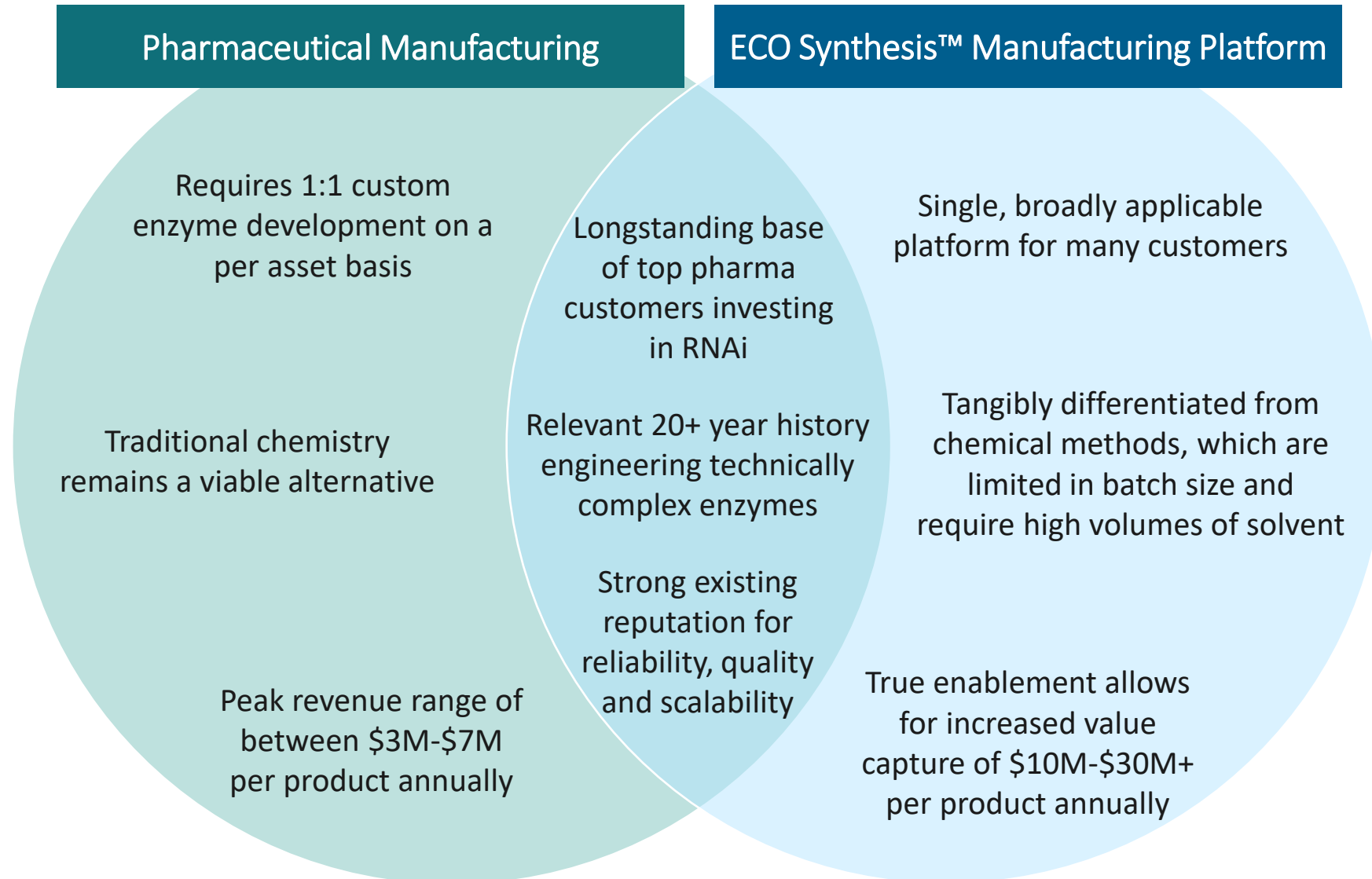
- ✓ De-bottlenecks current supply constraints with increased scale & efficiency
- ✓ Integrates with existing small molecule manufacturing facilities
- ✓ Saves \$Ms in purification and waste disposal costs

# ECO Synthesis™ Manufacturing Platform – (r)evolution in Progress

Set up for success based on two decades of expertise and experience in biocatalysis



# Leveraging Pharma Manufacturing Experience to Execute on Compelling ECO Synthesis™ Manufacturing Platform Opportunity



# Total Addressable RNAi Manufacturing Market Opportunity

## Estimated Annual RNAi Therapeutics Market Opportunity

Number of large indication RNAi assets approved by ~2030 <sup>1</sup>	15
	X
Annual kg demand / RNAi asset at peak <sup>2</sup>	2K kg
	=
Total annual kg demand at peak	30K kg
	X
Manufacturing cost / kg of API <sup>3</sup>	\$250K
	=
Peak annual RNAi manufacturing market opportunity	\$7.5B

## Why ECO Synthesis™ Manufacturing Platform is Positioned to Deliver in RNAi

- Obviates need for massive, early-stage capital investment (\$10-\$20B<sup>4</sup>) required for phosphoramidite chemistry to meet anticipated annual demand of ~30K kg by ~2030
- Adaptable technology with potential to manufacture a broad range of siRNA at commercial scale
- High purity output reduces downstream purification needs

<sup>1</sup>Assumes 35% of the 42 assets currently in Phase 2 & Phase 3 clinical trials are approved by 2030; based on data from Wong & Siah Biostatistics (2019)

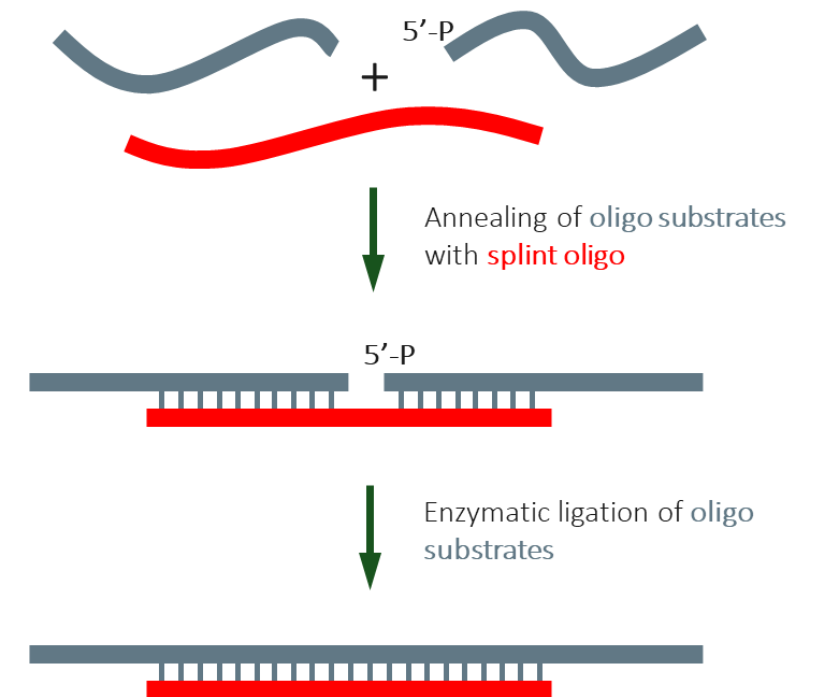
<sup>2</sup>Assumes 1 gram/patient based on current approved RNAi therapeutics; assumes an average treated population of 2 million patients/disease indication

<sup>3</sup>Assumes optimized phosphoramidite chemistry

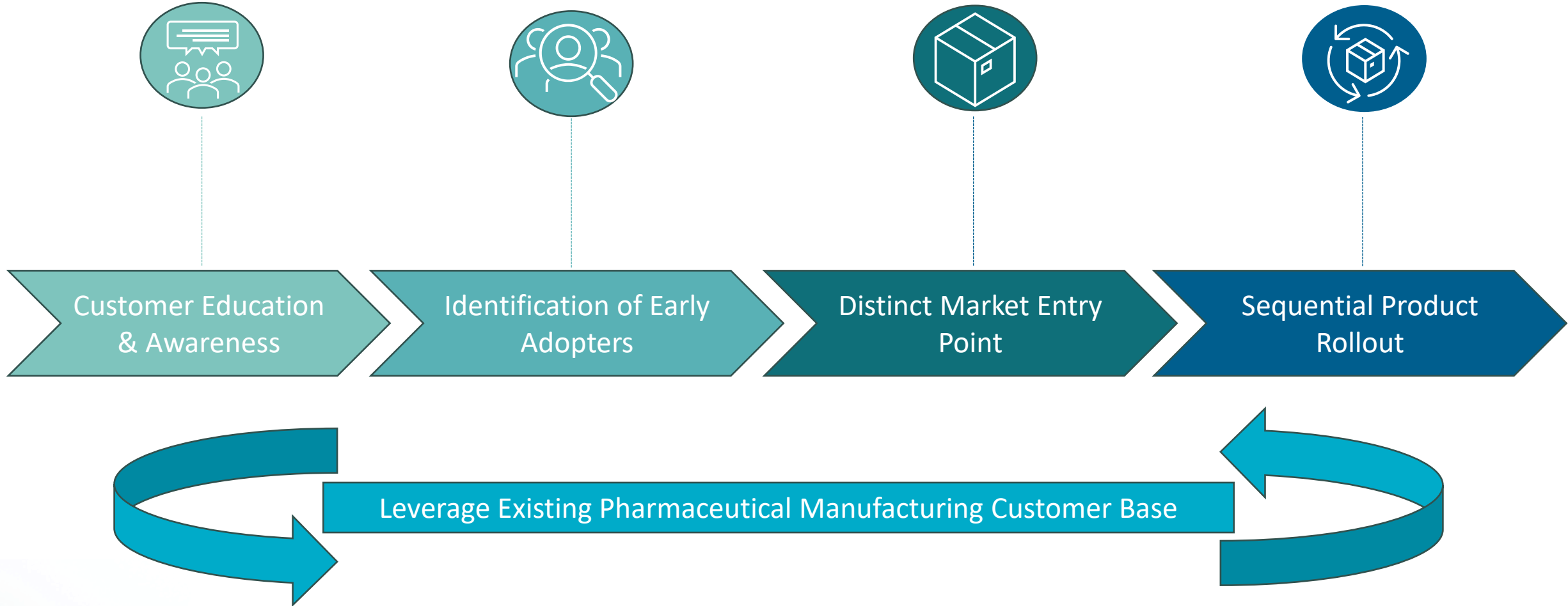
<sup>4</sup>Assumes \$0.7B capex required for manufacturing facility (Agilent) that can produce 1kg of siRNA per year

# Early RNAi Therapeutics Market Entry and Customer Engagement with an Engineered ecoRNA™ Ligase

- Double-stranded ecoRNA™ ligase offers a solution to reduce cost of manufacturing by integrating with existing phosphoramidite chemistries to join RNA fragments and form RNAs<sup>1</sup>
- Serves as RNAi therapeutics market entry point and enables earlier access to customers
- Enzyme currently in manufacturing for optimization and potentially offers an improved alternative to the early ligation technology on the market today
- Existing customized programs with large RNAi players; expect to make dsRNA ligase widely available in 2024



# ECO Synthesis™ Manufacturing Platform: Key Elements of Our Commercial Strategy



# Well Positioned to Maximize ECO Synthesis™ Manufacturing Platform Value Potential

## The Challenge



Traditional chemical synthesis alone is an expensive, time intensive and difficult option to meet the projected future wave of demand for RNAi therapeutics

## Our Solution



The ECO Synthesis™ manufacturing platform offers an enzymatic approach with potential to play an important role in meeting the anticipated RNAi therapeutics demand

**CODEXIS**®

## Our Advantages



The RNAi therapeutics landscape overlaps with our 20+ year Pharmaceutical Manufacturing history across infrastructure, experience, technology & commercial reach

## Our Financial Position



- Pro forma cash of ~\$70M as of 12/31/23<sup>1</sup>
- \$29M net proceeds from strategic debt financing in Feb 2024
- Path to potential positive cash flow expected around end of 2026



# Corporate Highlights

# Anticipated News Flow for ECO Synthesis™ Manufacturing Platform

TIDES USA - demonstrate clinically relevant, full-length siRNA synthesized enzymatically

ECO Synthesis™ manufacturing platform enters pre-commercial testing with select customers

ecoRNA™ ligase program available for customers

ECO Synthesis™ Innovation Lab build-out

Early commercial licenses to ECO Synthesis™ manufacturing platform

Achieve pilot scale production with ECO Synthesis™ Innovation Lab for pre-clinical use

ECO Synthesis™ manufacturing platform and process widely available for customers

2024

2025

2026

# Codexis: Strong Fundamentals and Positioned for Growth

Codexis is a well-funded, streamlined company with a profitable base business and a potentially transformational opportunity with the ECO Synthesis™ manufacturing platform

- Foundational Pharmaceutical Manufacturing business is profitable; expected to return to sustained growth with higher margins in 2024
- Significant opportunity to address anticipated wave of demand for siRNA therapeutics with the innovative ECO Synthesis™ manufacturing platform
- Uniquely positioned for success in siRNA market given longstanding history of engineering technically complex enzymes for existing large pharma customers
- Well-funded through key ECO Synthesis™ manufacturing platform milestones with a path to potential positive cash flow expected around end of 2026



# Thank You

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