



# Corporate Presentation

September 2024



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, our expectations regarding the potential revenues of Codexis’ Pharmaceutical Manufacturing business and that such business will experience mid-teens product revenue CAGR through 2030; 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; potential revenue opportunities of Codexis’ dsRNA ligase programs; 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’ expectations regarding 2H’2024 product revenues and growth and sources of future revenues, as well as its ability to achieve 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

Foundational CodeEvolver® Directed Evolution Platform Drives Exquisite Enzyme Engineering Capabilities

## Revenue Generating Pharma Manufacturing Business

- ✓ Foundational biocatalysis business in small molecule manufacturing
- ✓ Cash generating; anticipate mid-teens product revenue CAGR through 2030

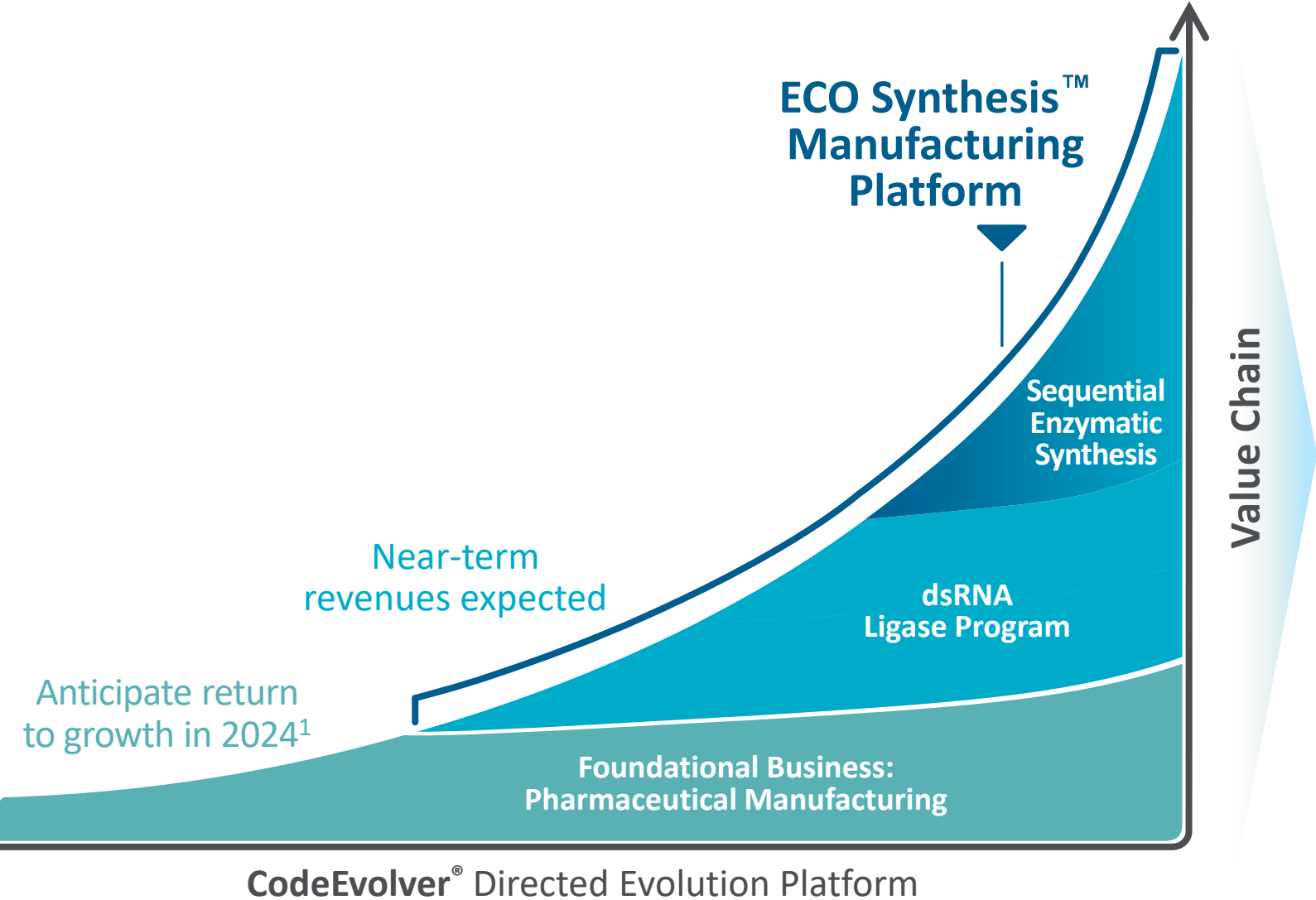
## RNA Manufacturing Services

- ✓ **ECO Synthesis™ manufacturing platform:** enzymatic RNA synthesis to meet future demand for RNAi therapeutics
  - dsRNA ligase
  - Sequential enzymatic synthesis
- ✓ **Codex® HiCap RNA Polymerase:** global exclusive license to  **aldevron®**

**\$73.2 Million** Cash / Cash Equivalents and Investments as of 6/30/24

Path to Potential Positive Cash Flow Around End of 2026

# Codexis' Path to Success



Path to positive cash flow around end of 2026

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Enabling full-scale production of siRNA

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

# Path to Positive Cash Flow Around End of 2026: Three Key Factors

**1**

**Strong 2H'24 product revenues**

Existing and expected orders drive near-term growth

**2**

**Pharma Manufacturing current commercial products and pipeline + additional dsRNA ligase orders**

Positioned to drive product revenue growth in 2025 & 2026

**3**

**Screening and evolution programs**

Anticipated R&D revenue from Pharma Manufacturing, dsRNA ligase screening and optimization services and ECO Synthesis™ Innovation Lab

# Pharmaceutical Manufacturing

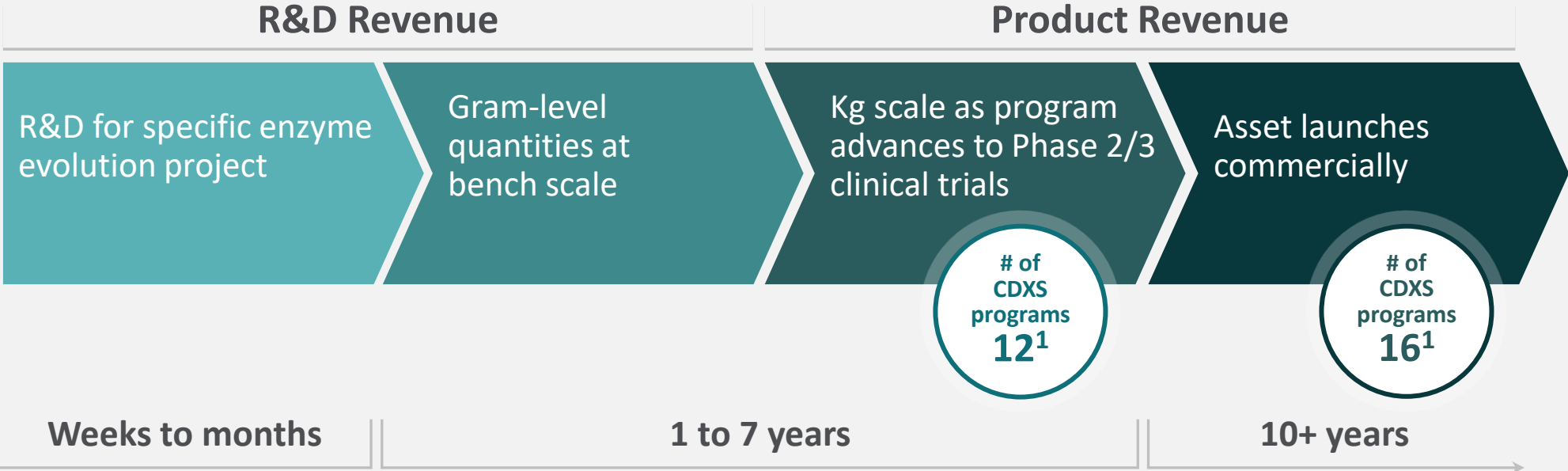
Evolved Enzymes for Biocatalysis  
of Small Molecule Manufacturing

# Pharma Manufacturing: Two Paths to Revenue

## Customer Engagement

### 1 “Off-the-shelf” Enzyme Solutions from Existing Libraries

### 2 Custom Enzyme Evolution



<sup>1</sup> Number of programs for which Codexis is selling biocatalysts to pharmaceutical manufacturers as of December 31, 2023

# Pharma Manufacturing: Pipeline Drives Revenue Growth

Anticipate Mid-Teens Product Revenue CAGR Through 2030 Based on Existing Commercial Products and Current Pipeline

## R&D Revenue

- Existing development-stage programs will fund future product revenue growth
- Sourcing additional pipeline programs to drive sustained revenue growth throughout the decade

## Product Revenue

- Return to sustainable growth in 2024
- Anticipate mid-teens CAGR through 2030 based on current commercial products and existing pipeline

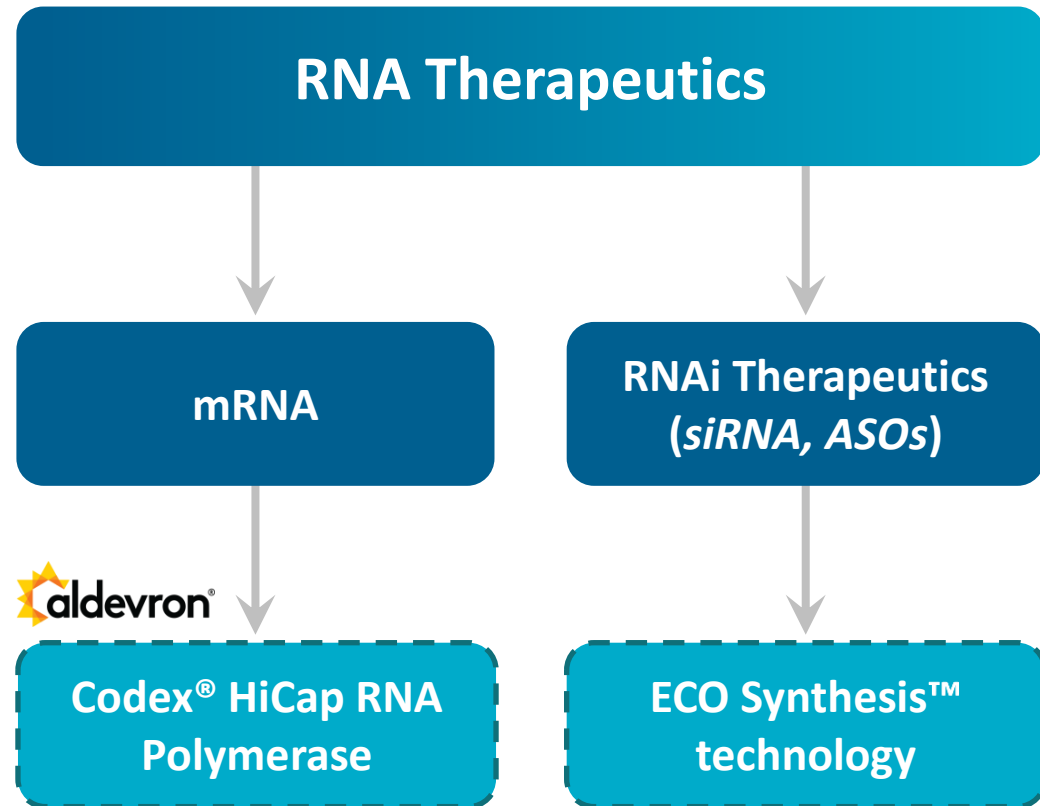
Strong Foundational Business Generating Cash



# RNA Manufacturing

Engineering the Next Generation of Enzymes  
for Oligonucleotide Manufacturing

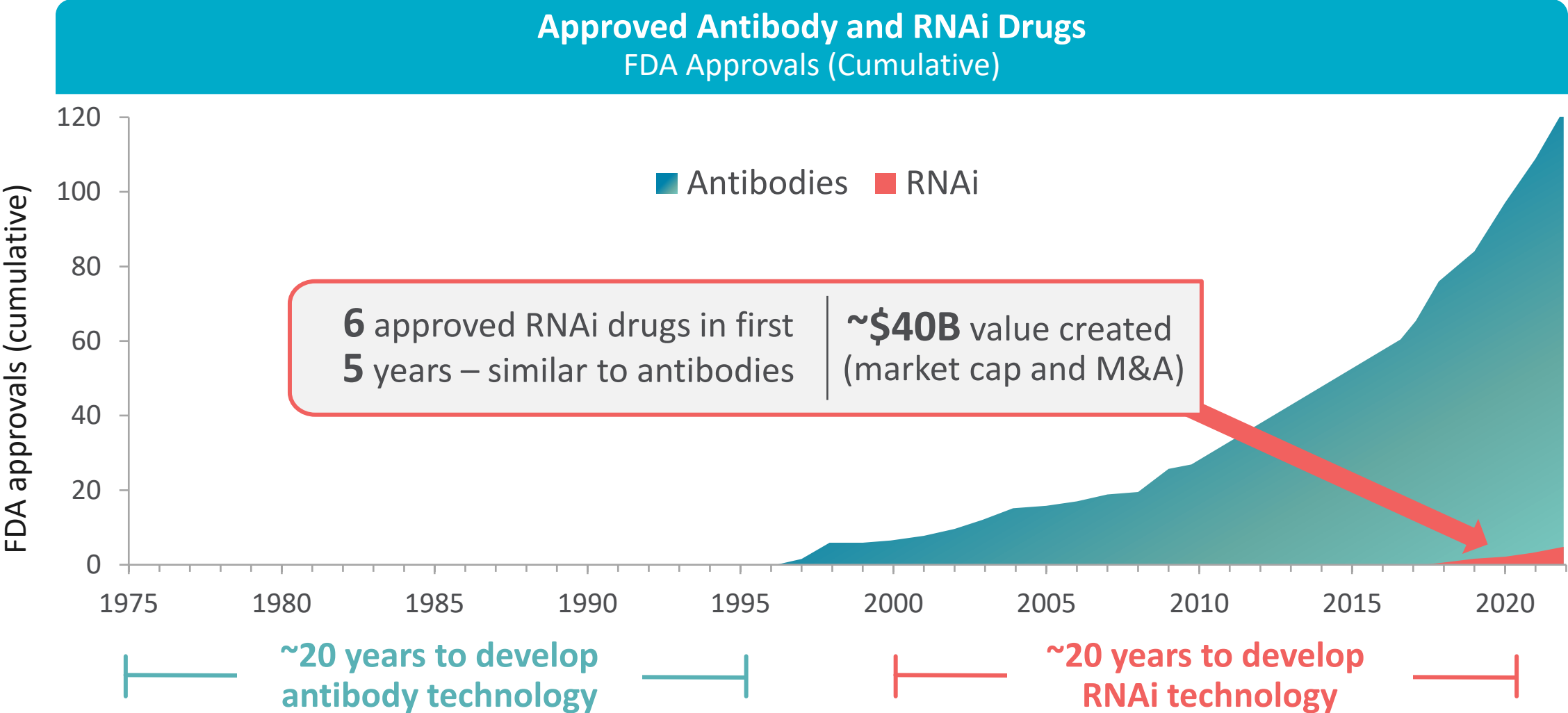
# RNAi Therapeutics – a Growing Modality



## siRNA: Natural Entry Point for ECO Synthesis™ Technology

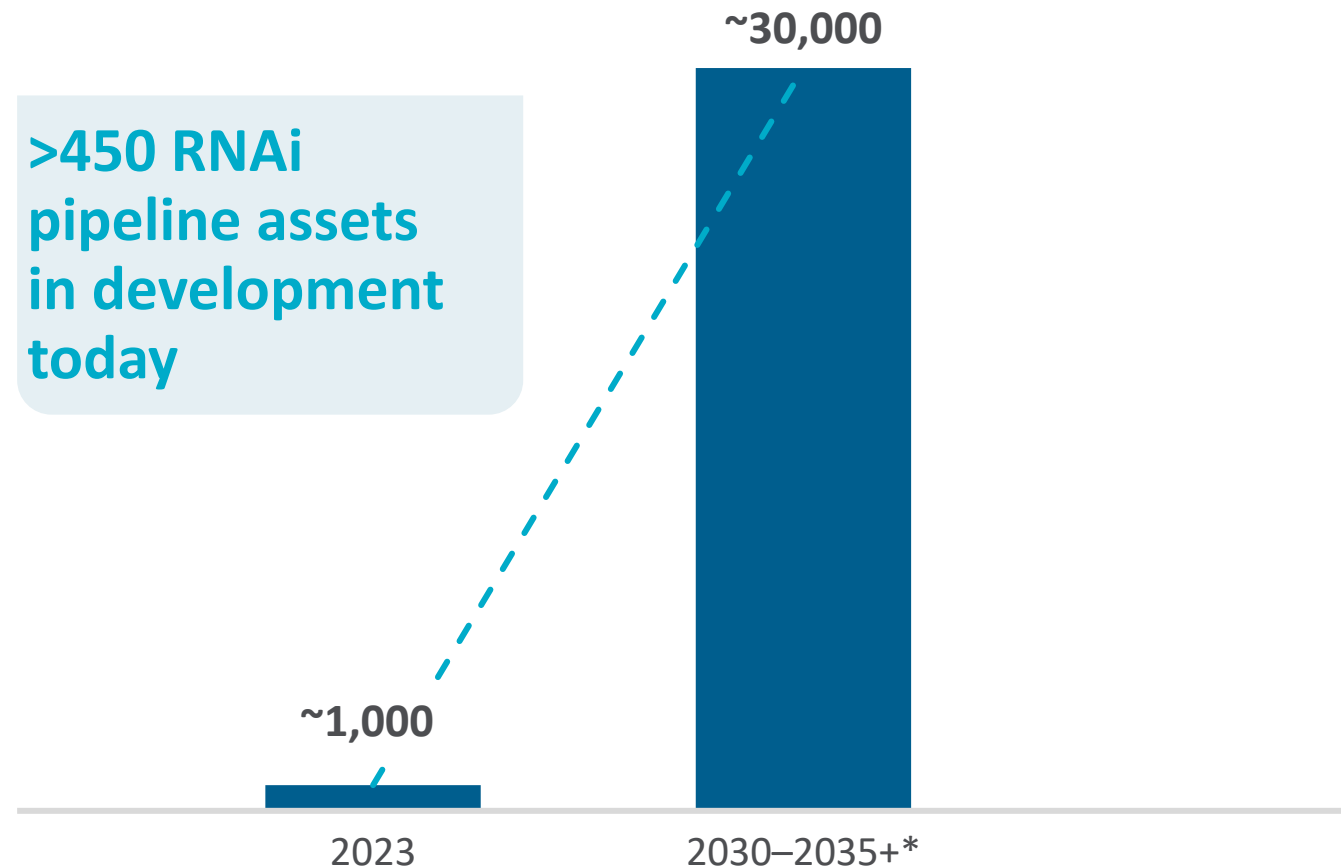
- Short, double-stranded oligonucleotides
- Selective knock-down of disease-related genes via sequence-specific mRNA degradation
- 6 approved therapies since 2018
- Approved for first large indication in 2021 (inclisiran)
- Potential application in additional large disease indications
- Currently manufactured using phosphoramidite chemistry

# RNAi Therapeutics – the Next Mab Modality?



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

## Worldwide RNAi Oligonucleotide Demand (Peak Annual RNAi Demand, kg)



Source: Codexis Market Research 2023

\* 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 Therapeutics Demand

## Challenges with Phosphoramidite Chemistry

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- Currently limited to **single-digit kg batch sizes**
- **Bottlenecks** for development-stage assets
- Requires **large volumes of toxic & flammable solvents**
- Produces **costly, harmful chemical waste**
- **Low purity output**
- **Significant capital investment** for raw materials, purification and waste disposal

## Significant CapEx Requirements

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



# Codexis is Positioned to Deliver Enzymatic Solutions for Growing RNAi Therapeutics Demand

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

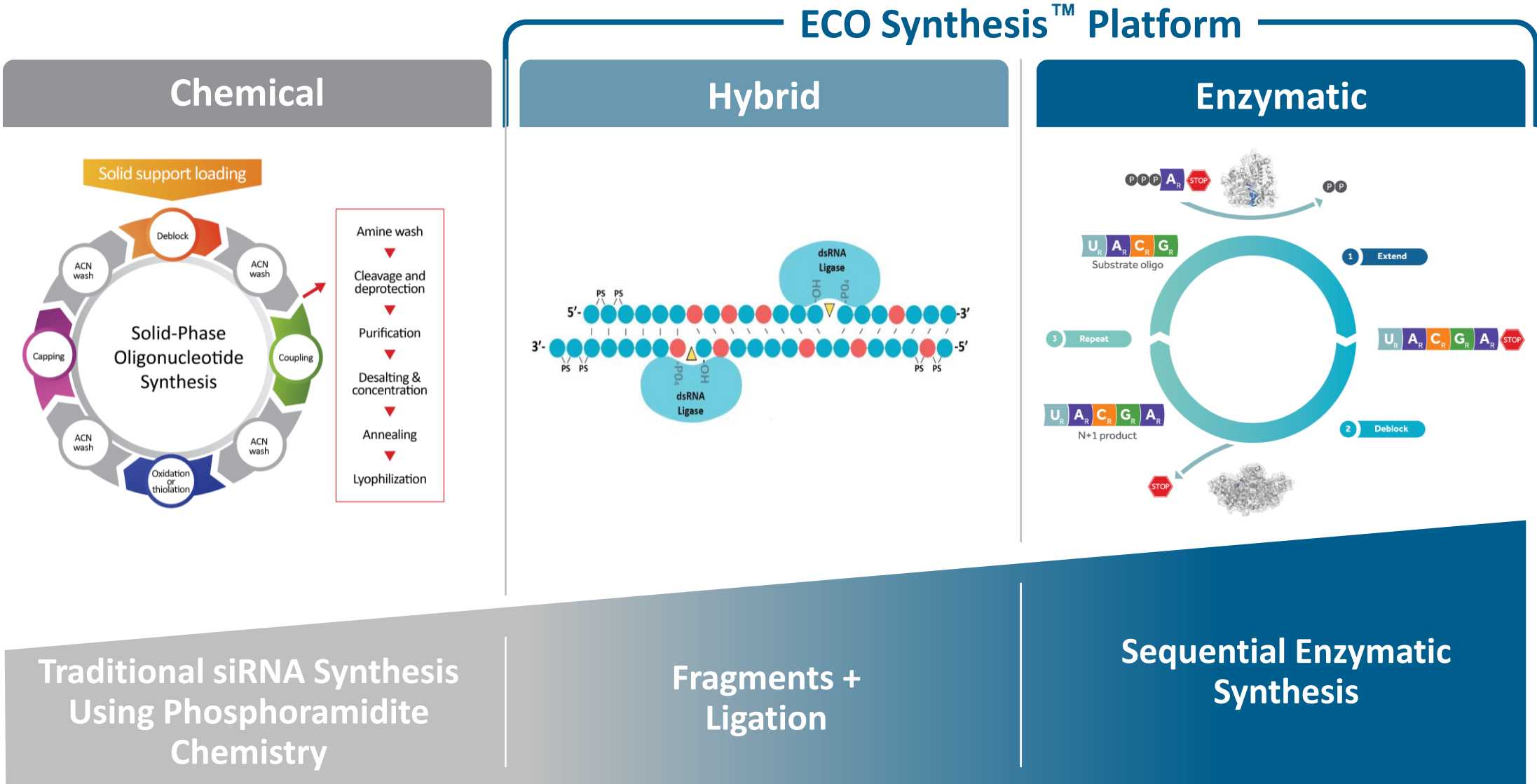
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Codexis is positioned to win based on **20-year history of engineering increasingly complex enzymes**

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Codexis' technical progress over the last 24 months has demonstrated that **enzymatic tools are here *now*** versus “years away”

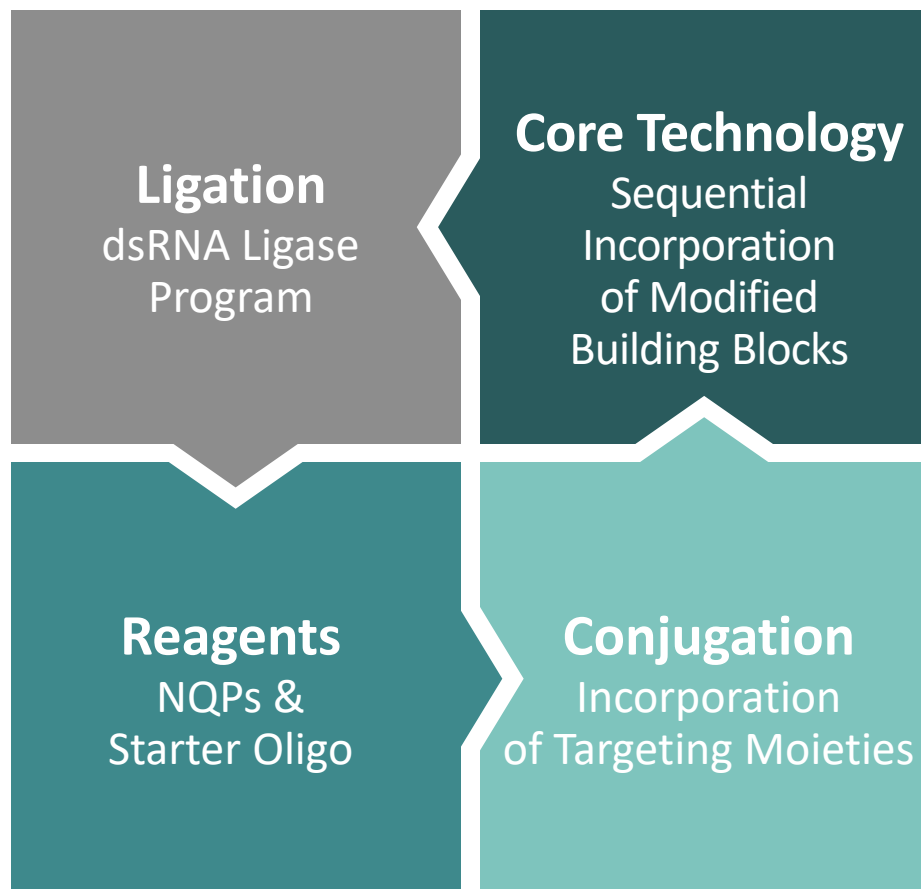
# Enzymatic Solutions Provide Optionality in siRNA Synthesis



# Our Solution: Building a Versatile Tool Kit to Synthesize RNA

## ECO: Enzyme-Catalyzed Oligonucleotide Synthesis

### ECO Synthesis™ Manufacturing Platform



### The Product



### Anticipated Revenue Streams

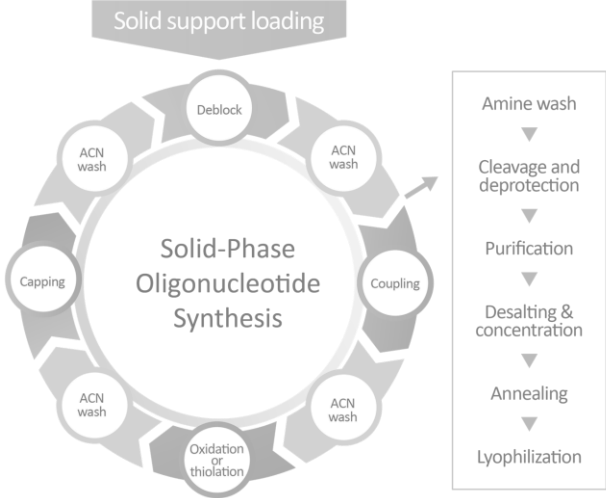
- ✓ Customized dsRNA ligases
- ✓ siRNA production
  - GLP material
  - GMP material
- ✓ Platform licenses (upfront payments, milestones, royalties, raw materials supply agreement)



# Hybrid dsRNA Ligase Approach: Near Term Revenues

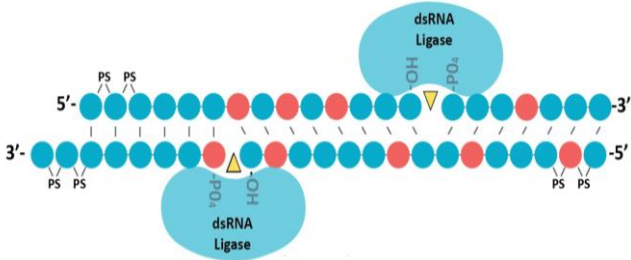
## ECO Synthesis™ Platform

### Chemical



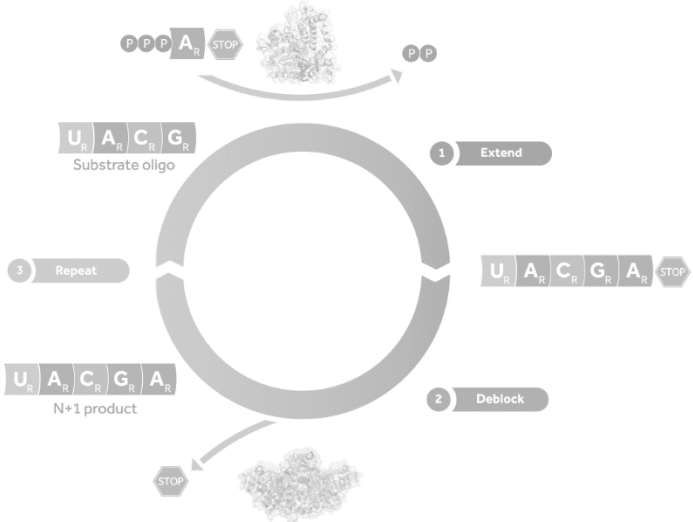
Traditional siRNA Synthesis Using Phosphoramidite Chemistry

### Hybrid



Fragments + Ligation

### Enzymatic



Sequential Enzymatic Synthesis

# dsRNA Ligase: Significant Per Asset Revenue Opportunity

## Pharma Manufacturing

**~\$5M**  
per Asset<sup>1</sup>

- Low price, high volume
- Thousands of dollars/kilogram

## dsRNA Ligase Program

**\$10M+**  
per Asset<sup>2</sup>

- High price, low volume
- Thousands of dollars/gram

## Large Indication siRNA Therapeutic Example<sup>2</sup>



**~\$1B**  
Projected peak sales of large indication siRNA asset



**~\$100M**  
COGS is ~10%



**20%**  
Potential COGS reduction from ligation



**\$20M**  
Pharma company savings



**\$10M**  
Codexis potential annual revenue

Repeatable, sustainable business expected to translate into meaningful revenues

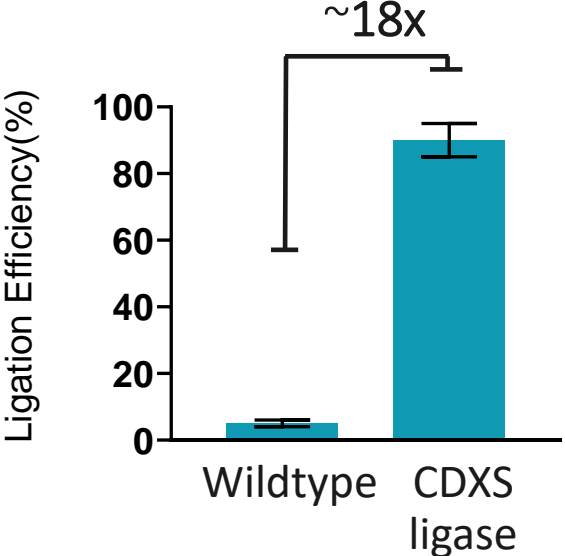
<sup>1</sup> Represents average projected 2024 revenue across Codexis' three largest Pharmaceutical Manufacturing enzymes

<sup>2</sup> Large pharma company guidance

# Engineered Ligases Enable Lower Manufacturing Costs

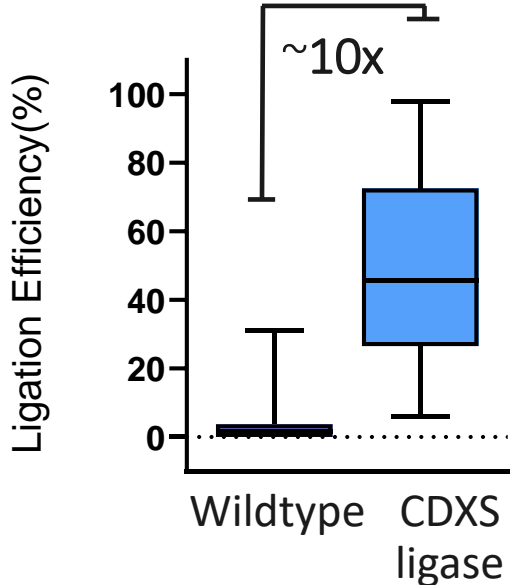
CDXS Variant Drives Valuable Economics through Improved Performance Metrics

## Improved Catalytic Activity



**Higher volumetric productivity**  
Potential cost savings via reduced time and purification needs; potential higher product yields

## Superior Performance Across 20+ Oligo Substrates



**Versatility**  
Broad tolerance of modified RNA oligo offers flexibility in design strategies

# dsRNA Ligase Program: Multi-Pronged Commercial Strategy

Variety of Approaches to Meet Customers Where They Are

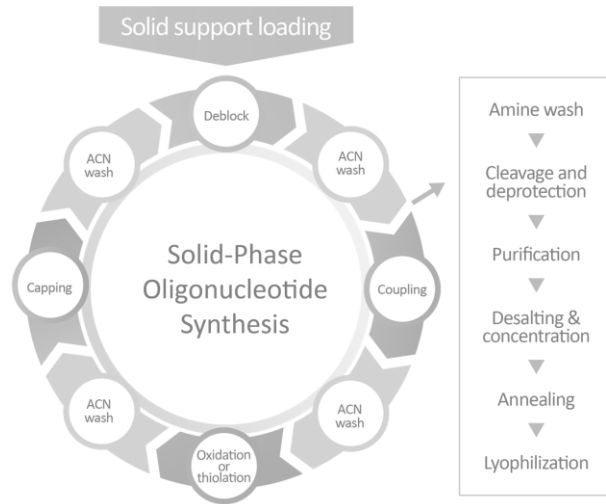


Offerings Designed to Encourage Rapid, Seamless Customer Uptake

# ECO Synthesis™ Manufacturing Platform: the Sequential Enzymatic Solution

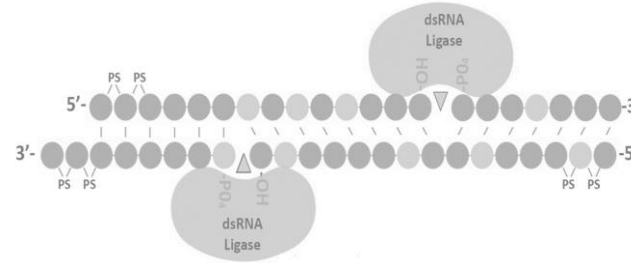
## ECO Synthesis™ Platform

### Chemical



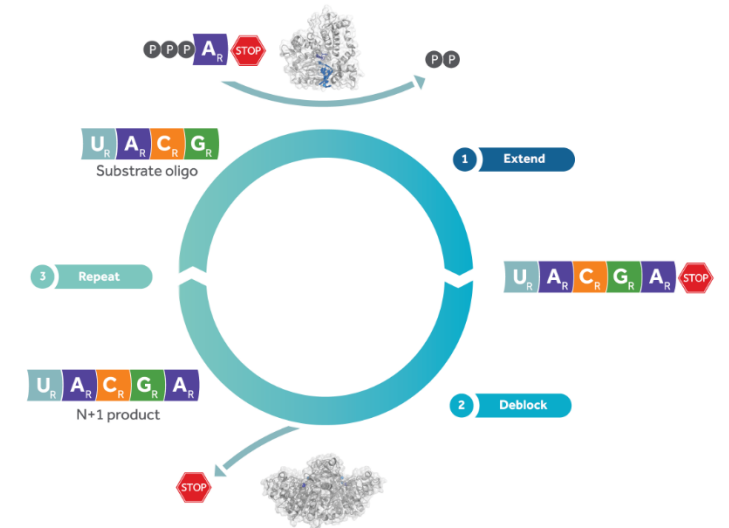
Traditional siRNA Synthesis  
Using Phosphoramidite  
Chemistry

### Hybrid



Fragments +  
Ligation

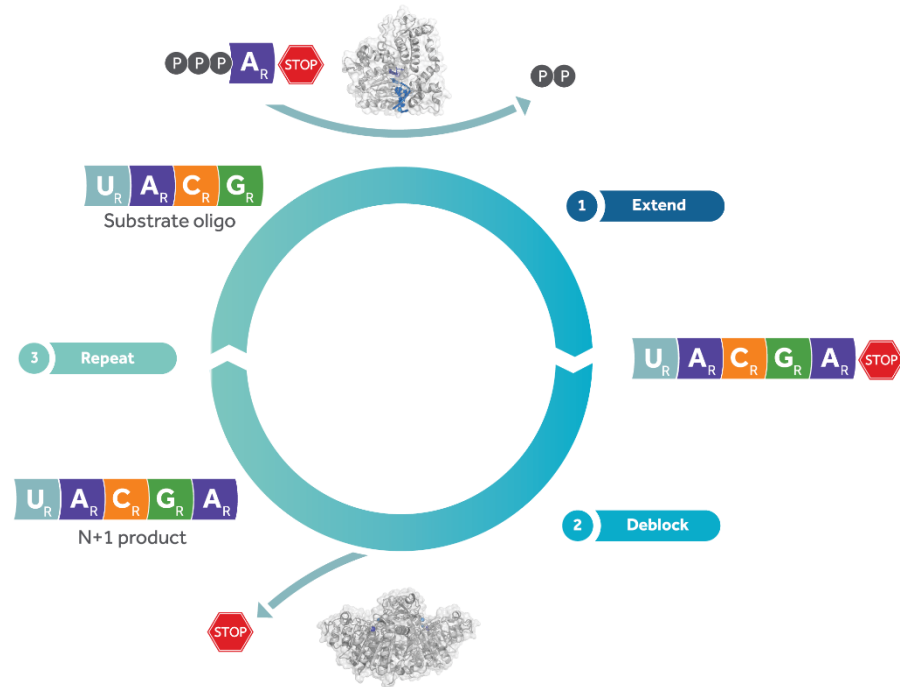
### Enzymatic



Sequential Enzymatic  
Synthesis

# Technical Overview: Sequential Enzymatic Synthesis

## ECO Synthesis™ Manufacturing Platform in Development



### Core Technology

Sequential addition of modified RNA nucleotides

### Reagents

Enzymatically generated NQPs (building blocks) & starter oligos

### Conjugation

Enzymatic attachment of targeting moieties

Leading the Way for a Full Platform of Sequential Enzymatic Synthesis

# ECO Synthesis™ Innovation Lab: First Step to Becoming a Full-Service Provider of siRNA

## Enables Process Development & Optimization

- Informs process conditions required for each molecule

## Offers Customers Path to GLP-Grade Material

- Enables toxicology studies through production of GLP material via ligation and/or sequential synthesis
- “Show and tell” bridges gap between concept and implementation of biocatalysis

## Supports GMP Scale Up

- Enables tech transfer to GMP facilities for clinical trial and commercial manufacturing

Continued Strong Engagement with Customers and Inbound Interest from Potential Partners

# Chemical Synthesis vs. ECO Synthesis™ Manufacturing Platform

## Phosphoramidite Chemistry

### Limited Scalability

- Delivers limited batch sizes (~5kg of RNA/batch)
- Capacity will be challenged to support future RNA demand

### Toxic Solvent Use

- Requires large volumes of toxic 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
- High purification costs
- Expensive waste disposal

## ECO Synthesis™ Manufacturing Platform

### Scalable

- High scalability designed to lower costs and lead times
- Flow process with immobilized enzymes enables volumetric reagent efficiency, delivering 10s to 100s of kg of RNA/batch

### Reduced Waste

- Aqueous reactions significantly decrease chemical waste streams
- Path to enzymatically created monomers

### High Purity

- Higher purity streamlines 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



# Total Addressable RNAi Therapeutics Manufacturing Market Opportunity

## Estimated Annual RNAi Therapeutics Market Opportunity

15

X

Number of large indication RNAi assets approved by ~2030<sup>1</sup>

2K kg

==

Annual kg demand / RNAi asset at peak<sup>2</sup>

20K kg

X

Total annual kg demand at peak

\$250K

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Manufacturing cost / kg of API<sup>3</sup>

\$7.5B

Peak annual RNAi manufacturing market opportunity

## Enzymatic Solutions:



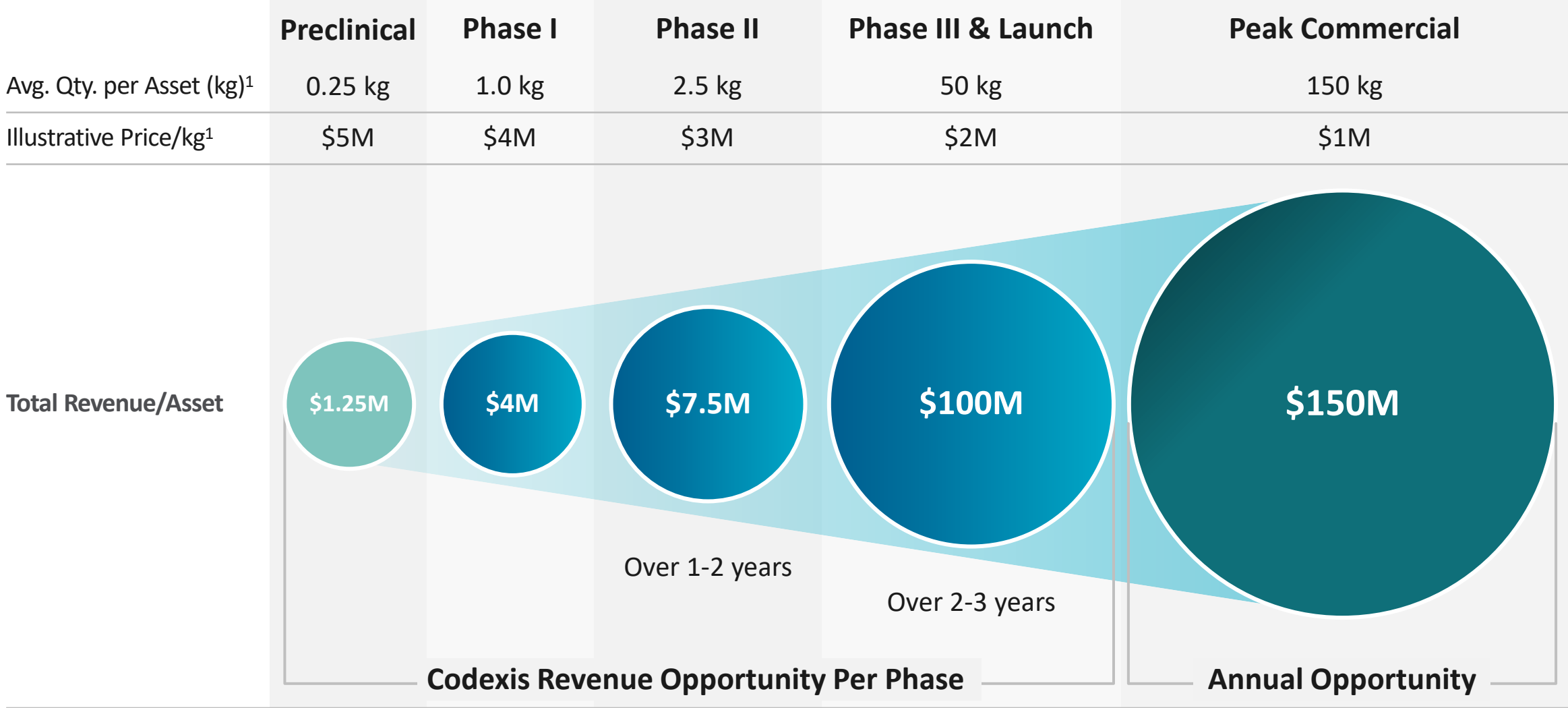
Obviate need for massive, early-stage capital investment (**\$10B–\$20B<sup>4</sup>**) required for traditional chemistry to meet anticipated annual demand of **~30K kg by ~2030**



Can be adapted to manufacture a broad range of siRNA at commercial scale

<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

# ECO Synthesis™ Manufacturing Platform Revenue Potential of a Single siRNA Therapeutic Asset by Stage



<sup>1</sup> Independent market research and feedback from potential customers; prices inclusive of CMC development-related services

# 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,  
Anylam 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



# Built to Win Based on Decades of Expertise in Biocatalysis

ECO Synthesis™ Manufacturing Platform – (R)evolution in Progress

1

**CodeEvolver®** – Leading protein engineering **technology**

2

50+ commercialized engineered **enzyme products**

3

Enzymatic (DNA) **oligonucleotide synthesis**  
(engineered TdT w/ >99.9% coupling efficiency)

4

**RNA Synthesis**  
(ECO Synthesis™ manufacturing platform)

# Corporate Highlights

# Anticipated News Flow for ECO Synthesis™ Manufacturing Platform

2024	2025	2026
<ul style="list-style-type: none"><li>✓ Demonstrate full-length, named siRNA compounds synthesized enzymatically</li><li>✓ Launch dsRNA ligase Screening and Optimization Services</li></ul>	<p>Achieve pilot scale production with ECO Synthesis™ Innovation Lab for GLP material</p>	<p>ECO Synthesis™ manufacturing platform widely available for customers</p>
<p>TIDES Europe</p>	<p>TIDES USA</p>	
<p>Technical collaborations with potential partners and customers</p>		
<p>ECO Synthesis™ Innovation Lab build-out complete</p>		

Streamlined & Positioned for Growth; Path to Profitability by End of 2026



# Thank You

CODEXIS®

Nasdaq: **CDXS**  
[www.codexis.com](http://www.codexis.com)