



# Corporate Presentation

November 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, our expectations regarding the potential revenues of Codexis’ Pharmaceutical Manufacturing business; 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, quality 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 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 customer uptake and revenue opportunities of Codexis’ dsRNA ligase program; Codexis’ expectations for the build-out of its planned ECO Synthesis™ Innovation Lab; timing of news updates regarding the ECO Synthesis™ platform and Codexis’ achievement of key milestones; and Codexis’ expectations regarding ability to and timing around reaching profitability, and length of cash runway. 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

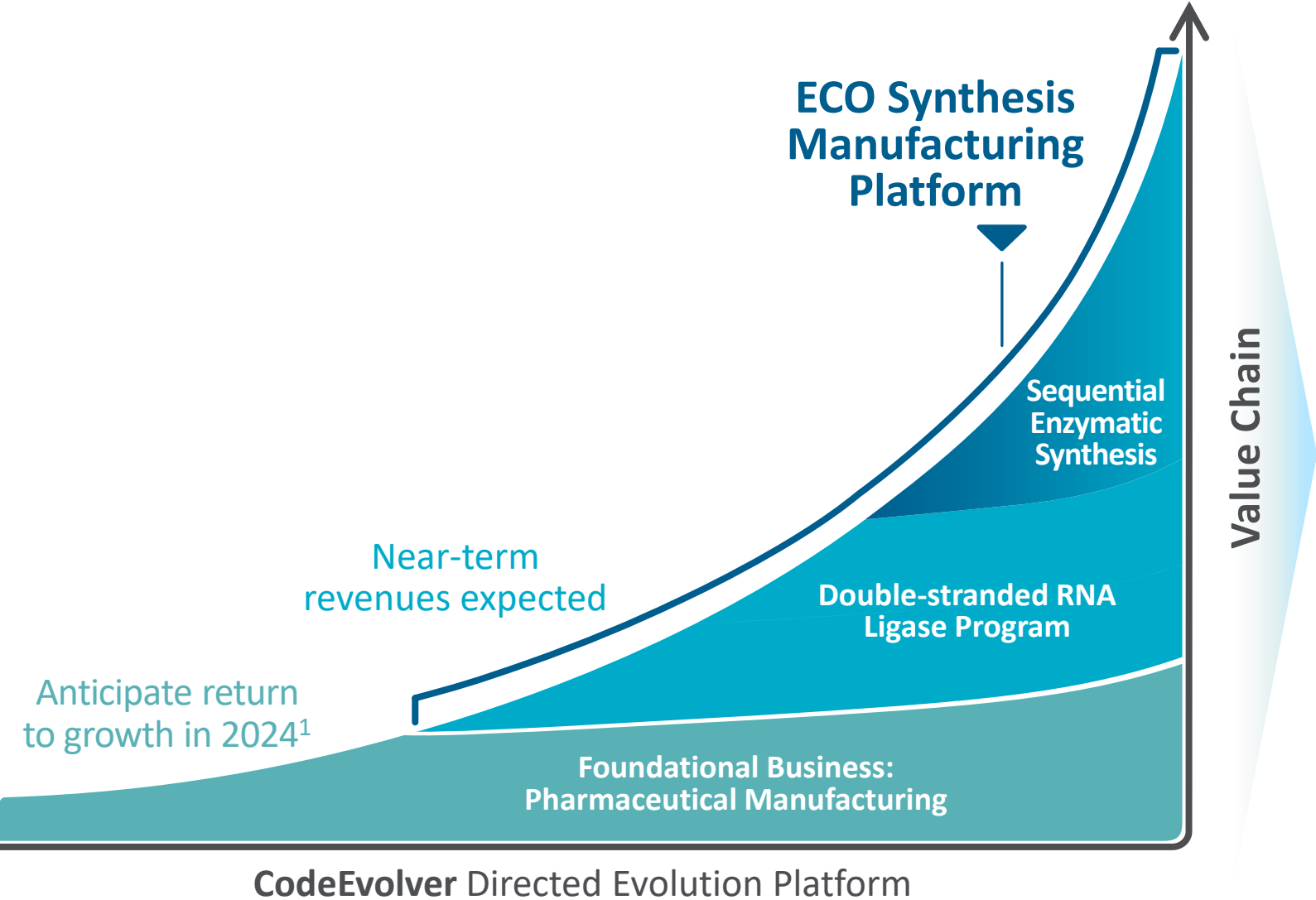
## RNA Manufacturing Services

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

**\$90 Million** Cash / Cash Equivalents  
and Investments as of 9/30/24

Path to Profitability By End of 2026;  
Cash Runway into 2027

# Codexis' Path to Success



Path to positive cash flow by end of 2026

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Enabling full-scale production of siRNA

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

# Clear Path to Profitability by End of 2026

## Pharmaceutical Manufacturing

- Existing products and customers
- Pipeline of higher-margin products expected to drive continued growth

## Double-Stranded RNA Ligase

- Expect increasing orders from existing customers

## Path to Profitability Supported by:

- \$90M in cash and equivalents as of 9/30/24
- Reasonable cash burn

ECO Synthesis Manufacturing Platform Will be Launched Off a Profitable Base Business

# Pharmaceutical Manufacturing

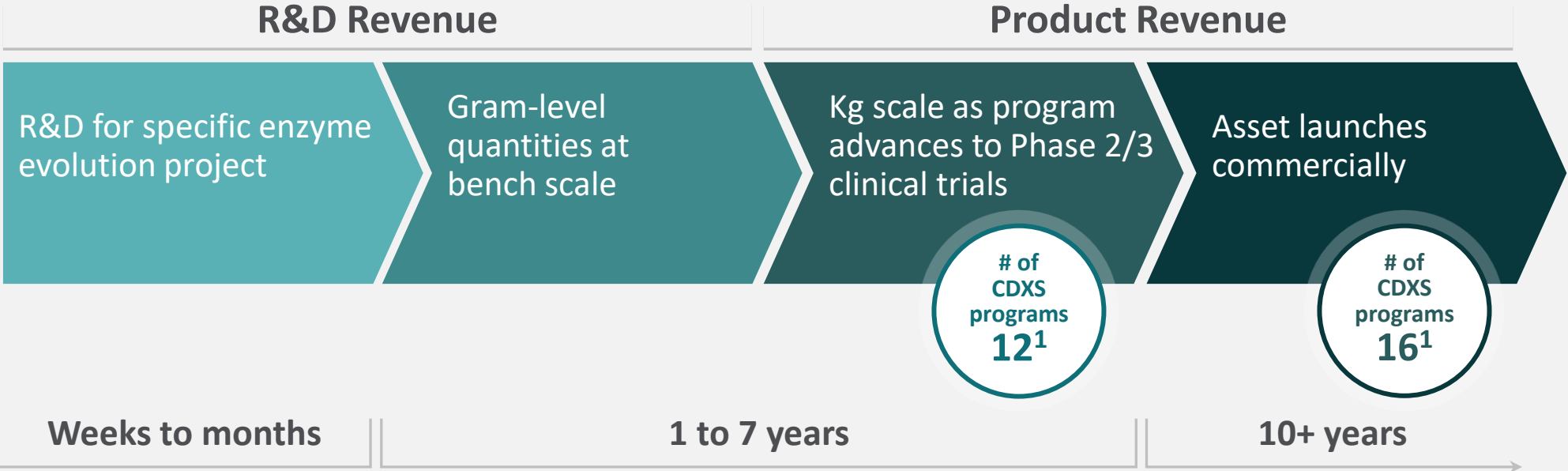
Evolved Enzymes for Biocatalysis  
of Small Molecule Manufacturing

# 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

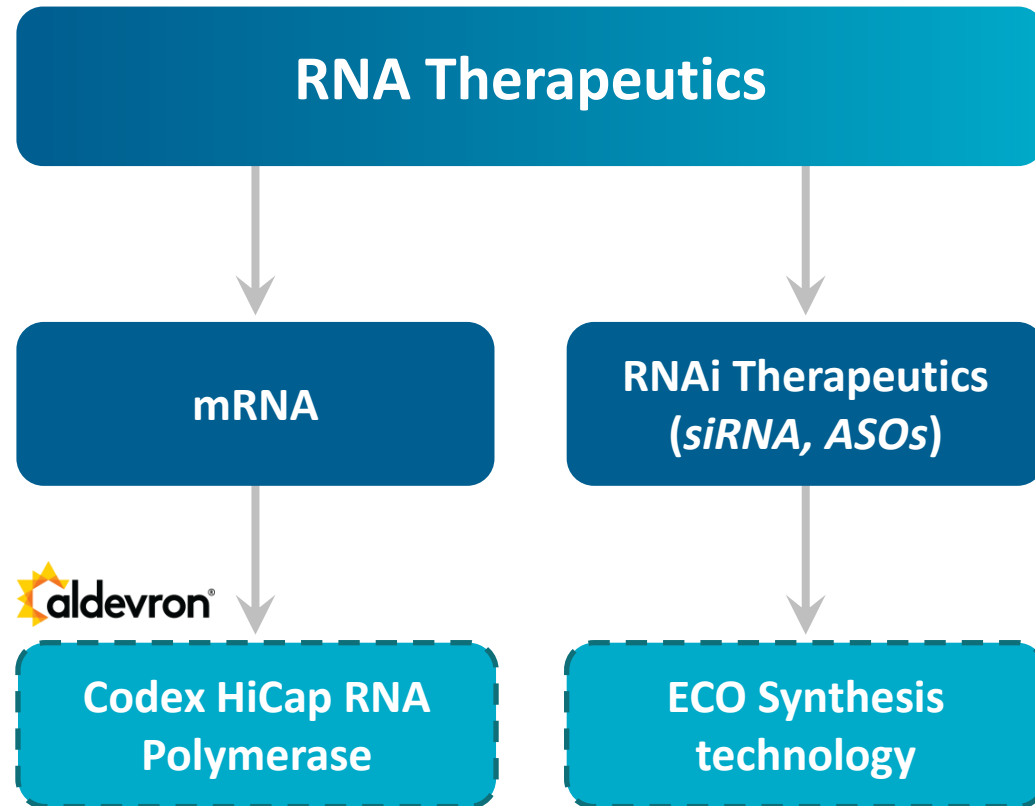
Strong Foundational Business Generating Cash



# RNA Manufacturing

Engineering the Next Generation of Enzymes  
for Oligonucleotide Manufacturing

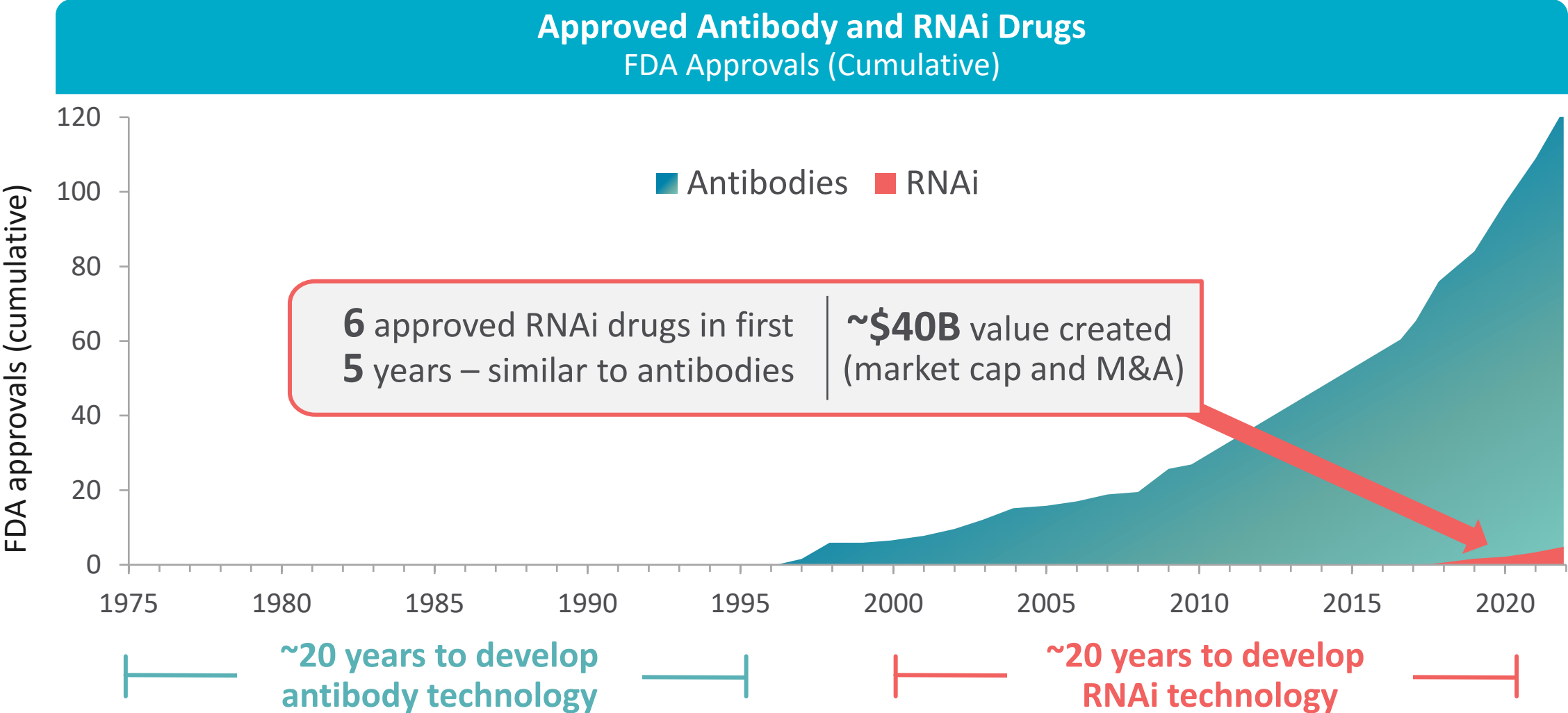
# RNAi Therapeutics – a Growing Modality



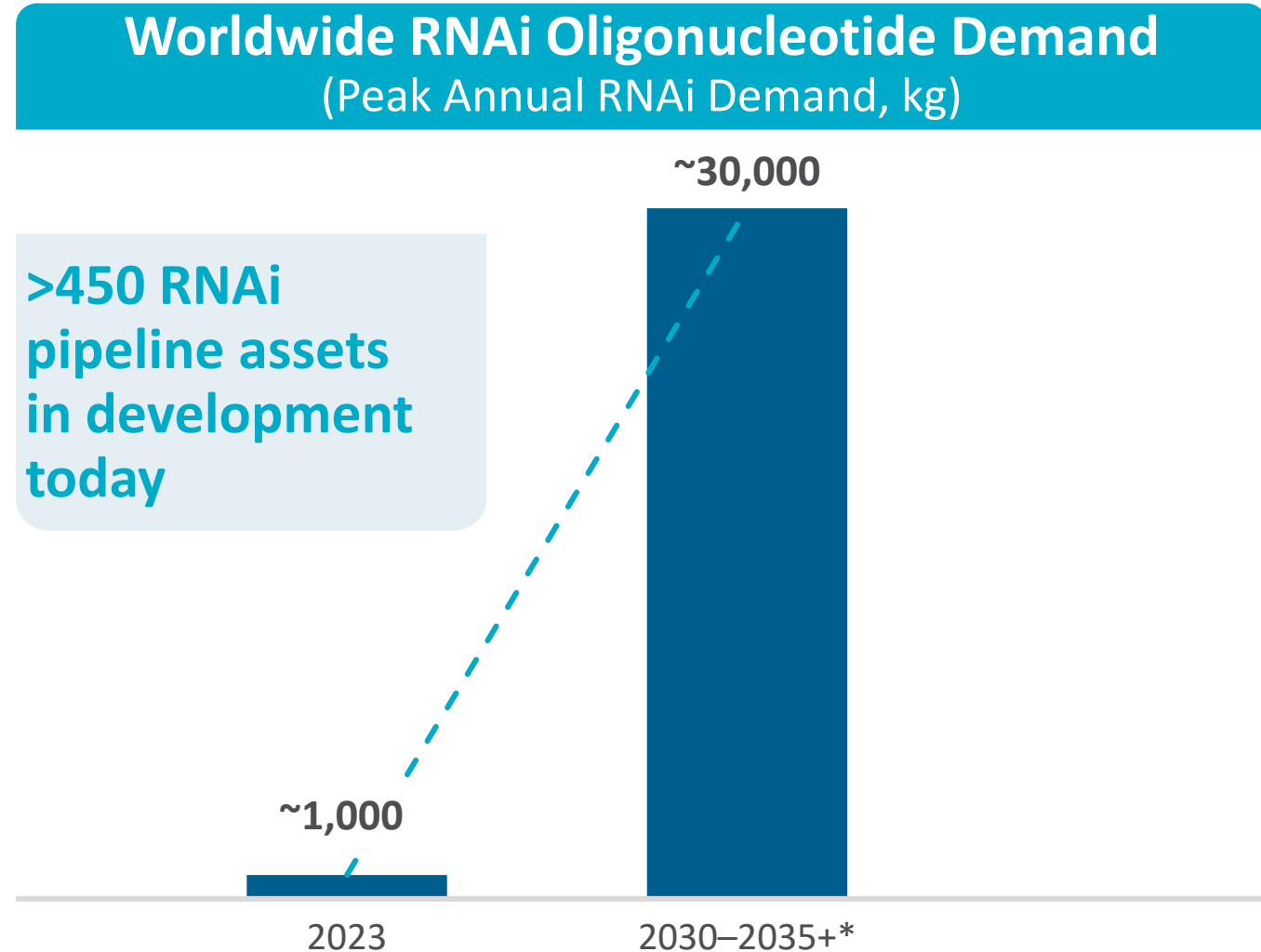
## siRNA: Natural Entry Point for ECO Synthesis Technology

- 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



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

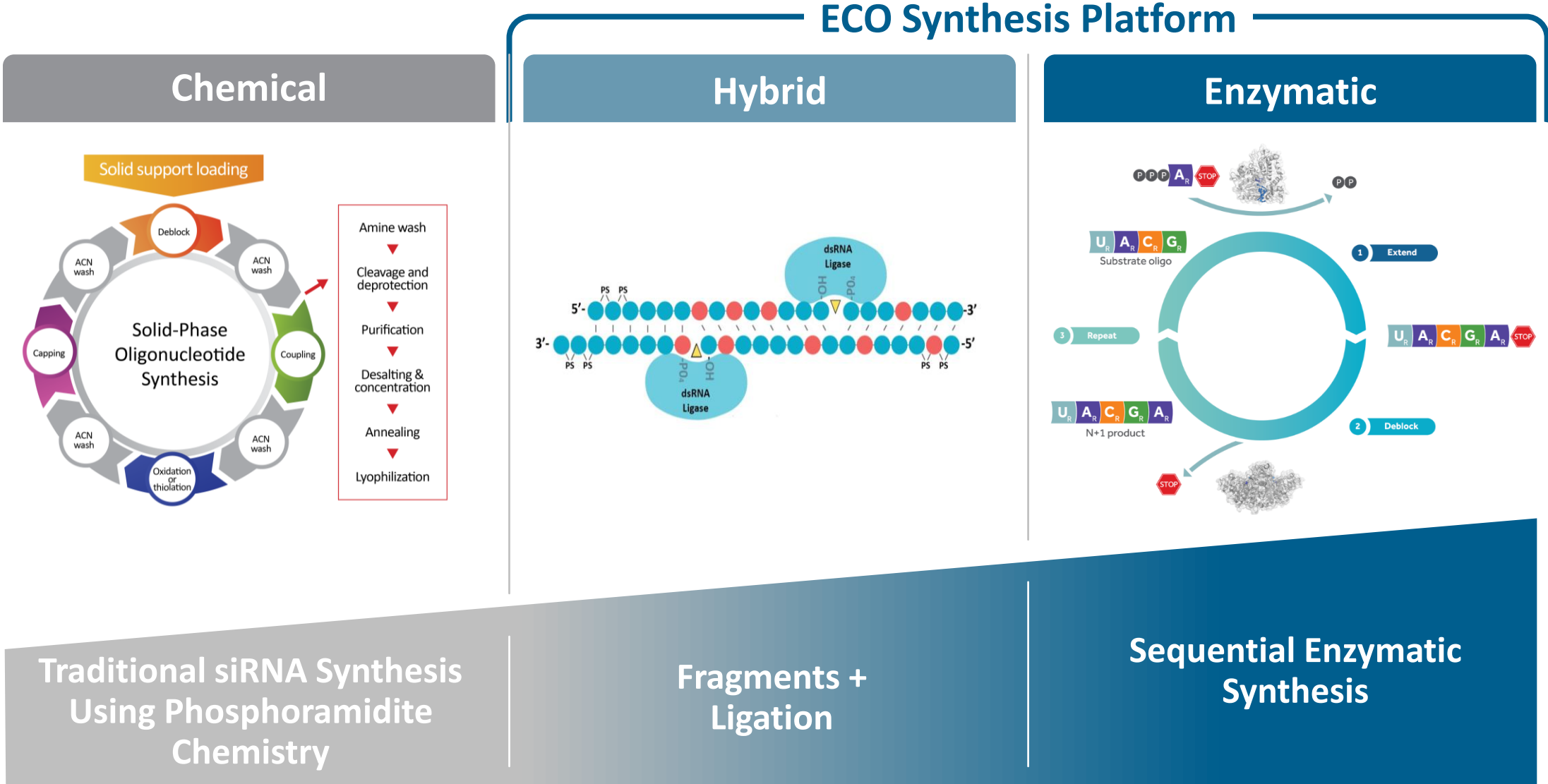
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Codexis is positioned to win based on **20-year history of engineering increasingly complex enzymes**

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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



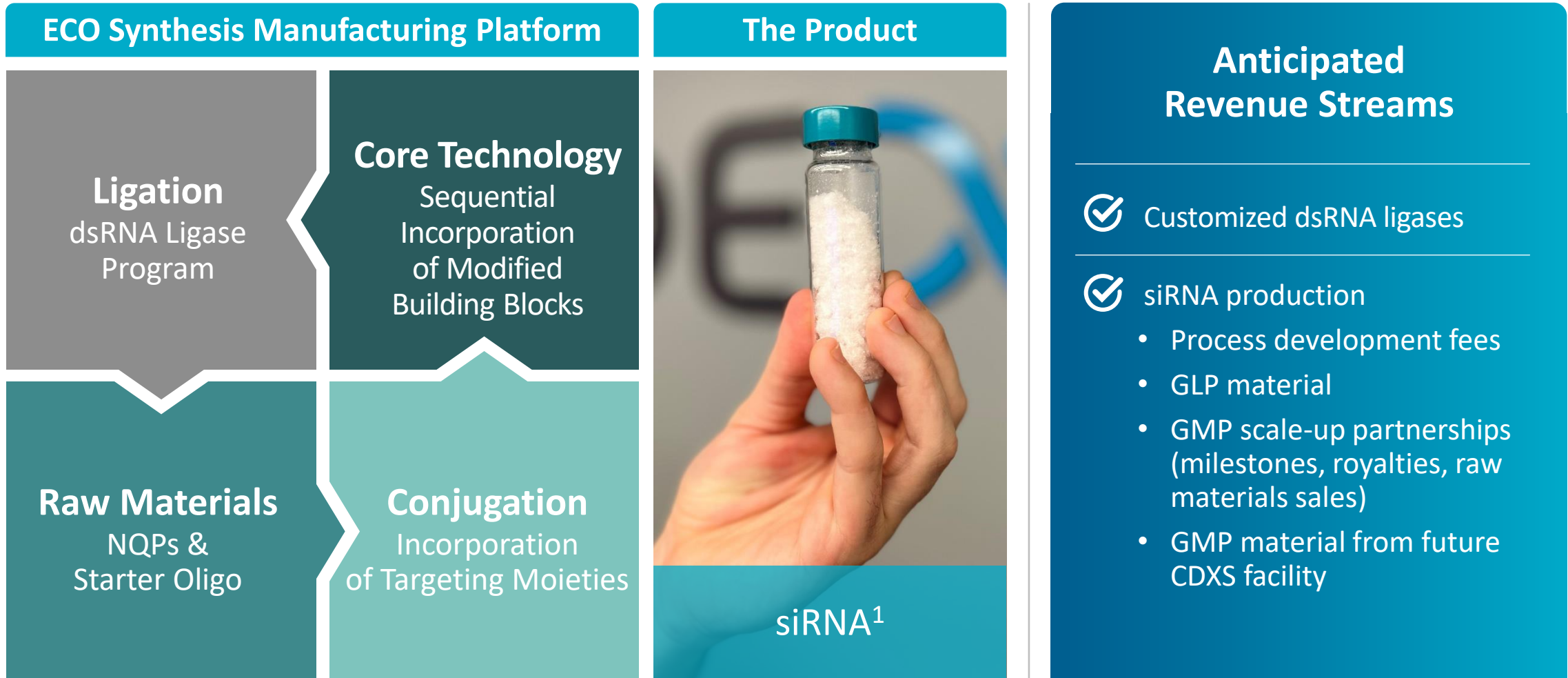
Traditional siRNA Synthesis Using Phosphoramidite Chemistry

Fragments + Ligation

Sequential Enzymatic Synthesis

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

**ECO:** Enzyme-Catalyzed Oligonucleotide Synthesis

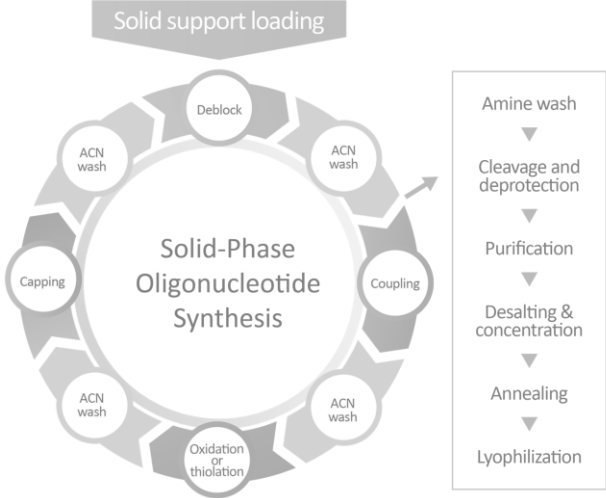




# Hybrid dsRNA Ligase Approach: Near Term Revenues

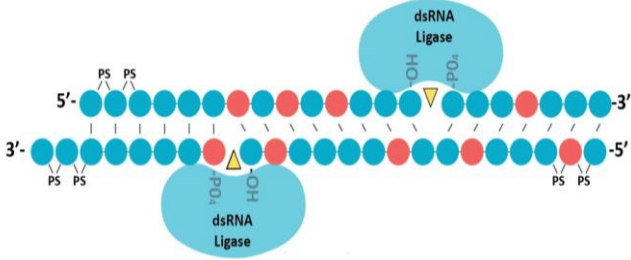
## ECO Synthesis Platform

### Chemical



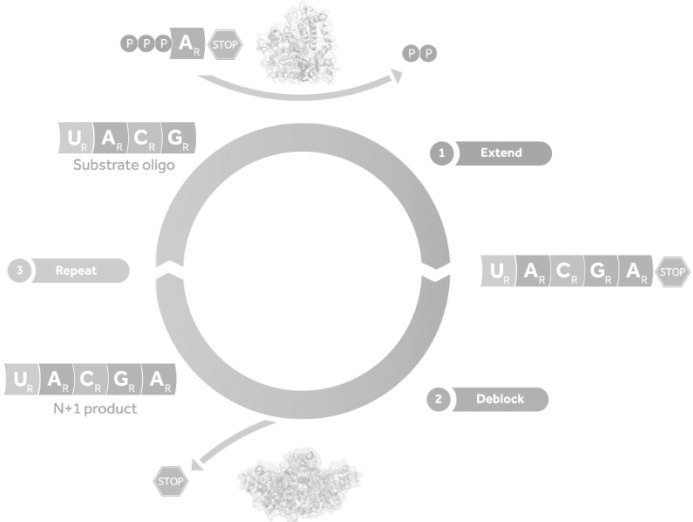
Traditional siRNA Synthesis Using Phosphoramidite Chemistry

### Hybrid



Fragments + Ligation

### Enzymatic

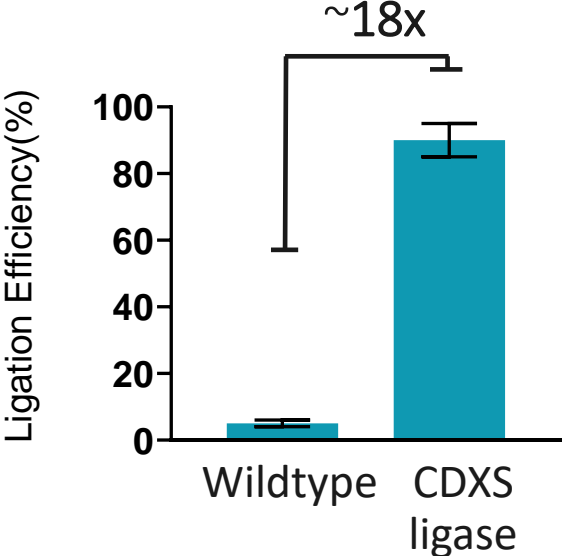


Sequential Enzymatic Synthesis

# Engineered Ligases Enable Lower Manufacturing Costs

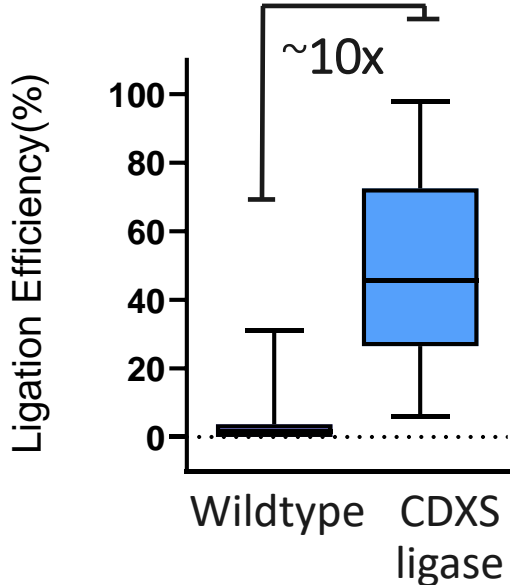
CDXS Variant Drives Valuable Economics through Improved Performance Metrics

## 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: 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

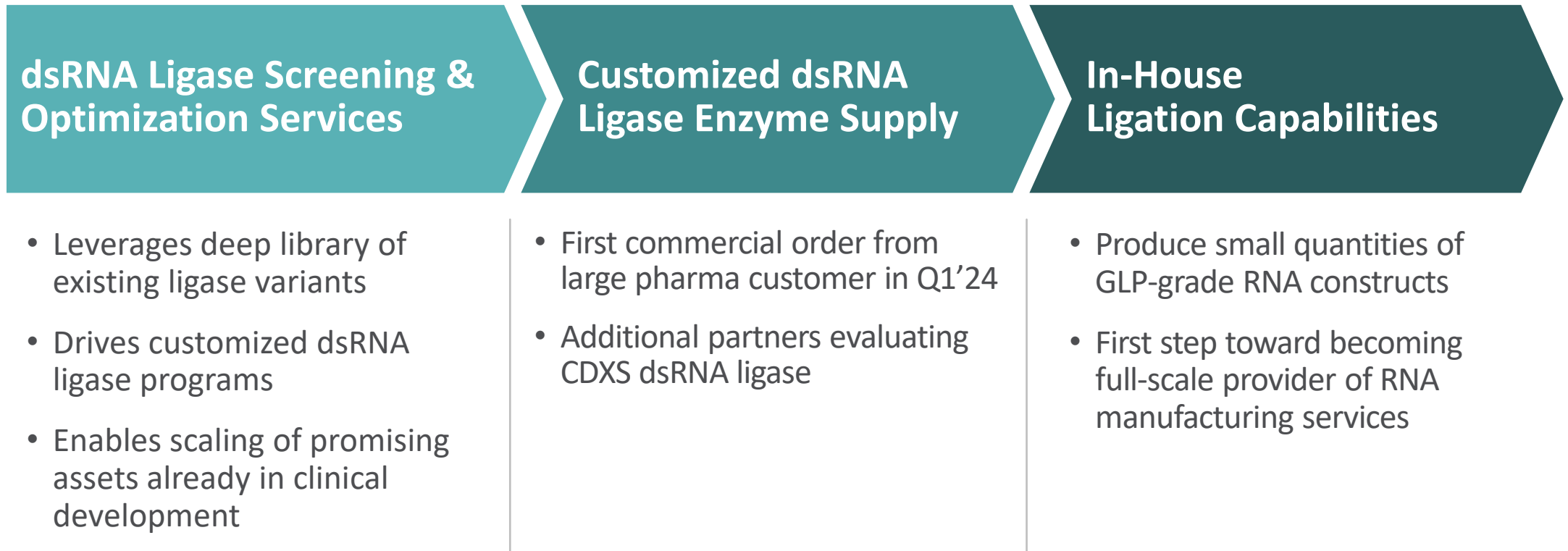
**Goal: Repeatable, sustainable business with meaningful revenues**

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

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

# dsRNA Ligase Program: Multi-Pronged Commercial Strategy

Variety of Approaches to Meet Customers Where They Are

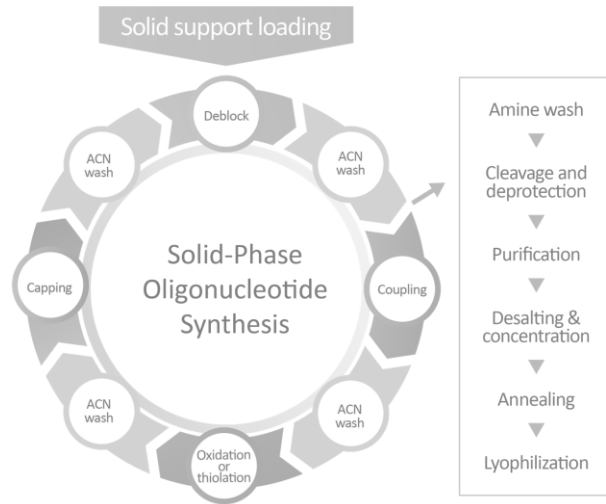


Offerings Designed to Encourage Rapid, Seamless Customer Uptake

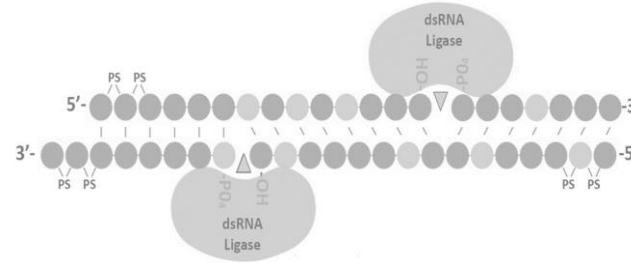
# ECO Synthesis Manufacturing Platform: the Sequential Enzymatic Solution

## ECO Synthesis Platform

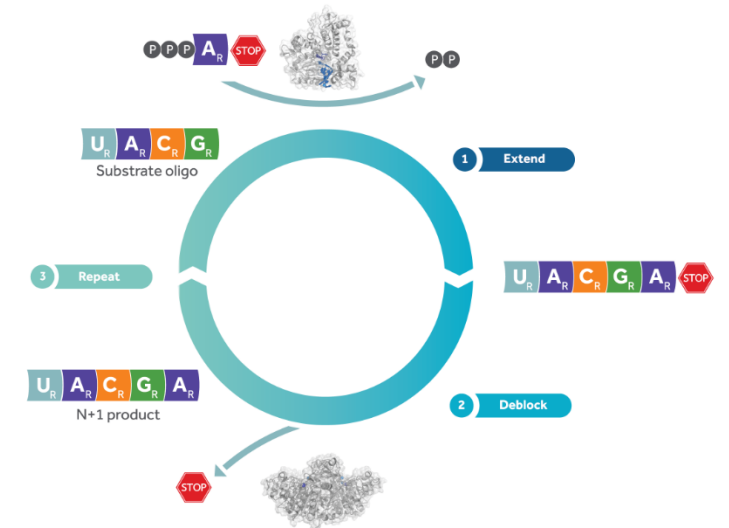
### Chemical



### Hybrid



### Enzymatic



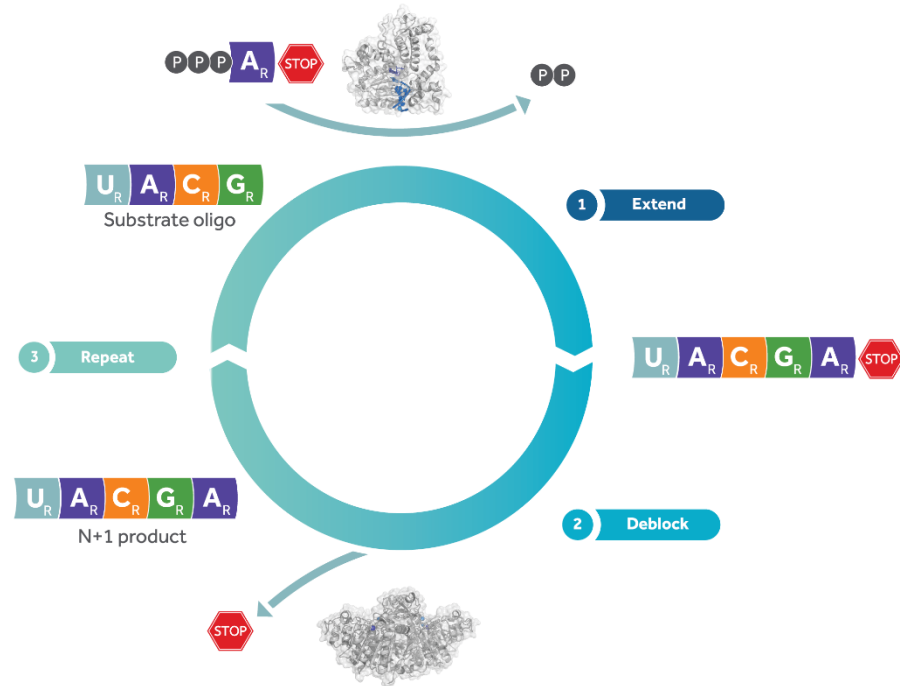
Traditional siRNA Synthesis  
Using Phosphoramidite  
Chemistry

Fragments +  
Ligation

Sequential Enzymatic  
Synthesis

# Technical Overview: Sequential Enzymatic Synthesis

## ECO Synthesis Manufacturing Platform in Development



### Core Technology

Sequential addition of modified RNA nucleotides

### Raw Materials

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 Platform: Demonstrating a Reliable Source of siRNA

## ECO Synthesis Innovation Lab

### Offers Customers Path to GLP-Grade Material

- Enables in-house manufacture of GLP-grade material for customers' preclinical studies
- Provides venue to demonstrate process scalability for larger production in clinical trials

### Supports GMP Scale Up

- Allows for tech transfer to GMP scale-up partners for clinical trial and commercial manufacturing

## Kilogram-Scale GMP Facility

### Provides siRNA for Early-Stage Clinical Trials

- Enable customers to conduct preclinical and early clinical-stage studies with Codexis
- Accelerate adoption of ECO Synthesis platform
- Allow for increased Codexis revenue capture over manufacturing life of a product

# 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

### Improved Quality

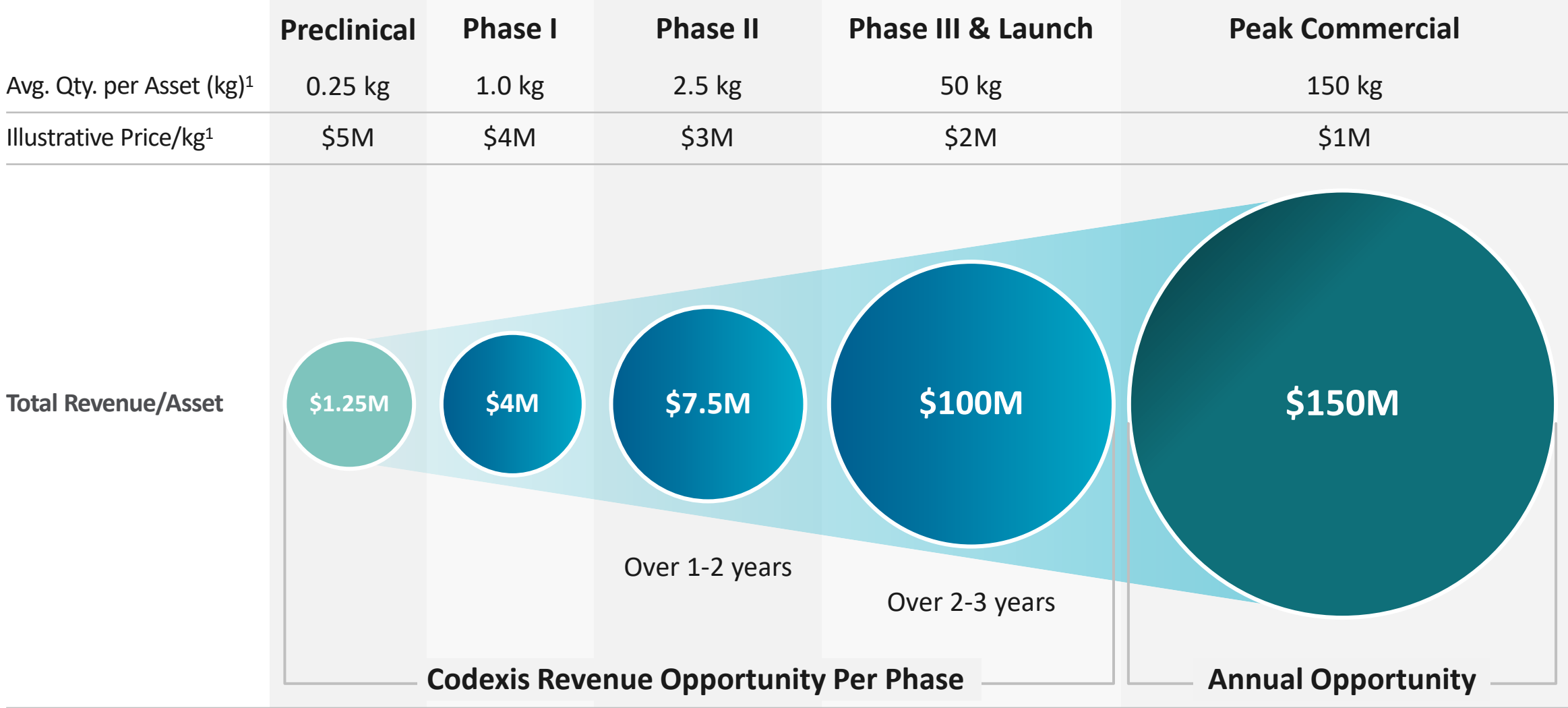
- Higher purity should streamline downstream purification needs and improve quality of final product

### Valuable Economics

- Increased scale, efficiency & product quality
- Saves \$Ms in purification and waste disposal costs
- Integrates with existing small molecule manufacturing facilities



# 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

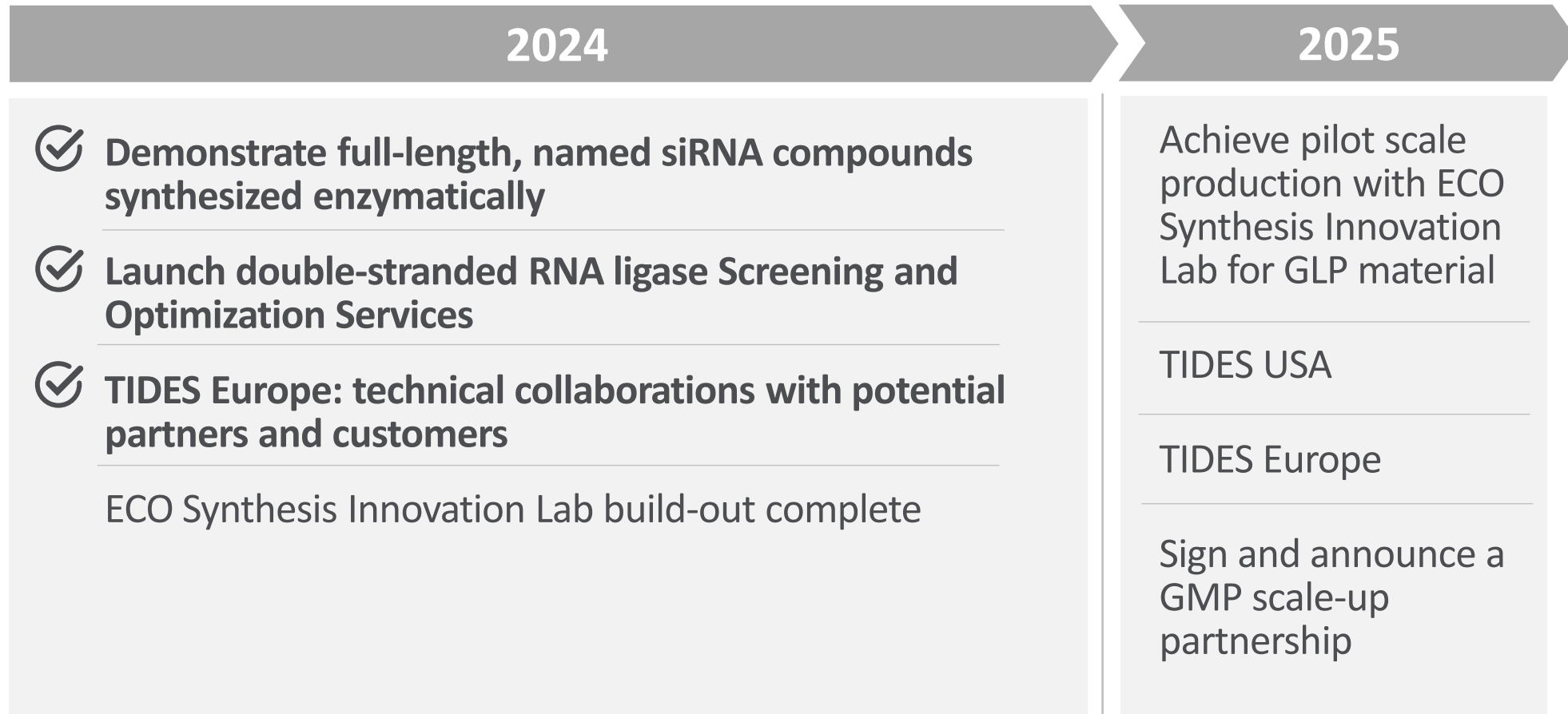
Enzymatic (DNA) **oligonucleotide synthesis**  
(engineered enzyme w/ >99.9% coupling efficiency)

4

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

# Corporate Highlights

# Anticipated News Flow for ECO Synthesis Manufacturing Platform



Path to Profitability by End of 2026



# Thank You

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