TIDES Europe: Codexis Presentation Overview

November 2024



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TIDES Europe: Key Highlights

- Successfully Made Inclisiran using the ECO Synthesis[™] Platform
 - First ever end-to-end enzymatic synthesis of a complete siRNA therapeutic
- Synthesized Inclisiran using Four Different Enzymatic Methods
 - Illustrates flexibility and reliability of ECO Synthesis platform
- Completed Multiple Proof-of-Concept Technical Collaborations
 - Bachem
 - Major siRNA drug innovator

TIDES Europe: Three Codexis Presentations

Joint Poster Presentation

 Demonstrate superior performance of Codexis double-stranded RNA ligase variant over wildtype enzyme with

BACHEM

Oral Presentation #1

 Showcase data from double-stranded RNA ligase customer case studies to highlight the benefits of ligase engineering and process optimization

Oral Presentation #2

 Compare various routes of enzymatic synthesis using the ECO Synthesis platform to manufacture a commercially approved siRNA therapeutic (inclisiran)



Joint Poster Presentation with Bachem

Data Provides Compelling External Validation of Superior Performance of Codexis Double-Stranded RNA Ligase Variant Over Wild-Type Enzymes

Codexis Double-Stranded RNA Ligase Demonstrates:

- Higher Volumetric Productivity
 - Enables manufacture of more siRNA drug substance with less enzyme
 - Exhibits faster and higher conversion of oligonucleotide fragments into full-length siRNA
 - Sets the stage for meaningful improvements in scalability
- Greater Substrate Versatility
 - Works across broad range of modified RNA building blocks used in siRNA today
 - Drives a more robust, higher-yielding manufacturing process
 - Positions ligase as a potential platform technology by enabling assembly of multiple siRNA assets using just one Codexis enzyme



Oral Presentation #1: Ligase Screening & Optimization Service Case Studies

Double-Stranded RNA Ligase Customer Case Studies Highlight Benefits of Enzyme Engineering and Process Optimization

Ligase Screening & Optimization Service:

- Accelerates Delivery of Lead Ligase Variants to Customers by Leveraging Codexis':
 - Extensive libraries of engineered enzymes
 - Longstanding expertise in optimizing process conditions for a specific asset
- Delivers Robust, In-Process Ligase Performance
 - Higher substrate loading
 - Faster reaction times
 - Improved conversion of oligo fragments into siRNA at elevated temperatures



Oral Presentation #2: Comparing Synthesis of Inclisiran Using Four Different Enzymatic Routes

Synthesis Routes

Sequential enzymatic synthesis of full-length siRNA asset using ECO Synthesis technology

Ligation of fragments produced by ECO Synthesis technology

Ligation of fragments produced by ECO Synthesis technology & chemical methods

Ligation of fragments produced by chemical methods

Key Takeaways:

- Codexis presented first-ever enzymatic synthesis of an entire approved siRNA therapeutic (inclisiran)
- Ligation using both enzymatically and chemically produced fragments resulted in full-length siRNA oligos of equal quality and yields
- Core ECO Synthesis technology achieved >98% coupling efficiency, in-line with chemical methods
- Data demonstrates broad applicability of enzymes in siRNA synthesis

Codexis has Demonstrated Process Development Capabilities for a Variety of Routes of Enzymatic siRNA Synthesis



Codexis at TIDES Europe







