Dicerna Pharmaceuticals Overview

Delivering RNAi-Based Breakthrough Therapies
Forward-Looking Statements

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Corporate Highlights

Dual-Approach Pipeline Strategy

• Rare inherited diseases involving the liver
  DCR-PH1: Primary Hyperoxaluria therapy
  Additional rare diseases (undisclosed)

• Genetically-defined cancers and oncogene targets
  DCR-MYC: Solid tumor therapy, initial target indication hepatocellular carcinoma
  KRAS targeted program (partnered with Kyowa Hakko Kirin)
  Additional oncogene targets (undisclosed)

Pipeline Creation Technology Portfolio

• “Dicer substrate” RNAi payload
  DsiRNA – DCR-MYC, KRAS program
  DsiRNA-EX – extended structure – DCR-PH1

• RNAi delivery to liver tissue and solid tumors
  EnCore tumor-centric lipid nanoparticle (LNP)
  Human-validated LNP
  DsiRNA-EX Conjugates – for subcutaneous dosing of liver-targeted therapy
<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Indication</th>
<th>Stage of Development</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rare Disease</strong></td>
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<tr>
<td>DCR-PH1 Targeting Glycolate Oxidase</td>
<td>Primary Hyperoxaluria 1</td>
<td>Research</td>
<td>Dicerna</td>
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<tr>
<td>Undisclosed Liver Programs</td>
<td>Other rare liver diseases</td>
<td>Preclinical</td>
<td>Dicerna</td>
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<tr>
<td><strong>Oncology</strong></td>
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<tr>
<td>DCR-MYC Targeting MYC</td>
<td>Hepatocellular Carcinoma and other solid tumors</td>
<td>Phase 1</td>
<td>Dicerna</td>
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<tr>
<td>KRAS Program (Partnered)</td>
<td>Solid tumors</td>
<td>Commercial Rights</td>
<td>Licensed to KHK worldwide; Dicerna option to co-promote in the US</td>
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Product Pipeline Strategy:
Rare inherited diseases involving the liver

DCR-PH1: Glycolate Oxidase (HAO1)-targeted therapy for Primary Hyperoxaluria 1
Primary Hyperoxaluria 1 Pathology

The abnormal liver metabolism of PH1 patients produces excess oxalate concentrated in the renal filtrate.

Calcium oxalate crystals form, inducing nephrocalcinosis.

Subsequent decline in kidney function results in systemic oxalosis (crystal deposition in other tissues).

Approximately 50% of PH1 patients will have kidney failure by age 30-35.
## DCR-PH1 for Primary Hyperoxaluria 1

Primary Hyperoxaluria 1 (PH1) is a rare genetic disease resulting in severe kidney damage caused by excess production of oxalate in the liver.

### Assessments

<table>
<thead>
<tr>
<th>Technical</th>
<th>Parameters</th>
<th>Investment thesis</th>
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</thead>
<tbody>
<tr>
<td>Validation</td>
<td>Genetic deletion of HAO-1 gene target in mice eliminates hyperoxaluria</td>
<td></td>
</tr>
<tr>
<td>Biomarker</td>
<td>Urinary oxalate &amp; urinary glycolate</td>
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</tbody>
</table>

### Clinical

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Parameters</th>
<th>Investment thesis</th>
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</thead>
<tbody>
<tr>
<td>High Unmet Need</td>
<td>No highly efficacious therapeutic options available</td>
<td>Potentially fatal in the absence of a liver-kidney transplant</td>
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<tr>
<td>Development</td>
<td>Phase 1 proof-of-concept by YE2015</td>
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### Marketability

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<thead>
<tr>
<th>Marketability</th>
<th>Parameters</th>
<th>Investment thesis</th>
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</thead>
<tbody>
<tr>
<td>Patient Numbers</td>
<td>Estimated genetic incidence of 8 per million</td>
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<tr>
<td>Competition</td>
<td>First-in-class opportunity</td>
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</tr>
<tr>
<td>Patient Advocacy</td>
<td>Oxalosis and Hyperoxaluria Foundation (OHF)</td>
<td></td>
</tr>
</tbody>
</table>
Blocking Glycolate Oxidase (HAO1) eliminates the key PH1 disease pathology

Metabolic Pathway

RNAi silencing of GO prevents oxalate over-production (substrate reduction therapy)

Mitochondrial metabolism

Glyoxylate

Oxalate

Mutations in this gene generate excess urinary oxalate (Primary Hyperoxaluria 1)

Glycine

Glycolate

GO (HAO1) glycinate oxidase

AGT1 (AGXT) alanine-glyoxylate aminotransferase

Hydroxyproline (from collagen)

Hydroxyproline → 4-hydroxy-2-oxoglutarate → pyruvate + glyoxylate

RNAi

Liver cell metabolism

Cytosol

Peroxisome

Mitochondrion

Liver cell metabolism

Dicerna pharmaceuticals
Anti-HAO1 DsiRNA Efficacy in a Mouse Model of PH1

- The PH1 mouse model carries the same gene knockout as human PH1 patients
- mRNA knockdown of the HAO1 gene is 97% after a single dose
- Oxalate levels are returned to near baseline levels, similar to normal mice

**Day**

**Urinary Oxalate Levels (vs PBS)**

- PBS
- Factor VII
- HAO1-1171
- HAO1-1378

Normal baseline oxalate
DCR-PH1: Payload and Delivery System

DsiRNA-EX – *extended Dicer substrate*

- Enhances immunosilencing
- Improves stability
- Dicerna proprietary

Lipid Nanoparticle Delivery System

- Tekmira LNP delivery system
- Validated in humans
- Streamlines DCR-PH1 development process
Delivery Technology for Future Liver-Targeted Programs

DsiRNA-EX-Conjugates for subcutaneous delivery

*extended Dicer substrate conjugates*

- Dicerna proprietary
- Enables subcutaneous delivery
- Being applied to multiple target opportunities
- First clinical candidate in 2015
Product Pipeline Strategy: Genetically defined cancers & oncogene targets

DCR-MYC: MYC-targeted therapy for solid tumors
# DCR-MYC for MYC-Related Cancers

MYC is frequently amplified in many tumor types. We have selected Hepatocellular Carcinoma (HCC) as our initial focus for DCR-MYC.

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<tr>
<td>Validation</td>
<td>MYC is frequently amplified in a wide-variety of tumors Anti-MYC treatment has powerful effects in animal models</td>
</tr>
<tr>
<td>Biomarker</td>
<td>FDG-PET imaging of tumor metabolic activity; MYC transcript</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
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<tr>
<td>High Unmet Need</td>
<td>Implicated in many tumor types</td>
</tr>
<tr>
<td>Development</td>
<td>Phase 1 trial multiple tumor types trial underway Phase 1 hepatocellular carcinoma trial initiating</td>
</tr>
<tr>
<td><strong>Marketability</strong></td>
<td></td>
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<tr>
<td>Patient Numbers</td>
<td>HCC is the third leading cause of cancer death worldwide ~695,000 deaths per year</td>
</tr>
<tr>
<td>Competition</td>
<td>First-in-class opportunity Only one approved systemic therapy for HCC (Nexavar)</td>
</tr>
<tr>
<td>Market</td>
<td>Nexavar sales in HCC are ~$780 million and growing</td>
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MYC: Frequently-Mutated “Undruggable” Oncogene Target

MYC Genomic Duplication or Higher Order Amplification Rate

- Hepatocellular 50%
- Breast 80%
- Colorectal 70%
- Gastric 51-77%
- Gynecological 90%
- Prostate 80-90%
- SCLC 18-30%

Genetic models show the powerful antitumor effects of MYC inhibition

Inhibition of Myc family proteins eradicates KRas-driven lung cancer in mice

Endogenous Myc maintains the tumor microenvironment

DCR-MYC Antitumor Efficacy Dose Response Curve

- Strong single-agent efficacy with DCR-MYC delivered intravenously
- Excellent tolerability profile in animal toxicology models
DCR-MYC Clinical Trial Plan

Two parallel phase 1 trials to establish proof-of-concept

Multiple tumor types trial (non-HCC)
- Enrolling at Univ. of Chicago and START (South Texas Accelerated Research Therapeutics)
- In dose escalation

Hepatocellular carcinoma trial
- IRB-approved, enrolling first patient
- Sites in US, South Korea and Singapore
- Additional sites to be added

Study Parameters for both trials
- Dose-escalation to determine maximum tolerated dose
- Expansion cohort treated at the maximum tolerated dose
- Primary objective: to determine safety and tolerability

Secondary Objectives for both trials
- Observe anti-tumor activity
- Assess reduction in tumor metabolic activity (FDG-PET)
- Observe direct impact of DCR-MYC on the MYC transcript (biopsy cohort)
DCR-MYC: Payload and Delivery System

**Dicer Protein**

- **Accumulation In Target Tissue**
- **Binding and Internalization**
- **Cytoplasmic Release**

**DsiRNA**
- Rossi patent estate
- Drives strand selectivity

**EnCore LNP**
- Tumor optimized
- Drives strand selectivity
- Envelope & Core structure
- Dicerna proprietary
# Product Candidate Pipeline

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<td>DsiRNA-EX + LNP</td>
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| **Undisclosed Liver Programs** | Other rare liver diseases | Research, Preclinical, Phase 1 | Dicerna |
| DsiRNA-EX-Conjugate | | | Dicerna |

| **DCR-MYC** | Hepatocellular Carcinoma and other solid tumors | Research, Preclinical, Phase 1 | Dicerna |
| Targeting MYC | | | |
| DsiRNA + EnCore LNP | | | |

| **KRAS Program (Partnered)** | Solid tumors | Research, Preclinical, Phase 1 | Licensed to KHK worldwide; Dicerna option to co-promote in the US |
| DsiRNA + KHK LNP | | | |

| **Undisclosed Oncology Programs (Partnered)** | Solid tumors | Research, Preclinical, Phase 1 | Dicerna |
| DsiRNA + EnCore LNP | | | |
| DsiRNA + KHK LNP | | | Licensed to KHK worldwide |
Key Upcoming Milestones

• DCR-PH1 Targeting Glycolate Oxidase (PH1)
  – Phase 1 initiation in 2015
  – Initial Phase 1 data in by YE2015

• DCR-MYC Targeting MYC (HCC and other solid tumors)
  – Phase 1 initiation in HCC in Q4 2014
  – Phase 1 data in mid-to-late 2015 from multiple tumor types trial

• Additional clinical candidate declaration

R&D Update Webcast scheduled for December 15th, 4:30 EST
High Value Product Opportunities
Rare inherited diseases involving the liver: DCR-PH1
Genetically-defined tumors and oncogene targets: DCR-MYC

Broad Liver and oncology RNAi platform capability
Ability to rapidly generate new therapeutic programs

Well Resourced to Drive Program Value
$111.9 million in cash at end of Q3 2014

Dicerna utilizes its RNAi platform to develop multiple, first-in-class programs against undruggable targets