Dicerna 2020 Virtual R&D Update: Nedosiran, RG6346 and Going Beyond GalXC™

August 6, 2020
Forward-Looking Statements

This presentation includes forward-looking statements. Such forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statements. Examples of forward-looking statements include, among others, statements we make regarding: (i) Phase 1 proof-of-concept data for RG6346, an investigational GalXC™ RNAi treatment candidate for chronic hepatitis B virus (HBV) infection in development with Roche; (ii) multidose data from the PHYOX™3 trial of nedosiran, an investigational GalXC RNAi treatment candidate for primary hyperoxaluria (PH), (iii) first preclinical data on Dicerna’s RNAi technology in extrahepatic tissues; (iv) the therapeutic and commercial potential of nedosiran and (v) clinical development timelines and review related to nedosiran and continued alignment on the regulatory pathway to approval. The process by which investigational therapies, such as nedosiran, could potentially lead to an approved product is long and subject to highly significant risks. Applicable risks and uncertainties include those relating to Dicerna’s clinical research and other risks identified under the heading "Risk Factors" included in the Company’s most recent filings on Forms 10-K and 10-Q and in other future filings with the Securities and Exchange Commission. These risks and uncertainties include, among others, the cost, timing and results of preclinical studies and clinical trials and other development activities by us and our collaborative partners; the likelihood of Dicerna’s clinical programs being executed on timelines provided and reliance on the Company’s contract research organizations and predictability of timely enrollment of subjects and patients to advance Dicerna’s clinical trials; the reliance of Dicerna on contract manufacturers to supply its products for research and development and the risk of supply interruption from a contract manufacturer; the potential for future data to alter initial and preliminary results of early-stage clinical trials; the impact of the ongoing COVID-19 pandemic on our business operations, including the conduct of our research and development activities; the regulatory review and unpredictability of the duration and results of the regulatory review of Investigational New Drug applications (INDs) and Clinical Trial Applications (CTAs) that are necessary to continue to advance and progress the Company’s clinical programs; the timing, plans and reviews by regulatory authorities of marketing applications such as New Drug Applications (NDAs) and comparable foreign applications for one or more of Dicerna’s product candidates; the ability to secure, maintain and realize the intended benefits of collaborations with partners; market acceptance for approved products and innovative therapeutic treatments; competition; the possible impairment of, inability to obtain, and costs to obtain intellectual property rights; possible safety or efficacy concerns that could emerge as new data are generated in R&D; and general business, financial, and accounting risks and litigation. The forward-looking statements contained in this press release reflect Dicerna’s current views with respect to future events, and Dicerna does not undertake and specifically disclaims any obligation to update any forward-looking statements.

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Today’s Speakers

Douglas M. Fambrough, Ph.D.
President and Chief Executive Officer
Dicerna Pharmaceuticals

Rob Ciappenelli, M.B.A.
Chief Commercial Officer
Dicerna Pharmaceuticals

Bernd Hoppe, M.D.
Vice President, Global Medical Affairs
Dicerna Pharmaceuticals

Bob D. Brown, Ph.D.
Chief Scientific Officer,
Executive Vice President of R&D
Dicerna Pharmaceuticals

Ralf Rosskamp, M.D.
Chief Medical Officer
Dicerna Pharmaceuticals

Man-Fung Yuen, M.D., Ph.D.
Chair Professor and Endowed Professor in Medicine of the Li Shu Fan Medical Foundation,
University of Hong Kong
<table>
<thead>
<tr>
<th>Session</th>
<th>Presenter(s)</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corporate Vision and Strategy</td>
<td>Douglas M. Fambrough, Ph.D.</td>
<td>10:00 – 10:10 a.m.</td>
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<tr>
<td>RG6346 Phase 1 Data and Next Steps</td>
<td>Bob D. Brown, Ph.D.</td>
<td>10:10 – 10:50 a.m.</td>
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<tr>
<td></td>
<td>Man-Fung Yuen, M.D., Ph.D.</td>
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<tr>
<td>Q&amp;A</td>
<td>All Presenters</td>
<td>10:50 – 11:00 a.m.</td>
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<tr>
<td>Nedosiran PHYOX™3 Data and Commercial Planning</td>
<td>Bernd Hoppe, M.D.</td>
<td>11:00 – 11:30 a.m.</td>
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<tr>
<td></td>
<td>Ralf Rosskamp, M.D.</td>
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<td>Rob Ciappenelli, M.B.A.</td>
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<tr>
<td>Going Beyond GalXC™</td>
<td>Bob D. Brown, Ph.D.</td>
<td>11:30 – 11:45 a.m.</td>
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<tr>
<td>Q&amp;A</td>
<td>All Presenters</td>
<td>11:45 – 12:00 p.m.</td>
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Vision and Strategy

Douglas M. Fambrough, Ph.D.,
President and Chief Executive Officer
VISION
Maximize the impact of RNAi on medicine

STRATEGY
Develop and commercialize our core high-probability-of-success programs either alone or in collaboration with partners

Broadly enable the use of our GalXC technology by collaborating with therapeutic area leaders on non-core opportunities
The RNAi Modality Has Come of Age

Liver targets formed the foundation for RNAi’s early success.

Today, RNAi technologies are exploring the vast opportunities outside the liver.
Expansive Opportunity for RNAi Throughout the Body

- Proprietary extended Dicerna structure provides unparalleled medicinal chemistry flexibility

- CNS collaboration with Lilly with multiple ongoing discovery programs

- Subcutaneous delivery for muscle and adipose tissue will be presented today

- Additional tissues under development
## Core Pipeline Candidates

<table>
<thead>
<tr>
<th>CANDIDATE / TARGET INDICATION</th>
<th>DISCOVERY/RESEARCH</th>
<th>PRECLINICAL</th>
<th>CLINICAL PROOF-OF-CONCEPT TRIALS</th>
<th>REGISTRATION TRIALS</th>
<th>DICERNA’S PRODUCT RIGHTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nedosiran</strong>&lt;br&gt;Primary Hyperoxaluria Types 1, 2, 3</td>
<td></td>
<td></td>
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<td>100%</td>
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<tr>
<td><strong>RG6346</strong>&lt;br&gt;Hepatitis B Virus</td>
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<td></td>
<td></td>
<td></td>
<td>U.S. opt-in*</td>
</tr>
<tr>
<td><strong>DCR-A1AT</strong>&lt;br&gt;ALN-AAT02&lt;br&gt;A1AT Liver Disease</td>
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<td>100% U.S. Alnylam ex-U.S. opt-in</td>
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<tr>
<td><strong>DCR-proprietary</strong>&lt;br&gt;Undisclosed</td>
<td></td>
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<td>100%</td>
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*Under the Dicerna-Roche agreement, Dicerna has the option to co-fund pivotal development, which if exercised, entitles Dicerna to receive enhanced royalties and co-promotion rights in the U.S.*
We Believe Dicerna Is Creating Best-In-Class Opportunities

**In Primary Hyperoxaluria**
Dicerna conducted fundamental disease research to develop the LDHA mechanism seeking to treat multiple forms of PH and potentially generate the most effective approach to PH1

**In Hepatitis B**
Dicerna’s X-sparing approach drives extended duration of effect that may lead to treatments that are both more convenient and more effective that non-X-sparing approaches

**In A1AT Liver Disease**
Dicerna and Alnylam have joined forces to potentially develop the best A1AT RNAi therapy for patients with A1AT liver disease

**In Extending RNAi Throughout the Body**
Dicerna’s proprietary RNAi configuration provides unparalleled medicinal chemistry flexibility to potentially create molecules that transcend cell-type specificity and move toward general solutions to RNAi therapy in multiple cell types and tissues
Deep Collaboration Pipeline

Over 15 Preclinical Targets In Process Across Multiple Therapeutic Categories

- **Liver-Related Diseases**
  - NASH
    - DCR-LIV2
  - Liver-Related Diseases
    - DCR-COMP1
    - DCR-COMP2
    - DCR-COMP3
    - DCR-COMP4

- **Cardiometabolic, Neurodegeneration, Pain, Undisclosed**
  - Chronic HBV
    - DCR-RG1
  - Multiple potential targets
    - LY3561774
    - LY3819469
    - DCR-CM4
    - DCR-CM5
    - DCR-NEURO1
    - DCR-NEURO2
    - DCR-LLY9
    - DCR-PAIN1
    - DCR-PAIN2
    - DCR-LLY10

- **Rare Diseases**
  - Multiple targets
    - DCR-COMP1
    - DCR-COMP2
    - DCR-COMP3
    - DCR-COMP4

- **Preclinical Discovery Stage**
  - Nov. 2017
  - Oct. 2018
  - Oct. 2019
  - Nov. 2019

30+ potential targets
Multiple targets selected
Dicerna retains opt-in rights

$175M upfront
$75M total annuals
$50M equity

$200M upfront
$100M upfront
$100M equity

$100M upfront
$100M equity

$100M upfront
$75M total annuals
$50M equity

• 1 NASH Target
  • $5M option
  • exercised

• 4 complement-
  • mediated targets
  • $20M option
  • exercised

• Up to 8
cardiometabolic
targets, liver and
non-liver
• Neurodegeneration
  & pain targets
• DRNA retains rights
to certain neuro
orphan indications

• RG6346 and
  multiple potential
  HBV-related
targets
• DRNA option to co-
  fund development
  and co-promote in
  U.S.

• 30+ potential
targets for liver-
related CM diseases
• 2 Novo programs:
  DRNA opt-in
• DRNA retains rights
to 2 new orphan
programs (Novo
retains opt-in rights)

Dicerna retains opt-in rights

Nov. 2017
Oct. 2018
Oct. 2018
Oct. 2019
Nov. 2019

Successfully Executing on High-Value Collaboration Strategy
HBV HBsAg Reduction: The X-Sparing Hypothesis

Bob D. Brown, Ph.D.

Chief Scientific Officer, Executive Vice President Research & Development
Hepatitis B: A Severe, Global Unmet Medical Need

- Significant worldwide prevalence: ~292 million infected
- Causes more than 887,000 deaths per year
- Current treatments are rarely effective in achieving functional cures
- Dicerna is collaborating with Roche to develop RG6346 and potentially other agents for the treatment of HBV

The Promise of RNAi for the Treatment of Chronic HBV
Organization of the HBV Genome Enables Effective RNAi Targeting of Multiple Viral Functions

Overlapping mRNAs and protein-coding regions enable targeting multiple HBV genes with a single GalXC trigger

There are two conserved regions to target within the virus.

Which is best?
Or should you target both?

**S gene (HBsAg)**
Surface protein. Involved in viral coat and immune tolerizing agent

**P gene**
Polymerase. Involved in viral genome production

**C gene**
Core protein. Involved in capsid assembly and viral gene regulation

**X gene**
Involved in maintenance of cccDNA and viral gene regulation

**Conserved S Region**
Silences S, P and C encoding mRNAs
*RG6346 targets this region*

**Conserved X Region**
Silences S, P, C and X encoding mRNAs
Superior HBsAg Reduction When Targeting Only the Conserved S Region

Striking Differences Between Targeting S Region Alone vs. S and X Regions in a Preclinical Model

- Conserved S Region only: ≥3.9 log reduction, long duration of activity
- Conserved S & X Regions: 3.0 log reduction, shorter duration of activity

The hydrodynamic injection (HDI) mouse model only introduces the HBV genome into mouse hepatocytes, so should reflect natural HBV gene regulation

- Targeting the Conserved X Region leads to more rapid HBsAg rebound
- Result is reproducible when different sequences within the regions are targeted

These findings predict a longer duration of effect for candidate therapeutics that target solely the Conserved S Region
Known X Gene Function Supports Role as an S Gene Regulator
Leaving X Gene Function Intact is Predicted to Give Better HBsAg Suppression

- HBV X protein has been characterized as a “rheostat” controlling the balance between active viral replication and cccDNA-mediated production of aviral particles (circulating HBsAg)
- Targeting the Conserved S Region with RG6346 leaves the X protein encoding mRNA intact
  - Remaining X protein drives residual Core protein into the cytoplasm
  - Cytoplasmic Core protein cannot act as a transcriptional activator
  - Less HBsAg is produced

HBV Core Protein

- Immunohistochemical staining of mouse liver sections for HBV Core protein reveals differential subcellular localization in the HDI-HBV plasmid model
- Silencing of X gene leads to nuclear localized Core protein likely driving additional S expression
Phase 1 Trial: RG6346 for the Treatment of Hepatitis B Virus (HBV) Infection

Man-Fung Yuen, D.Sc., M.D., Ph.D.

Chair Professor & Endowed Professor in Medicine, Li Shu Fan Medical Foundation; Chief of the Division of Gastroenterology & Hepatology and Deputy Head of the Department of Medicine, Queen Mary Hospital, the University of Hong Kong
• A therapeutic expert and pioneering clinical researcher leading numerous studies on novel antiviral and immunomodulatory agents for the treatment of chronic hepatitis B virus infection

• Research includes prevention, natural history, molecular virology, treatment of chronic hepatitis B and C and hepatocellular carcinoma and is actively involved with cutting-edge research on novel markers for hepatitis B infection and occult hepatitis B infection

• One of the top internationally known researchers in the field of hepatitis B, with more than 430 papers published in world-renowned medical journals

• First bachelor’s degree of medicine in 1992; three doctoral degrees:
  – Doctor of Medicine with Sir Patrick Manson Gold Medal in 2001
  – Doctor of Philosophy in 2005
  – Doctor of Science in 2017
Disclosures

• Dr. Yuen is currently a principal investigator for Dicerna’s HBVS-101 study and was a member of our clinical advisory board that was held in 2019. Dr. Yuen has received compensation from Dicerna for both these activities. His role as an investigator in the HBVS-101 study and as a member of Dicerna’s clinical advisory board makes him uniquely qualified to present at today’s R&D event and share his perspective and experience. Dr. Yuen is receiving fair market value compensation from Dicerna for the services he is providing today on our behalf. Dicerna’s compensation to Dr. Yuen for his services today are not intended in any way to influence any future prescribing decision for any Dicerna compound in development or in return for any recommendation now or in the future to use any Dicerna product.
Global Impact: Still Increasing HBV Disease Mortality

- Unlike HIV, tuberculosis, and malaria, mortality from viral hepatitis is increasing.
- Putting it into context: mortality from HBV-related diseases *each year* is higher than current worldwide mortality from COVID-19.

Source: WHO Global Health Estimates 2016
Present Treatment Aims/Goals

HBsAg Clearance Remains Key to Chronic Hepatitis B Virus Treatment Paradigm

<table>
<thead>
<tr>
<th>Virologic response</th>
<th>Biochemical and liver synthetic test improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. ↓ HBV DNA to undetectable</td>
<td>ALT, bilirubin, albumin</td>
</tr>
<tr>
<td>2. ↓ cccDNA</td>
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</table>

Histologic improvement

Serologic responses

HBeAg loss/seroconversion
HBsAg loss/seroconversion

Aims:
Prevent progression to cirrhosis, Hepatocellular Carcinoma and death

- The new treatment paradigm is to continue CHB treatment until HBsAg seroclearance is achieved for both HBeAg-positive and HBeAg-negative CHB patients, potentially resulting in functional cure
- Treatment guidelines from APASL, EASL and AASLD all agree that this is the optimal endpoint

Source: WHO Global Health Estimates 2016
# RG6346 Phase 1: Three-Part Safety, Tolerability, PK/PD Study in Adult Healthy Volunteers and Participants With Chronic Hepatitis B

*Includes Placebo-Controlled Studies in Both NUC-Naïve and NUC-Experienced Participants*

<table>
<thead>
<tr>
<th>Group</th>
<th>Study Design</th>
<th>Status</th>
<th>Dose cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong></td>
<td>Placebo-controlled (2:1 active vs placebo), single-ascending-dose study in healthy volunteers</td>
<td>Completed n=30</td>
<td>RG6346 dose cohorts: 0.1, 1.5, 3.0, 6.0, 12.0 mg/kg</td>
</tr>
<tr>
<td><strong>B</strong></td>
<td>Placebo-controlled (5:3 active vs placebo), single-dose study in participants with no prior use of nucleoside or nucleotide analogue (NUC) therapy (NUC-naïve) with chronic HBV infection</td>
<td>Ongoing n=9*</td>
<td>RG6346 dose cohort: 3.0 mg/kg (NUCs initiated after 12 wks)</td>
</tr>
<tr>
<td><strong>C</strong></td>
<td>Placebo-controlled (2:1 active vs placebo), multiple-ascending-dose study in NUC-experienced participants with chronic HBV infection</td>
<td>Ongoing n=18 Currently dosing 6.0 mg/kg cohort</td>
<td>RG6346 dose cohorts: 1.5, 3.0, 6.0 mg/kg; 4 monthly doses</td>
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</tbody>
</table>

- **Key Study Inclusion/Exclusion Criteria:**
  - HBeAg positive with HBsAg >1000 IU/mL or HBeAg negative with HBsAg >500 IU/mL; NUC naïve with screening serum HBV DNA >2000 IU/mL and ALT ≥35 U/L (males) or ≥30 U/L (females)
  - Clinical history compatible with compensated liver disease, with no evidence of cirrhosis
  - Group C: continuously on NUC therapy for at least 12 weeks prior to screening

- **After completion of the treatment period, study participants with ≥1 log HBsAg reduction are followed in a conditional follow-up period (CFU)**

*One additional subject was enrolled in Group B (total N=9) to replace a subject determined to be ineligible after the study dose had been administered.*
## Patient Baseline Characteristics Well Balanced Across Cohorts

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<tr>
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<th>COHORT C</th>
<th>COHORT B</th>
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<tbody>
<tr>
<td></td>
<td>1.5 mg/kg (N=4)</td>
<td>3 mg/kg (N=4)</td>
</tr>
<tr>
<td>Age at Screening (years) Mean (SD)</td>
<td>37.8 (6.7)</td>
<td>46.5 (5.8)</td>
</tr>
<tr>
<td>Gender n (%)</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>3 (75.0%)</td>
<td>2 (50.0%)</td>
</tr>
<tr>
<td></td>
<td>1 (25.0%)</td>
<td>2 (50.0%)</td>
</tr>
<tr>
<td>Race n (%)</td>
<td>Asian</td>
<td>Native Hawaiian or Other Pacific Islander</td>
</tr>
<tr>
<td></td>
<td>4 (100%)</td>
<td>0</td>
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<tr>
<td></td>
<td>0</td>
<td>0</td>
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<tr>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Weight (kg) Mean (SD)</td>
<td>59.9 (18.9)</td>
<td>63.2 (11.9)</td>
</tr>
<tr>
<td>HBSAg Day 1 Predose Value (log10 IU/mL) Mean (SD)</td>
<td>3.48 (0.29)</td>
<td>3.62 (0.59)</td>
</tr>
<tr>
<td>HBeAg Positive n (%)</td>
<td>2 (50.0%)</td>
<td>2 (50.0%)</td>
</tr>
<tr>
<td>HBV DNA (log10 IU/mL) Mean (SD)</td>
<td>1.60 (1.04)</td>
<td>1.00 (0.00)</td>
</tr>
<tr>
<td>ALT (U/L) Mean (SD)</td>
<td>12.75 (4.57)</td>
<td>14.25 (9.78)</td>
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</tbody>
</table>
RG6346 Showed Strong, Durable Reduction in HBsAg Levels at All Doses

Lowest Dose Cohort Had Mean HBsAg Reduction Maintained Through Day 336 (Still Ongoing)

- At Day 112 (end of treatment), mean HBsAg log10 IU/mL reduction from baseline in Group C was:
  - 1.39 (SD 0.38) for 1.5 mg/kg cohort
  - 1.80 (SD 0.57) for 3 mg/kg cohort
  - 1.84 (SD 0.79) for 6 mg/kg cohort
- Mean max. HBsAg log10 IU/mL reduction was 1.88 (SD 0.52) for 3 mg/kg cohort; 1.84 (SD 0.79) for 6 mg/kg cohort
- 6 mg/kg cohort ongoing
  - Only 2 of 4 participants had reached Day 112 as of data analysis cutoff
- Longest-treated participant in 1.5 mg/kg cohort had 2.21 log10 IU/mL reduction at Day 392
- 6 of 10 Group C participants who completed Day 112 had HBsAg <100 IU/mL at last reported visit

Results shown as of June 25, 2020 data cutoff; 4 participants dosed with RG6346 in each dosing cohort at each time point unless otherwise noted
Interim Results: Maximum HBsAg Change From Baseline for all Group C Participants Who Reached at Least Day 112

No Significant Difference in Max. HBsAg Change From Baseline for HBeAg+ vs. HBeAg- Participants

- 80% of subjects on active treatment had >1.5 log10 IU/mL reduction
- Greatest max reduction: 2.7 log10 IU/mL

Data reflect participants who have completed the treatment period, i.e., Day 112
RG6346 Led to Reduction in HBV-DNA in NUC-Experienced Patient With Previously Incomplete Response

Patient Experienced Drop to Levels Below the Limit of Quantification When RG6346 Added

Results shown as of June 25, 2020 data cut
Treatment With RG6346 + NUCs Resulted in Reductions in Key Viral Markers Across All Group C Dose Levels

Mean HBcrAg Reductions

Mean HBeAg Reductions

HBeAg: minimum n=2 for each dose cohort; full data not collected for 1.5 mg/kg cohort.

HBcrAg: 1.5 mg/kg cohort n=4; 3 mg/kg cohort n=4; 6 mg/kg cohort n=3
Two Additional Group B NUC-Naïve Patients Had Similar Responses

ALT Elevation Associated With Reductions in HBsAg, Other Viral Markers

Synthetic and Excretory Liver Function Preserved

Patient from Group B, 3 mg/kg cohort
NUC-Naïve Patient With Transient ALT Elevation and Overall Preserved Liver Function Suggests Flare With Enhanced Host Immune Response

ALT Elevation Coincides With Decline in HBV-DNA and HBsAg Reduction

Relationship of ALT Flare and Reduction in HBsAg and HBV-DNA
NUC-Experienced Patient Had Mild Serum ALT Elevation Associated With 2.5 Log10 IU/mL HBsAg Reduction

Patient’s ALT Elevation Also Associated With Preserved Liver Synthetic and Excretory Function

- All HBV-DNA and HBV-RNA values, at all time points, for this participant were BLQ
In the Phase 1 Patients, RG6346 Appeared To Be Safe and Generally Well Tolerated as of the Interim Analysis

No Dose Effect on Liver Function Tests Observed in Healthy Volunteers at Dosages ≤12 mg/kg

• No serious adverse events (SAEs) associated with RG6346 observed as of June 25, 2020 in Groups B or C
  – One participant in Group A (healthy volunteer on placebo) experienced one SAE not related to study drug
• No dose-limiting toxicities
• No safety-related discontinuations
• No dose/exposure dependent increase in frequency or severity of safety parameters: AEs, safety labs, ECG or vital signs
  – In all participants with flares, or flare-like ALT/AST elevations, overall liver synthetic and excretory functions were preserved
  – No cases of simultaneous elevations of ALT >3x ULN and total bilirubin >2x ULN
• The most commonly reported AEs were related to the injection site
  – All injection site reactions (ISRs) were mild with exception of a single patient who had two moderate ISRs
Preliminary Data Demonstrates RG6346 Was Generally Well Tolerated With Four Monthly Doses

<table>
<thead>
<tr>
<th>COHORT C</th>
<th>COHORT B</th>
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<tbody>
<tr>
<td>1.5 mg/kg (N=4)</td>
<td>3 mg/kg (N=4)</td>
</tr>
<tr>
<td>Number of participants with at least 1 possibly-related AE</td>
<td>2</td>
</tr>
<tr>
<td>Number of participants with at least 2 AEs (^1)</td>
<td></td>
</tr>
<tr>
<td>Injection site erythema, Injection site vesicles, Injection site bruising, Injection site rash, Injection site pain (^2)</td>
<td>2 Mild</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
</tr>
<tr>
<td>ALT increased, AST increased, GGT increased (^3)</td>
<td>0</td>
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</tbody>
</table>

\(^1\) MedDRA Preferred Term (PT) aggregated based on similarity.
Possibly, Probably, or Definitely Drug-Related AEs in ≥ 2 participants

\(^2\) Inclusive of all ISRs regardless of onset time < 4 hours or ≥ 4 hours (≥ 4 hours case is defined as ISR by protocol)

\(^3\) May be associated with treatment-induced enhanced immune responses
Participants treated with RG6346 and concomitant NUC therapy had meaningful and sustained reductions in HBsAg for all dose levels at end of treatment period

- 80% of subjects on active treatment had >1.5 log10 IU/mL reduction
- In the 3 mg/kg and 6 mg/kg cohorts the mean HBsAg reduction was ≥1.8 log10 IU/mL at Day 112
- Mean maximal HBsAg log10 IU/mL reduction from baseline in Group C was*:
  - 1.88 (SD 0.52) for 3 mg/kg cohort
  - 1.84 (SD 0.79) for 6 mg/kg cohort
- Greatest max reduction: 2.7 log10 IU/mL
- First dosed patient in ongoing study has reached Day 392 with 2.21 log10 IU/ml reduction in HBsAg

Several participants treated with RG6346 exhibited self-resolving ALT elevations with overall preserved liver function suggesting ALT flares potentially as a result of treatment-induced enhanced immune responses

No differences in HBsAg reductions were noted between HBeAg+ and HBeAg- participants

In the Phase 1 patients, RG6346 appeared to be safe and generally well tolerated as of the interim analysis

Study ongoing; two of four participants treated with RG6346 6 mg/kg have not reached Day 112

*Mean max not included for Group C 1.5 mg/kg cohort due to patient replacement
RG6346 Phase 1: Encouraging HBsAg Reduction and Duration of Response

- Phase 1 proof-of-concept study confirms X-sparing hypothesis and potential for best-in-class activity
- Innovative and thoughtfully designed development strategy provided additional insight to RG6346 effect
  - HBsAg reduction and long duration of action indicate potential for best-in-class profile as part of potential HBV therapeutic cure regimen
- Trial ongoing; additional participants in Group C expected to complete treatment period in September
  - May see additional dose response from two ongoing participants in 6 mg/kg dosing cohort
- ALT elevations consistent with enhanced immune responses (“flares”) observed in Group B and Group C participants
- Plan to present Phase 1 data at future scientific conference
- Under the agreement, Roche will be responsible for initiating Phase 2 development of RG6346
Our Investigators & Site Teams

- Dr. Edward Gane
- Dr. Jung-Hwan Yoon
- Dr. Man-Fung Yuen
- Dr. Pisit Tangkijvanich
- Dr. Alexander Thompson
- Dr. Tien Huey Lim
- Dr. Wattana Sukeepaisarnjaroen
- Dr. Won Kim
- Dr. William Sievert

Our Partners

- Innocent Clement
- Hardean Achneck
- Mark Pirner
- Wendy Cyr
- Jeremy Cronin
- Andrew Henderson
- Shuli Yu
- Mark Bercy
- Susan Griffin
- Jing Yu
- Dhruv Patel
- Bob Brown
- Jennifer Lockridge
- Jing Zhou
- Lara Curtin

Thank You especially to our participants and all the people who care for them

The Dicerna Team, particularly...
HBV Q&A

All Presenters
Primary Hyperoxaluria: Unmet Need and Treatment Paradigm

Bernd Hoppe, M.D.
Vice President, Global Medical Affairs, Head of the German Hyperoxaluria Center and Professor of Pediatrics at University of Cologne
PH: A Family of Rare Disorders Causing Hepatic Oxalate Overproduction Resulting in Life-Threatening Kidney Damage

In all PH subtypes, LDH is Believed to Catalyze the Conversion of Glyoxylate to Oxalate

PH Liver enzyme deficiencies
cause glyoxylate dysregulation. In PH, LDH transforms some of the excess glyoxylate into oxalate.

Renal damage
is caused by Calcium Oxalate crystals that primarily lead to nephrolithiasis and/or nephrocalcinosis, but also induces chronic inflammation, which results in progressive kidney damage, Chronic Kidney Disease, and later systemic oxalate deposition.

Abbreviations: CKD, chronic kidney disease; LDH, lactate dehydrogenase; CaOx, calcium oxalate
PH Is More Common Than Previously Thought, Affecting an Estimated 8,500 People in the U.S.

Expected U.S. prevalence from genetic studies¹²: 1:58,000 or ~8,500 people

>80% of patients currently undiagnosed¹

Approximately 11% of patients with a clinical phenotype consistent with PH have no known PH mutation detected

Expected Prevalence*

| PH1 | ~2,700 |
| PH2 | ~1,700 |
| PH3 | ~4,100 |

Expected Ratio*

| PH1 | 32% |
| PH2 | 20% |
| PH3 | 48% |

*Prevalence based on PH mutant alleles found in the National Heart, Lung, and Blood Institute Exome Sequencing Project (NHLBI ESP) and calculated according to Hardy-Weinberg equilibrium for each PH type using the sum of all alternate PH1, PH2, or PH3 alleles (known, or known and scored as pathogenic) and all wild type alleles.
Kidney Stones Are a Hallmark of All PH Subtypes

<table>
<thead>
<tr>
<th>Stone Burden</th>
<th>CaOx Stones\textsuperscript{10}</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PH 1</strong></td>
<td>73%-100% of patients have stones\textsuperscript{1,2}</td>
</tr>
<tr>
<td><strong>PH 2</strong></td>
<td>83%-100% of patients have stones,\textsuperscript{3-5} <em>many before age 4 years</em></td>
</tr>
<tr>
<td><strong>PH 3</strong></td>
<td>Nearly 100% of patients have stones,\textsuperscript{6-9} <em>most before age 4 years</em></td>
</tr>
</tbody>
</table>

**Appearance before treatment** \textsuperscript{11-13}

- Light whitish or pale yellow surface color
- Loose aggregations of different-sized crystals
- Median size: 1.6 cm (range, 0.5-4.5 cm)

*Abbreviation: CaOx, calcium oxalate.*

A Single Kidney Stone in Children and Recurrent Stones in Adults Can Be Signs of PH

Warning signs can include one or a combination of the following symptoms\(^1\text{-}^{11}\):

- Family history of kidney or bladder stones
- A single kidney stone in children
- Recurrent UTIs, flank pain, hematuria
- CKD with no known etiology
- Recurrent stones in adults
- Nephrocalcinosis
- Severe infantile form: Failure to thrive, ESRD, severe retinal abnormalities
- Systemic oxalosis

**Kidney Function**\(^12\)

<table>
<thead>
<tr>
<th>GFR (mL/min/1.73 m(^2))</th>
<th>CKD Stage 1</th>
<th>CKD Stage 2</th>
<th>CKD Stage 3</th>
<th>CKD Stage 4</th>
<th>CKD Stage 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥90</td>
<td>Mild renal impairment</td>
<td>Kidney damage, mild loss of kidney function</td>
<td>Moderate to severe loss of kidney function</td>
<td>End-stage renal disease (ESRD)</td>
<td></td>
</tr>
<tr>
<td>60-89</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-59</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>15-29</td>
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<tr>
<td>&lt;15</td>
<td></td>
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</tr>
</tbody>
</table>

**Plasma Oxalate**\(^13\)

Abbreviations: CKD, chronic kidney disease; ESRD, end-stage renal disease; UTIs, urinary tract infections.

PH Often Has Early Onset, But Patients Can Vary in Symptom Timing and Kidney Function

<table>
<thead>
<tr>
<th>Symptom Onset</th>
<th>Age at Diagnosis</th>
<th>Kidney Function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PH Type 1</strong></td>
<td><strong>PH Type 2</strong></td>
<td><strong>PH Type 3</strong></td>
</tr>
<tr>
<td>Median (age)</td>
<td>Median (range)</td>
<td></td>
</tr>
<tr>
<td>3.9 - 5.2 years (0-66 years)</td>
<td>8.1 years (0-72 years)</td>
<td>10% have ESRD by age 1 year</td>
</tr>
<tr>
<td>PH Type 2</td>
<td>3.2 years (1.0-11 years)</td>
<td>9 years (2-32 years)</td>
</tr>
<tr>
<td>3.2 years</td>
<td>&gt;50% have CKD stage 2+</td>
<td>&gt;50% have CKD stage 2+</td>
</tr>
<tr>
<td>PH Type 3</td>
<td>0.75 - 2.6 years (0.1-31 years)</td>
<td>1.5 years* (0.7-13 years)</td>
</tr>
<tr>
<td>0.75 - 2.6 years</td>
<td>14%-30% with CKD</td>
<td></td>
</tr>
</tbody>
</table>

*Limited data, N=4 patients.

Abbreviations: CKD, chronic kidney disease; ESRD, end-stage renal disease.

Renal Damage Caused by Oxalate May Not Be Reversible and Progresses to Systemic Oxalosis

1. Progressive CaOx crystal deposition, recurrent stones, but especially inflammation, and interstitial fibrosis lead to ESRD\(^1,2\)*.

2. As glomerular filtration rate declines, oxalate is inadequately filtered by the kidneys, resulting in increased plasma oxalate values and then *systemic oxalosis*\(^2\).

CaOx crystals are deposited in tissue throughout the body, especially the skeleton\(^3\).

- Bone fractures, bone deformation, inhibited bone growth, anemia, severe pain\(^4,5\).
- Retinopathy\(^4,5\).
- Cardiomyopathy, conduction disturbances\(^4,5\).
- Skin ulcers, nodules\(^4,5\).
- Retinal CaOx deposits\(^6\).
- Crystal deposits at finger tip\(^6\).
- CaOx deposits in the bone\(^6\).
- CaOx deposits in the heart\(^6\).

Abbreviations: CaOx, calcium oxalate; ESRD, end-stage renal disease.

Multiple Studies Show That Earlier Diagnosis Is Needed to Improve Patient Outcomes and Preserve Renal Function

42% of patients with PH experience a significant delay in diagnosis\textsuperscript{1}
Patients experience 3.4 ± 5.4 years between first symptom presentation and diagnosis

One study reported that\textsuperscript{2} 27% of patients are diagnosed at ESRD, with delay of 3.5 years after symptom onset

A separate study found that\textsuperscript{3} ~5% are diagnosed after kidney transplant
19% of those diagnosed after transplant are not diagnosed until after first transplant failure

Abbreviations: ESRD, end-stage renal disease.
Current Treatments for PH Do Not Stop Disease Progression and Can Contribute to Patient Burden

**Oxalate Reduction**

- **Aggressive hydration**\(^1\)
  - 2-3 liters water/per 1m\(^2\) BSA/day
  - Gastrostomy tube for infants or adults struggling with water intake

- **Pyridoxine (vitamin B6)**
  - For a subset of patients with PH1 only\(^1\)
  - Multiple tablets per day

- **Crystallization inhibition**\(^1\)
  - Alkaline citrate or orthophosphate
  - 3-4 times daily application

- **Dietary changes**\(^1\)
  - Avoidance of oxalate-rich foods recommended

**Kidney Stone Management\(^1-4\)**

- Percutaneous nephrolithotomy (PCNL) or ureteroscopy

**Renal Replacement Therapy**\(^1\)

- Intermittent hemodialysis (HD), additional peritoneal dialysis (PD) in some patients

**Organ Transplant**

- Simultaneous liver/kidney transplant for PH 1
- Isolated kidney transplantation for PH 2 patients

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
Nedosiran for the Treatment of Primary Hyperoxaluria

Ralf Rosskamp, M.D.
Chief Medical Officer
Nedosiran Is Designed to Inhibit the Final Common Step in Oxalate Production

Known Types of Primary Hyperoxaluria

<table>
<thead>
<tr>
<th>Type</th>
<th>Genetic Mutation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH1</td>
<td>AGXT</td>
<td>Glyoxylate in PH1 only</td>
</tr>
<tr>
<td>PH2</td>
<td>GRHPR</td>
<td>Glyoxylate</td>
</tr>
<tr>
<td>PH3</td>
<td>HOGA1</td>
<td>Glyoxylate</td>
</tr>
</tbody>
</table>

Nedosiran blocks final common pathway of oxalate production by silencing LDHA

Kidney function preservation

GO = glycolate oxidase
LDHA = lactate dehydrogenase A

Calcium oxalate crystallization

Impacted by ESRD and systemic oxalosis

Kidney stones
Human Genetic Deficiency Supports Safety of Liver LDHA Inhibition

14 Case Reports of Humans Naturally Deficient for LDHA, With No Liver Dysfunction Reported

- LDHA is involved in the inter-conversion of lactate to pyruvate
- Human data in PHYOX1 in HVs up to 12mg/kg of nedosiran show no changes in plasma lactate and pyruvate concentrations over placebo
- Preclinical studies of nedosiran in mice do not show changes in plasma lactate and pyruvate concentrations over placebo, in both resting and exercised mice

14 Case Reports of Humans Naturally Deficient for LDHA, With No Liver-Related Abnormalities Reported

- Of the 14 case reports, six were women


*Of the 14 case reports, six were women
Final Results From PHYOX1 Single-Dose Phase 1 Study of Nedosiran in Participants With PH1 or PH2

**PHYOX1: Mean Urinary Oxalate Levels by Dose***

<table>
<thead>
<tr>
<th>PH Type</th>
<th>Dose (mg/kg)</th>
<th>Pts. Reaching Normalization or Near-Normalization (%)</th>
<th>Max Reduction Uox (%) Mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH1</td>
<td>1.5 (n=5)</td>
<td>3 (60)</td>
<td>51 (28-72)</td>
</tr>
<tr>
<td></td>
<td>3.0 (n=6)</td>
<td>5 (83)</td>
<td>73 (62-80)</td>
</tr>
<tr>
<td></td>
<td>6.0 (n=4)</td>
<td>4 (100)</td>
<td>78 (35-100)</td>
</tr>
<tr>
<td>PH2</td>
<td>1.5 (n=1)</td>
<td>0 (0)</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>3.0 (n=2)</td>
<td>2 (100)</td>
<td>54 (42-66)</td>
</tr>
</tbody>
</table>

*Days with at least two values in both dosing groups
ClinicalTrials.gov: NCT03392896
Abbreviation: BSA=body surface area
Monthly Dosing is a Simple Choice for Participants and May Safeguard Against Sudden Oxalate Spikes

Monthly Dosing Supports Comprehensive Coverage, Convenience and Safety Advantage

- **Consistency** - Based on modeling and simulation of PK and PD data from the PHYOX1 Study
  - Modeling shows that highest percentage of participants reach normal Uox levels with monthly dosing
  - Monthly dosing was superior compared to a loading-dose regimen with nedosiran after 6 months of treatment

- **Simple and Convenient** - Monthly dosing will be at home with pre-filled syringes for adults and adolescents
  - Monthly dosing is easy to remember and may lead to better adherence
  - Facilitates establishment of treatment routine and provides consistent protection
  - Patient and physician preference study in migraine show no difference between monthly and quarterly regimen

- **Safety Advantage** - A missed dose in a monthly regimen is unlikely to lead to sudden spike in Uox
  - When reaching normal Uox concentrations, participants may be weaned off their supportive therapy including hyperhydration and potassium citrate
  - PH participants are vulnerable to sudden increases in Uox, which may lead to renal failure within days

Abbreviations: PK, pharmacokinetics; PD, pharmacodynamics

PHYOX3 Clinical Trial Design
3-Year Open-Label Extension Study for Participants With PH1, PH2 or PH3 From Another PHYOX Study

**Key evaluation objectives:**
- Effect on estimated glomerular filtration rate (eGFR)
- Effect on new stone formation and nephrocalcinosis
- Effect on Uox levels
- Safety and tolerability when administered monthly

**Nedosiran once-monthly dosing regimen:**
- Fixed-dose regimen in participants 12 years and older
  - Participants weighing ≥50 kg, receive dose of 170 mg (1 mL)
  - Participants weighing <50 kg, receive dose of 136 mg (0.8 mL)
- Initially, weight-based dose in participants 11 years and younger

**enrollment**

For single-dose studies, after Uox rebound

For PHYOX2, immediate rollover

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\[ \text{year 1} \] \[ \text{year 2} \] \[ \text{year 3} \]

\[ \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \uparrow \]

\[ \text{enrollment} \]

= Office visit for dosing and safety assessment

= At-home dosing

*If single-dose studies, after Uox rebound.*

*For PHYOX2, immediate rollover.*
Demographics and Baseline Uox Values for PHYOX3
Data Reflect 11 Participants Who Rolled Over From PHYOX1 and Have Reached Day 120 (5 Doses)

• PHYOX3 BSA corrected baseline values are lower compared to PHYOX1 BSA corrected baseline values
  – Average 0.926 mmol/1.73m² BSA/24hr for PHYOX3, versus 1.323 mmol/1.73m² BSA/24hr for PHYOX1
  – Some PHYOX1 participants had not returned to 80% of baseline
  – PHYOX1 baseline (mean of 2 screening values) used for comparison as this is the only real pre-treatment value
  – For reference, the pivotal PHYOX2 BSA corrected baseline is currently at 1.409 mmol/1.73m² BSA/24hr

### Table: 301 participants (101 rollover) (N=11)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>Min, Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27.0 (8.57)</td>
<td>26</td>
<td>16, 46</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>12 - 17 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 (90.9)</td>
<td>≥18 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th></th>
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<tbody>
<tr>
<td>Male</td>
<td>7 (63.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4 (36.4%)</td>
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<table>
<thead>
<tr>
<th>Race</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Asian</td>
<td>1 (9.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>5 (45.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not recorded</td>
<td>5 (45.5%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Hispanic or Latino</td>
<td>10 (90.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not recorded</td>
<td>1 (9.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline eGFR (mL/min/BSA) (n=9)</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>Min, Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>75.3 (22.86)</td>
<td>82</td>
<td>36, 102</td>
</tr>
<tr>
<td>≥ 30 and &lt; 45 mL/min/BSA</td>
<td>2 (22.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 45 mL/min/BSA</td>
<td>7 (77.8%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline 24Hr Urinary Oxalate (mmol/24Hr/BSA)</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>Min, Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.926 (0.272)</td>
<td>0.922</td>
<td>0.557, 1.448</td>
</tr>
<tr>
<td>PH Type</td>
<td>Type 1</td>
<td>Type 2</td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>8 (72.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 2</td>
<td>3 (27.3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time since PH Diagnosis (months)</th>
<th>Mean (SD)</th>
<th>Median</th>
<th>Min, Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>222.29 (109.656)</td>
<td>197.27</td>
<td>50.2, 475.9</td>
</tr>
</tbody>
</table>

Based on availability of data as of July 10, 2020
Abbreviation: BSA=body surface area
PHYOX3 BSA Corrected Mean 24-Hour Uox Absolute Values for Participants With 5 Doses of 170 mg of Nedosiran

- Day 120 BSA corrected mean value for all participants (n=11): 0.524 mmol/1.73m² BSA/24hr

For both PHYOX1 and PHYOX3 the first dose was administered Day 1 after baseline (BL= Day 0)
PHYOX3 Mean Percent Reduction of Uox Values for Participants With 5 Doses of 170 mg of Nedosiran

Mean Reduction From PHYOX1 Pre-Treatment Baseline

- Day 120 mean reduction value for all participants (n=11): 54.3%

For PHYOX3 the first dose was administrated Day 1 after baseline (BL= Day 0)
Normalization and Near-Normalization of Uox Levels

Normalization: Uox at or below 0.460 mmol/1.73m² BSA/24 hr
Near Normalization: Uox between 0.460 and 0.600 mmol/1.73m² BSA/24 hr (~130% of normal)

<table>
<thead>
<tr>
<th>PH Type</th>
<th>Pts. Reaching Normalization at Day 120 (%)</th>
<th>Pts. Reaching Normalization or Near-Normalization at Day 120 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH1 (n=8)</td>
<td>5 (63)</td>
<td>8 (100)</td>
</tr>
<tr>
<td>PH2 (n=3)</td>
<td>1 (33)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>PH1+PH2 (n=11)</td>
<td>6 (55)</td>
<td>9 (82)</td>
</tr>
</tbody>
</table>

- As of interim analysis, five participants have reached normal Uox concentrations at 3 consecutive visits and are eligible for weaning off disease management, including hyperhydration
- For PH1 participants, the average Uox level achieved is in the normal range (mean Uox= 0.404 mmol/1.73m² BSA/24 hr, 66% reduction)
## Similarities and Differences Between PHYOX3 Open-Label Extension Study and PHYOX2 Pivotal Registration Study

<table>
<thead>
<tr>
<th></th>
<th>PHYOX₂</th>
<th>PHYOX₃</th>
</tr>
</thead>
</table>
| **Patient Population** | PH1 and PH2 participants  
Ages 6 and above | PH1, PH2 and PH3 participants  
PHYOX1 rollover participants are 12 and above, younger ages may enroll from other trials; siblings of participants may also enroll |
| **Evaluation Period** | 180-days | 3-years |
| **Primary Endpoint** | Uox AUC from Day 90-180 | eGFR |
| **Uox Completeness Criteria** | Strict rules | Initially guidelines, now consistent with PHYOX2 |
| **Uox Measurements** | Monthly | Monthly measurements for PHYOX1 rollover participants; others quarterly |
| **Study Design** | Double-blind, placebo controlled  
Randomized 2:1 drug:placebo | Open-label |
**PHYOX3 Interim Safety Data**

- Favorable risk/benefit profile in this study
- AEs mostly related to SC injection
- Drug-related ISRs in 3/16 participants
- ALT elevations <2.5 ULN; both participants started study with elevated ALT
- One SAE of nephrolithiasis
- No other clinically significant laboratory abnormalities, ECG findings and vital signs

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<table>
<thead>
<tr>
<th>Category</th>
<th>301 Study n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total TEAEs</td>
<td>16 (94.1)</td>
</tr>
<tr>
<td>TEAEs occurring in &gt;=10% of participants in group (n, %)</td>
<td></td>
</tr>
<tr>
<td>Injection site discomfort</td>
<td>6 (35.3)</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>6 (35.3)</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>4 (23.5)</td>
</tr>
<tr>
<td>Flank pain</td>
<td>3 (17.6)</td>
</tr>
<tr>
<td>Injection site discoloration</td>
<td>3 (17.6)</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>Injection site atrophy</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>Injection site hematoma</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>ISRs (n, %)</td>
<td>3 (17.6)</td>
</tr>
<tr>
<td>TEAEs leading to discontinuation of study treatment (n, %)</td>
<td>0</td>
</tr>
<tr>
<td>TEAEs leading to study withdrawal (n, %)</td>
<td>0</td>
</tr>
<tr>
<td>Death (n, %)</td>
<td>0</td>
</tr>
<tr>
<td>Serious TEAEs (n, %)</td>
<td>1 (5.9)</td>
</tr>
<tr>
<td>Severity of TEAEs (n, %) [1]</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>12 (70.6)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (17.6)</td>
</tr>
<tr>
<td>Severe</td>
<td>1 (5.9)</td>
</tr>
</tbody>
</table>

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*Treatment-emergent adverse event (TEAE) is defined as any adverse event that begins on or after the first dose of study intervention. Safety population n = 16; [1] The severity shown is the greatest severity reported for a particular subject (Severe > Moderate > Mild)*

*Abbreviations: SC, subcutaneous; BL, baseline, ALT, alanine transaminase; ULN, upper level of normal, ECG, electrocardiograph*  
*Based on availability of data as of July 10, 2020*
## Pivotal Study Package

<table>
<thead>
<tr>
<th>Trial</th>
<th>Description/Details</th>
<th>Status</th>
<th>PH Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHYOX₂</td>
<td>Study 201: Pivotal, double-blind, randomized, placebo-controlled trial (2:1 randomization) Monthly fixed-dose, enabling prefilled syringes at launch</td>
<td>Enrolling n~36</td>
<td>1,2</td>
</tr>
<tr>
<td>PHYOX₃</td>
<td>Study 301: Long-term, multidose, open-label extension study open to all participants in PHYOX trials and siblings</td>
<td>Enrolling</td>
<td>1,2,3</td>
</tr>
</tbody>
</table>

## Additional Supportive Studies

<table>
<thead>
<tr>
<th>Trial</th>
<th>Description/Details</th>
<th>Status</th>
<th>PH Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHYOX₄</td>
<td>Study 104: Double-blind, randomized, placebo-controlled study in participants with primary hyperoxaluria type 3 (PH3)</td>
<td>Enrollment Q3 2020</td>
<td>3</td>
</tr>
<tr>
<td>PHYOX₇</td>
<td>Study 204: Multidose trial in participants (birth to adult) with PH and end-stage renal disease (ESRD)</td>
<td>Enrollment Q4 2020</td>
<td>1,2</td>
</tr>
<tr>
<td>PHYOX₈</td>
<td>Study 203: Open-label study in children 0-5 yrs</td>
<td>Enrollment Q1 2021</td>
<td>1,2</td>
</tr>
<tr>
<td>PHYOX犰X</td>
<td>Study 502: Natural history study to evaluate association between Uox and stone formation rate</td>
<td>Initiation Q3 2020</td>
<td>3</td>
</tr>
</tbody>
</table>
Nedosiran Summary

• PHYOX3 Day 120 results in line with expectations from single-dose PHYOX1 study
  – Already a high percentage of participants with normalization/near-normalization at Day 120
  – High Uox percent reduction despite low baseline
  – Average Uox for PH1 participants at Day 120 was in the normal range (Uox = 0.404 mmol/1.73m² BSA/24 hr)

• Five participants have reached normal Uox concentrations at 3 consecutive visits and are eligible for gradual fluid reduction

• Monthly nedosiran administration appears safe and generally well tolerated
  – Low rate of injection-site reactions
  – No evidence of changes to blood lactate or pyruvate levels

• Expect comprehensive label including all ages in participants with relatively intact renal function (GFR ≥ 30mL/min/BSA) at time of launch

• Nedosiran fixed dose monthly dosing regimen for participants 12 years and above is simple and will avoid oxalate spikes
  – We expect monthly weight-based dosing regimen for children <12 years of age

• Agreement with FDA on path to full approval for PH1 and PH2

• Safety data from participants with severe renal impairment (GFR <30 mL/min/BSA) will be included with the NDA
  – Currently 6 compassionate-use cases in young participants undergoing hemodialysis
Our Investigators & Site Teams Screening and Enrolling Participants

- Dr. Gema Ariceta
- Dr. Michelle Baum
- Dr. Vladimir Belostotsky
- Dr. Pierre Cochat
- Dr. Martin Coenen
- Dr. Georges Deschenes
- Dr. Francesco Emma
- Dr. Tom Forbes
- Dr. Jaap Groothoff
- Dr. Shuzo Hamamoto
- Dr. John Lieske
- Dr. Graham Lipkin
- Dr. Shabbir Moochhala
- Dr. Michael Moritz
- Dr. Chebi Mourani
- Dr. Gesa Schalk
- Dr. Burkhard Toenshoff
- Dr. Anna Wasilewska
- Dr. William Wong

Thank You to all those who make these studies possible!

Our Patients and Advocacy Organizations

The Dicerna Team, particularly...

- Jay Russak
- Katelyn Berteletti
- James Park
- Kelly Barrios
- Bernd Hoppe
- Bob Brown
- Natalie Pursell
- Cheng Lai
Nedosiran Business Planning

Rob Ciappennelli
Chief Commercial Officer
Nedosiran: The Only RNAi Drug Candidate in Development for All PH Types

Limited Disease Awareness, Education and Resources to Efficiently Diagnose PH

**Estimated PH Diagnosis Rates**

<table>
<thead>
<tr>
<th></th>
<th>PH1</th>
<th>PH2</th>
<th>PH3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Diagnosis Projections^</td>
<td>~40% – 50%</td>
<td>~10%</td>
<td>~7%</td>
</tr>
</tbody>
</table>

*Nedosiran’s target profile provides a comprehensive treatment option for all PH patients with convenient once monthly dosing, including self administration*

**Dicerna estimates nedosiran global sales > $500M**

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*Prevalence based on PH mutant alleles found in the National Heart, Lung, and Blood Institute Exome Sequencing Project (NHGRI ESP) and calculated according to Hardy-Weinberg equilibrium for each PH type using the sum of all alternate PH1, PH2, or PH3 alleles (known, or known and scored as pathogenic) and all wild type alleles. 1. Hopp K, et al. J Am Soc Nephrol. 2015;26(10):2559-2570. 2. U.S. Census Bureau population on a date: February 20, 2020. United States Census Bureau website, 2020.

^Sources: Dicerna internal estimates PH claims/registry analysis and scientific advisors. Analyst Projections.
Multiple Important Clinical, Regulatory and Infrastructure Milestones Projected Over Next Two Years

2020
- Establish Medical Group

2021
- Stand Up Commercial
- Build Enterprise Infrastructure
- Launch Readiness Preparations

2022
- PHYOX Clinical Trial Results Expected
- Target Regulatory Filings
- Potential Approvals

Dicerna
Establishing Product Strategy and Business Infrastructure to Drive Nedosiran Global Commercialization

### Operations Overview

<table>
<thead>
<tr>
<th>U.S. Launch Readiness</th>
<th>Outside the U.S. Launch Preparations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Teams / Infrastructure:</strong></td>
<td><strong>Partnering:</strong></td>
</tr>
<tr>
<td>• Commercial: Patient Advocacy, Patient Services, Marketing, Market Access, Insights/Analytics and Commercial Operations</td>
<td>• Active partner discussions with regional and multi-national pharma/biotech commercial groups</td>
</tr>
<tr>
<td>• Enterprise: Medical Affairs, Regulatory, Compliance, Legal, Technical Operations, IT and Finance</td>
<td></td>
</tr>
<tr>
<td><strong>Planning:</strong></td>
<td><strong>Market Engagement:</strong></td>
</tr>
<tr>
<td>• Strategic Product Plan (e.g. positioning, branding…etc.)</td>
<td>• Market Assessments</td>
</tr>
<tr>
<td>• Product Launch Infrastructure</td>
<td>• EMA and PMDA discussions</td>
</tr>
<tr>
<td><strong>Patient:</strong></td>
<td>• European Primary Hyperoxaluria Patient Advocacy</td>
</tr>
<tr>
<td>• Patient advocacy grant - “FDA Voice of the Patient” event led by the Oxalosis and Hyperoxaluria Foundation October 5, 2020</td>
<td>Sept 19, 2020 Annual Patient Meeting</td>
</tr>
</tbody>
</table>

*Building foundation to support patients through Dicerna’s growing portfolio*
Nedosiran: Setting the Stage for Commercial Success

• Nedosiran has potential to address all patients with PH, regardless of type
  – Mechanism: Nedosiran silences LDHA, the ultimate step in the oxalate production pathway
  – Development Plan: Comprehensive PHYOX development program to evaluate all types of PH
  – Dosing Format: Simple, once-monthly, self-administered subcutaneous injections in patients ≥12 years

• Data from PHYOX3 present competitive product profile
  – Achievement of 100% normal or near-normal response in participants with PH1
  – Five of the 17 participants enrolled in the trial achieved normal Uox at three consecutive visits, making them eligible for gradual reduction in fluid intake

• Commercial preparations underway, with key infrastructure in place and fit-to-purpose as key development and regulatory milestones are achieved

• Target NDA submission: Q3 2021
Extrahepatic Platform

Bob D. Brown, Ph.D.

Chief Scientific Officer, Executive Vice President Research & Development
Platform Expansion to Achieve Effective Extrahepatic Delivery
Including Central and Peripheral Nervous Tissues and Other Extrahepatic Tissues

![Diagram showing nucleic acid constructs with variable secondary structures and chemical compositions](image)

- **GalXC**
  - 1st Generation GalXC
  - GalNAc Sugars to bind hepatocyte ASGPR

- **New NA Platforms**
  - Novel nucleic acid constructs with variable secondary structures and chemical compositions
  - ± Non-GalNAc ligands (e.g. small molecules, peptides, Fabs, etc.)

- **Our RNAi platform provides remarkable flexibility for medicinal chemistry optimization and expansion**
  - We are modifying the fundamental nucleic acid composition of oligonucleotides to enhance drug-like properties
  - Optimization of nucleic acid composition alone can drive significant extrahepatic delivery function
  - We are utilizing a broad range of molecular weights, secondary structures and chemistries

- **Targeting moieties are not required for effective extrahepatic delivery**
  - Targeting moieties can enhance delivery efficiency after medchem optimization, if needed

- **We are testing potent hits against multiple neurological and systemic extrahepatic targets**

- **These platform advancements can deliver nucleic acid therapeutics with non-RNAi mechanisms of action**
  - Enables potential expansion into new target/indication opportunities

**Abbreviations:** NA, nucleic acid; SAR, structure-activity relationship
Many neurological disorders are not cell type specific, highlighting the need for a platform that enables delivery and potency in a variety of cell types.

Modified siRNA payloads have been designed against cell type-specific mRNAs to enable specific cell-type challenges to be identified and overcome:

- Astrocytes
- Oligodendrocytes
- Neurons

Our modified platforms are capable of dose-dependent and durable target mRNA suppression after intrathecal injection.

CNS platforms can be tuned to enhance activity and durability in distinct cell types to treat a variety of neurological diseases.

Abbreviation: CNS, central nervous system
Medchem/SAR Activity in Mouse CNS After Intrathecal Administration

One 300 µg Dose (≈10 mg/kg equivalent), Target Knockdown at Day 7 vs. Day 28

- Sense (passenger) strand modifications alone can increase RNAi potency and duration of action
- Initial SAR characterizations in the CNS includes potency, duration and tolerability
- CD68 and other CNS markers of inflammation demonstrate tolerability in both rodents and NHP
Delivery of Novel Constructs via I.T. versus I.C.M. Administration in Rats Yields Consistent CNS-Wide Target mRNA Knockdown

Efficient mRNA Target Reduction Independent of Route of Administration
CNS Tissue Distribution After Intracisternal and Intrathecal Administration

Bulk Distribution of RNAi Payload Throughout Rat CNS by in situ Hybridization (ISH) Detection

- In situ hybridization visualization of bulk test article tissue distribution in the CNS vs the route of administration

- Effective target knockdown from the forebrain to the lumbar region and in DRG over a two order of magnitude difference in drug exposure

**Abbreviation:** aCSF, artificial cerebrospinal fluid; DRG, dorsal root ganglia
Durable CNS Target mRNA Knockdown After a Single Dose in Rats

1 mg Dose, i.t.

- Sustained control of target mRNA reduction for at least 160 days (ongoing)
- The duration of target knockdown is not dependent on the magnitude of initial knock down
Widespread Therapeutic Target mRNA Reduction in Nonhuman Primate (NHP) CNS by RNAi in the Absence of Complex Conjugation

Broad Distribution and Target mRNA Reduction 28 Days After a Single 45 mg i.c.m. Dose

Target mRNA Reduction Throughout Primate CNS at Day 28

- Prefrontal Cortex
- Frontal Cortex (grey matter)
- Frontal Cortex (white matter)
- Parietal Cortex (grey matter)
- Parietal Cortex (white matter)
- Temporal Cortex (grey matter)
- Temporal Cortex (white matter)
- Occipital Cortex (grey matter)
- Occipital Cortex (white matter)
- Midbrain
- Cerebellum
- Brainstem
- Cervical SC (grey matter)
- Cervical SC (white matter)
- Thoracic SC (grey matter)
- Thoracic SC (white matter)
- Lumbar SC (grey matter)
- Lumbar SC (white matter)
Cellular Uptake in NHP CNS After Intracisternal Administration

High Resolution Images Reveal Delivery and Intracellular Accumulation in Multiple Cell Types

- In situ hybridization (ISH) visualization of test article at 20x magnification
- RT-PCR of target mRNAs confirms intracellular delivery and target knockdown
New Indications Are Enabled by Delivery To Extrahepatic Non-Neural Tissues Using Nucleic Acid Platforms Without GalNAc

10 mg/kg Subcutaneous Dose in Mice, Target Silencing Measured 14 Days Post-Dose

- Optimized chemistries enables delivery to multiple tissues beyond the liver
- Delivery to multiple tissues expands the range of important cardiovascular and metabolic targets to access
- Peripheral tissue delivery is independent of Apolipoprotein E, including muscle
Flexible Subcutaneous Dosing Regimens Yield Equivalent Extrahepatic Target Knockdown

*Mice, 15 mg/kg Total Exposure, Subcutaneous Administration*

- Multiple effective dosing regimens support flexible subcutaneous clinical development strategies
Rodents Are Predictive of Extrahepatic Activity in NHPs

*Mouse Sampled at Two Weeks; NHP Samples at Four Weeks*

- SAR and medchem screening in rodents enables rapid, reliable translation into monkeys.
Broadly Distributed Activity Is Observed Within Individual Tissue Types in Nonhuman Primates

Target mRNA Measured 4 Weeks After a Single Subcutaneous Dose

- Up to 85% target reduction detected in both peripheral tissue types in cynomolgus monkeys
- Onset of RNAi activity was 1-2 weeks post-dose
- No adverse effects observed at either dose level
Expansion of Dicerna’s Therapeutic Nucleic Acid Platforms and Programs

**Going Beyond GalXC**

- We are developing nucleic acid technologies independent of the hepatic GalNAc/ASGPR system

- Chemical and structural modifications of our clinical-stage GalXC platform have:
  - Increased the intrinsic drug-like properties of our RNAi and non-RNAi nucleic acid platforms
  - Lowered barriers to intracellular delivery beyond hepatocytes, including systemic and CNS applications
  - Enabled additional mechanisms of action to expand our target/indication spaces beyond RNAi applications

- We are applying these advances to a range of indications beyond the liver
  - Indications in the CNS, peripheral nervous system and muscle
  - Indications requiring simultaneous liver and adipose tissue targeting, such as cardiometabolic diseases
Closing Remarks

Douglas M. Fambrough, Ph.D.,
President and Chief Executive Officer
Dicerna: Well Positioned for Near- and Long-Term Success

Diversified Core & Collaborative Pipelines Plus Expanding Technology Platforms to Drive Growth

• **Core pipeline** of early and late-stage assets with multiple development milestones over next year+
  – Nedosiran: A potential best-in-class therapeutic for PH1, PH2 and PH3
  – RG6346: A Potential best-in-class therapeutic for the treatment of chronic HBV
  – A1AT: Dicerna/Alnylam collaboration to bring forward best A1AT program

• **Collaborations** with leading global pharmaceutical and biotech companies expected to yield multiple clinical programs over the coming years and have the potential to provide significant financial upside

• **Unparalleled medicinal chemistry flexibility** has enabled us to expand beyond GalNAc mediated delivery to the liver and allows us to create nucleic acid molecules that may address additional tissues and indications

• **Strong balance sheet** with cash into 2023 provides runway through projected nedosiran commercialization
Q&A

Dicerna Management Team