ALN-HBV, an Investigational RNAi Therapeutic for the Treatment of Hepatitis B Virus (HBV) Infection

July 28, 2015
Agenda

Welcome
• Joshua Brodsky
  Senior Manager, Investor Relations and Corporate Communications

Introduction
• John Maraganore, Ph.D.
  Chief Executive Officer

Overview of Hepatitis B Virus Infection
• Edward Gane, MBChB, M.D., FRACP, MNZM, Professor of Medicine, University of Auckland,
  and Chief Hepatologist, Transplant Physician, Deputy Director of New Zealand Liver Transplant Unit, Auckland
  City Hospital

Patient Advocacy: The Changing Landscape of HBV
• Su Wang, M.D., MPH
  Board Member, World Hepatitis Alliance and Medical Director of Center for Asian Health at Saint Barnabas
  Medical Center

Q&A Session
• With Dr. Gane and Dr. Wang

ALN-HBV Program
• Laura Sepp-Lorenzino, Ph.D.
  Vice President, Entrepreneur-in-Residence

Q&A Session
Reminders

• Event will run for approximately 90 minutes
• Q&A Session at end of each presentation
  ◦ Submit questions at bottom of webcast screen
  ◦ Questions may be submitted at any time
• Replay, slides and audio available at www.alnylam.com
Alnylam Forward Looking Statements

This presentation contains forward-looking statements, within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. There are a number of important factors that could cause actual results to differ materially from the results anticipated by these forward-looking statements. These important factors include our ability to discover and develop novel drug candidates and delivery approaches, successfully demonstrate the efficacy and safety of our drug candidates, obtain, maintain and protect intellectual property, enforce our patents and defend our patent portfolio, obtain regulatory approval for products, establish and maintain business alliances; our dependence on third parties for access to intellectual property; and the outcome of litigation, as well as those risks more fully discussed in our most recent quarterly report on Form 10-Q under the caption "Risk Factors." If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. All forward-looking statements speak only as of the date of this presentation and, except as required by law, we undertake no obligation to update such statements.
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Q&A Session
Alnylam RNAi Therapeutics Strategy
A Reproducible and Modular Path for Innovative Medicines

1. Liver-expressed target gene
   • Involved in disease with high unmet need
   • Validated in human genetics
   • GalNAc-siRNA enables SC dosing with wide therapeutic index

2. POC achieved in Phase 1
   • Blood-based biomarker with strong disease correlation
     ◦ e.g., Serum TTR, thrombin generation, hemolytic activity, LDL-C, HBsAg levels

3. Definable path to approval and market
   • Established endpoints
   • Focused trial size
   • Large treatment effect
   • Collaborative approach with physicians, regulators, patient groups, and payers
# Alnylam Development Pipeline

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<th>Category</th>
<th>Discovery</th>
<th>Development</th>
<th>Phase 1</th>
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Q&A Session
CHRONIC HEPATITIS B
Promising New Treatments

Ed Gane
NZ Liver Transplant Unit
Auckland Hospital
Global Burden of Chronic HBV Infection

World population
6 billion

2 billion with evidence of HBV infection

400 million with chronic HBV

25% die of cirrhosis or liver cancer

Margolis et al, 1991
HCC has a High Burden of Disease

- 4th most common cancer worldwide
- 3rd most common cancer-related death

HBV is the most common cause of HCC

The 50 year History of Hepatitis B

- 1965: Australian Antigen discovered in leukaemia
- 1967: link with serum hepatitis
- 1970: first specific serologic tests
- 1971: WHO recommend screening of blood donors
- 1972: Dane particle visualised on EM
- 1976: Plasma-derived subunit HBV vaccine
- 1980: Clinical trial (Merck) of MS-2 in MSM in NYC
- 1981: First link between HBV and HCC (Beazley)
- 1983: Vaccine/HBIG to prevent vertical transmission
- 1987: National neonatal HBV vaccine program (Taiwan)
- 1992: Effective therapy for CHB (Interferon)
- 1997: Effective oral antiviral therapy (lamivudine)
- 1999: First APASL HBV Consensus Meeting
Goals of treatment in CHB: APASL Consensus Statement 2005

“The ultimate long-term goal is prevention of cirrhosis, decompensation and HCC, and prolong survival.

Sustained viral suppression is the key to the reduction or prevention of hepatic injury and disease progression.

Therefore, the primary goal of treatment for chronic hepatitis B is to eliminate or permanently suppress HBV….. ”

Liaw YF et al. JGH 1999
Benefits of Long-term Oral Antiviral Therapy:
(i) Viral Suppression during 8 years of Tenofovir

- 99.6% overall response at Year 8
- 98% overall response at Year 8

Benefits of Long-term Oral Antiviral Therapy
Viral Suppression may reverse cirrhosis

Baseline: Ishak Stage 6

Week 48: Ishak Stage 6

Week 240: Ishak Stage 2
Benefits of Long-term Oral Antiviral Therapy

Viral Suppression may prevent fibrosis

♦ Patients in Long-term Tenofovir Studies 102/103
  – 348 had liver biopsies at baseline, 1 and 5 years

Benefits of Long-term Oral Antiviral Therapy
Viral Suppression may prevent HCC

Cirrhosis Asian Lamivudine Multicenter study
RCT of 651 Pts with compensated HBV-cirrhosis

* If exclude 5 HCC cases in yr 1 ⇒ HR = 0.47; P = 0.052

Liaw et al, NEJM 2004;
Benefits of Long-term Oral Antiviral Therapy
Viral Suppression may prevent HCC

- Meta-analysis of 5 RCTs, case control & cohort studies

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Nucleotide/side analogues n/N</th>
<th>Placebo / no treatment n/N</th>
<th>RR (random) 95% CI</th>
<th>RR (random) 95% CI</th>
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<tbody>
<tr>
<td>Liaw, 2004 (29)</td>
<td>17/436</td>
<td>16/215</td>
<td>0.52 [0.27, 1.02]</td>
<td>0.52 [0.27, 1.02]</td>
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<td>Matsumoto, 2005 (30)</td>
<td>4/377</td>
<td>50/377</td>
<td>0.08 [0.03, 0.22]</td>
<td>0.08 [0.03, 0.22]</td>
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<td>Papatheodoridis, 2005 (31)</td>
<td>5/201</td>
<td>15/195</td>
<td>0.32 [0.12, 0.87]</td>
<td>0.32 [0.12, 0.87]</td>
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<td>Yuen, 2007 (32)</td>
<td>1/142</td>
<td>3/124</td>
<td>0.29 [0.03, 2.76]</td>
<td>0.29 [0.03, 2.76]</td>
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<td>Eun, 2007 (33)</td>
<td>5/111</td>
<td>36/111</td>
<td>0.14 [0.06, 0.34]</td>
<td>0.14 [0.06, 0.34]</td>
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<tr>
<td>Total (95% CI)</td>
<td>1267</td>
<td>1022</td>
<td>0.22 [0.10, 0.50]</td>
<td>0.22 [0.10, 0.50]</td>
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</table>

Total events: 32 (Nucleotide/side analogues), 120 (Placebo/no treatment)
Test for heterogeneity: $\chi^2 = 12.57, df = 4 \ (P = 0.01), I^2 = 68.2\%$
Test for overall effect: $Z = 3.65 \ (P = 0.0003)$
Benefits of Long-term Oral Antiviral Therapy
Viral Suppression may prevent Decompensation

Cirrhosis  Asian Lamivudine  Multicenter study
• 436 Patients received Lamivudine for 3 years

Liaw et al, NEJM 2004;
Benefits of Long-term Oral Antiviral Therapy
Viral Suppression may rescue Decompensation

Perrillo et al. 2001 (n = 27)
- 79%

Untreated historical controls
De Jongh et al. 1992
- 14%

Benefits of Long-term Oral Antiviral Therapy
Reduce the demand for Liver Transplantation

- **NZLTU Trends in HBV Transplants (1999-2014)**
  - 602 liver transplants; 121 (20%) for HBV

NZLTU data 1999-2014
Benefits of Long-term Oral Antiviral Therapy
Reduce the demand for Liver Transplantation

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NZLTU data 1999-2014
Benefits of Long-term Oral Antiviral Therapy
Reduce the demand for Liver Transplantation

- **OPTN Trends in Waiting Lists (1985-2006)**
  - 113,927 listed; 47923 (4.2%) for HBV

Benefits of Long-term Oral Antiviral Therapy

<table>
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<tr>
<th>Benefits</th>
<th>Short-term goal</th>
<th>Medium-term goal</th>
<th>Long-term goal</th>
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<td>Mortality reduction</td>
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<td>Transplant need reduction</td>
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<td>HCC reduction</td>
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<td>Cirrhosis reduction</td>
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<td>Fibrosis regression</td>
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<td>HBsAg seroclearance</td>
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<td>Histological improvement</td>
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<td>HBeAg loss-seroconversion (HBeAg(+) patient only)</td>
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<td>HBV DNA negativity</td>
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<td>ALT normalisation</td>
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Most chronic hepatitis B patients are not treated

China

120 MILLION
chronic HBV carriers

~50,000,000
meet criteria for treatment

~8,000,000
are treated

USA

1.2-2 MILLION
chronic HBV carriers

~500-800,000
meet criteria for treatment

~75,000
are treated
Disadvantages of Long-term Oral Antiviral Therapy

1. Cost of life-long therapy
   - Highest burden in low income countries
   - Patient can afford only fixed duration of therapy

2. Risk of viral rebound ➔ severe flares
   - Due to Non-adherence (can't afford therapy)
   - Due to emergence of resistance

3. Direct toxicity of oral antivirals
   - Tenofovir ➔ bone disease, nephrotoxicity
   - Entecavir ➔ risk of mutagenesis?
   - Adefovir/Lamivudine ➔ risk of HCC
     - A181T mutation ➔ oncogenic truncated S proteins

HBV CURE
HBV Cure

Finite treatment duration

Absence of HBV DNA and antigens

Cessation of all treatment

Prevention of liver complications
How can we cure HBV?...

♦ Currently, HCV is curable, unlike HIV and HBV\(^1\)–\(^3\)

HCV

![HCV diagram](image)

- Viral RNA
- TREATMENT: Lifelong suppression
- No reservoir of infection
- HCV clearance
- CURE\(^4\)

HIV

![HIV diagram](image)

- Proviral DNA
- TREATMENT: Lifelong suppression

HBV

![HBV diagram](image)

- cccDNA: covalently closed circular DNA
- Nucleus
- TREATMENT: Lifelong suppression

cccDNA: covalently closed circular DNA; SVR: sustained virological response

1. Pawlotsky JM. J Hepatol 2006;44:S10–3;
New Targets for HBV “Cure”
New Targets for HBV “Cure”

- cccDNA silencing
- Inhibit protein translation by siRNA
- Core inhibitors
  - Novira
  - Bayer
  - Assembly
  - Gilead
  - Janssen
  - Roche
- HBsAg release Inhibitor
  - NAP

- Immunodulators
  - TLR agonists
  - T-cell vaccines
  - PD-1/PD-L1 blockade

- RT Pol Inhibitors
  - Nucleotide analogues
  - Non-Nuc analogues
  - RNAseH inhibitors

- Entry Inhibitors
  - Myrcludex
HBV CURE Conclusions

- Viral suppression with oral antiviral therapy can prevent disease progression and liver-related complications.
- Current duration of OAV is lifelong with high cost and risk of breakthrough from non-adherence/resistance.
- Future therapies will aim to induce HBsAg loss and enable discontinuation of long-term therapy.
- Ultimate goal of CHB management will be to develop a new targeted therapy which can provide “HBV Cure” after a finite duration of treatment.
HBV CURE: Conclusions

• HBV Cure programs stem from better understanding of HBV lifecycle and identification of new targets

• Target patient population still undefined but ideal therapy will work in both “immune active” and “immune tolerant” phases of chronic hepatitis B

• Safety will be the priority for these new therapies, in order to avoid severe hepatitis flares and other toxicity

• Convenient administration will be important (oral, subcut, weekly or monthly dosing)

• HBV cure will ultimately require agents which target multiple steps of HBV replication, thereby inactivating cccDNA and restoring host immune responses
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The Hepatitis B Epidemic

• 350-400 M with chronic hepatitis B (CHB) worldwide\(^1\)
  – More prevalent than HIV (35M) and HCV (170M) globally
  – 1 in 20 are infected, 75% live in Asia, major health disparity

• Leading cause of primary liver cancer (HCC) worldwide\(^2\)
  – HCC rates increasing in US (MMWR 2010)
  – 4-5,000 deaths a year in US due to cirrhosis and liver cancer

• 2/3 of those infected are unaware

• 1 of 4 with CHB may develop cirrhosis or HCC
  – Early intervention can prevent & cost-effective\(^3\)

Large Gaps in HBV Screening and Care

Persons unaware of their infection

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Q&A Session
Hepatitis B Virus (HBV) Infection

Chronic HBV (CHB) infection is significant WW problem
- One third of world population infected
- 400M people with chronic disease
  - 25M in U.S./EU
- Most unaware of infection
- High prevalence expected for next 3 decades
  - Despite availability of HBV vaccine

Clinical manifestations severe
- Chronic inflammation leading to cirrhosis and hepatocellular carcinoma (HCC)

Current therapies not curative and have significant limitations
- Reduce viral load, resulting in improved liver histology, decrease in cirrhosis and HCC but do not eliminate virus

Future therapies aim to enable “functional cure”
- Regain sustained immune control over infection, with eventual elimination of viral cccDNA

http://www.hepb.org/hepb/statistics.htm
Novel CHB Therapies Aim to Cure

**Goal: Enable Functional Cure**
- Achieve state of immunological control of infection
  - HBsAg sero-clearance and sero-conversion
- Prevent progression of disease to cirrhosis, liver failure or HCC
- Clearance of circulating viral DNA, normalization of ALT and histology

**Inhibit Viral Lifecycle**
- Reduce circulating virus and inhibit new/re-infection
- Entry, nucleocapsid assembly, cccDNA maintenance inhibitors complement novel reverse transcriptase inhibitors (NUCs)
- Silencing of viral transcripts

**Reduce Tolerogenic Proteins**
- HBsAg secretion inhibitors
- Knockdown of HBsAg and HBeAg

**Break Immune Tolerance**
- Boost immune response to aid in clearing virus
- TLR7 agonist, therapeutic vaccines, immune checkpoint inhibitors
- Knockdown of PD-L1
HBV Targeting with RNAi Therapeutics

Compact genome, overlapping transcripts
- 3.2 kb partially double stranded DNA genome
- Replication occurs through RNA intermediate
- 4 overlapping viral transcripts encoding 7 viral proteins translated across 3 reading frames

Single siRNA can silence viral products
- pgRNA replication intermediate
- Polymerase, Core, HBsAg, HBeAg, X protein

RNAi Therapeutics for HBV
Efficacy in HBV-Infected Chimpanzees (1/3)

Dose-dependent antiviral response with intra-animal ascending doses

- Mean 2.9 \(\log_{10}\) decrease in viral DNA day 2-6 post 0.5 mg/kg dose
  - >4 \(\log_{10}\) reduction in circulating viral DNA achieved in highest titer animal
- Mean 2.0 \(\log_{10}\) reduction in HBsAg at 0.5 mg/kg dose
  - Up to 2.3 \(\log_{10}\) reduction achieved

Plasma Viral Load (bDNA)

Plasma HBsAg (Surface Antigen)

*low titer animal dropped below LLOQ from day 23-day 98

Meyers, TIDES, May 2014
RNAi Therapeutics for HBV
Efficacy in HBV-Infected Chimpanzees (2/3)

Potential evidence for therapeutic flare

- ALT normalized in highest titer chimp
- Possible therapeutic immune flare in 2/4 chimps
  - Correlated with small increases in IL6 and IFNg

High baseline ALT reversed with siRNA treatment

2x ALT increase consistent w/ therapeutic immune flare

Meyers, TIDES, May 2014
**RNAi Therapeutics for HBV**

**HBV-Infected Chimpanzees (3/3)**

**High threshold for selection of resistance as monotherapy**
- Illumina deep sequencing applied to viral DNA plasma from chimps pre- and post-multiple dose treatment
- HBV sequence complementary to siRNA target site showed no enrichment of potentially resistant virions

<table>
<thead>
<tr>
<th>Chimp</th>
<th>Target Site snp*</th>
<th>day -342</th>
<th>day -7</th>
<th>day 105</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
| D     | Snp 1, position 3
      Snp 2, position 3
      Snp 3, position 14 | 2.5%     | 3%     | 4.2%    |
|       |                                      | 1.2%     | 1.4%   | 1.8%    |
|       |                                      | 0%       | 0%     | 5.4%    |

*relative to 5’ antisense start*
Regulus RG-101

- GalNAc-anti miR122 for HCV
- Phase Ia: single 2 & 4 mg/kg SC dose was efficacious and well tolerated
  - 15/28 pt BLOQ at 8 wk post dose
  - 7/28 pt BLOQ at 20 wk post dose
- No decreased efficacy in cirrhotic pt
# ALN-HBV Development Candidate Selected

<table>
<thead>
<tr>
<th></th>
<th>ALN-HBV</th>
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</thead>
<tbody>
<tr>
<td>Site</td>
<td>X-orf</td>
</tr>
<tr>
<td># viral RNA silenced</td>
<td>All (3.5, 2.4, 2.1, 0.7 kb)</td>
</tr>
<tr>
<td>Viral RNA Silencing ED$_{50}$</td>
<td></td>
</tr>
<tr>
<td>P ORF PCR</td>
<td>19 pM</td>
</tr>
<tr>
<td>S ORF PCR</td>
<td>12 pM</td>
</tr>
<tr>
<td>Homology (Gen. A-J)</td>
<td>&gt;97%</td>
</tr>
<tr>
<td>Pan-genotypic silencing</td>
<td>Confirmed (A-J)</td>
</tr>
<tr>
<td>PK / stability</td>
<td>Matches ESC profile</td>
</tr>
<tr>
<td>Rat exploratory toxicology</td>
<td>No findings</td>
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</tbody>
</table>

**Pan Genotypic Silencing**

- Reporter assay
- Rat Liver Histopathology 100 mg/kg qWx3

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**Graph**

Pan Genotypic Silencing

% Reporter Expression Remaining

100 mg/kg qWx3

10nM

**Legend**

- A
- B
- C
- D
- E
- F
- G
- H
- I
- J
Potent, Multi-Log HBsAg KD in Murine Model

- Mouse model with AAV-HBV vector, single SC dose of siRNA at 3 mg/kg
- ALN-HBV DC achieves potent knockdown of HBsAg
  - Up to 3.6 $\log_{10}$ reduction; mean 1.6 $\log_{10}$ reduction 15 days after single dose
- Specificity confirmed with control siRNA

**ALN-HBV**

Mean $\Delta_{(0-15d)} = -1.57 \pm 0.81 \log_{10}$

Max $\Delta_{(0-15d)} = -3.63 \log_{10}$

**mTTR Control**

Mean $\Delta_{(0-15d)} = +0.0035 \pm 0.46 \log_{10}$
Durable, Multi-Log HBsAg KD in Murine Model

Durable HBsAg suppression >4 months after 3 mg/kg qWx3

% HBsAg Plasma Levels (Normalized to d0)

Time (days)

AAV-HBV 10^{11} VG

ALN-HBV 3 mg/kg qwk x3, SC
Clinical Development Plan
ALN-HBV for the Treatment of Chronic Hepatitis B

Robust development plan to maximize product opportunity

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
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<tbody>
<tr>
<td>SAD HV</td>
<td>+ NUC</td>
</tr>
<tr>
<td>SAD CHB + NUC</td>
<td>+ NUC + Immune therapy</td>
</tr>
<tr>
<td>MAD CHB + NUC</td>
<td>+ NUC + Other</td>
</tr>
</tbody>
</table>

Key Objectives
- Safety
- PK
- HBsAg silencing: extent and duration
- Initial dose finding
ALN-HBV Product Opportunity

Significant potential for CHB functional cures

• Finite duration of treatment, aimed at enabling cures
  ◦ Sustained Viral Responses (SVRs) after short treatment period (<6 months) as fixed
dose combination with SOC NUCs (and/or IFN)
• Potent and durable silencing of all HBV gene products
  ◦ Elicit multiple synergistic antiviral mechanisms
• Improved compliance due to wide therapeutic index and convenience of
infrequent subcutaneous dosing
• Pan-genotypic, conserved site, and combination with NUCs increases barrier for
development of resistance
• Excellent tolerability profile would support combination with less tolerated immune
therapies
• RNAi combination approach feasible
  ◦ Pathogen and host factors
• Expected efficacy across CHB patient segments, including young immune tolerant
and patients outside treatment guidelines
• Rapid physician/patient acceptance of novel treatment paradigm
ALN-PDL: Liver-Restricted Immune Reactivation

• Obligate liver pathogens exploit tolerant environment and enhance immune suppression\textsuperscript{1}
  ◦ Exhaustion of adaptive immunity
  ◦ Active suppression of innate immunity

• Liver-intrinsic immunosuppressive mechanism provide target opportunities

• Liver targeting will result in organ specific immune modulation, reducing the risk of systemic immuno-toxicity\textsuperscript{2}

ALN-PDL could de-repress intrahepatic T cell and NK cell responses to HBV, while avoiding the immunotoxicity of systemic immune de-repression

\textsuperscript{1}Ferrari C., Liver Int. 35, 121–128 (2015), \textsuperscript{2}Gelao et al., Toxins 6, 914-933 (2014)
ALN-HBV and ALN-PDL in Chronic Hepatitis B

**ALN-HBV**

**Inhibit Life Cycle**
- KD replication template, core, polymerase, surface, X-protein

**Eliminate cccDNA**
- Prevent new synthesis
- Eliminate existing pool
- Non-cytolytic (KD core, X)
- Cytolytic (CTL, NK cells)

**Break Immune Tolerance – Enhance Host Immunity**
- Reducing expression of tolerogenic antigens (HBsAg, HBeAg, core)
- Release of PD-1/PD-L1 immune checkpoint in hepatocytes
Summary

- Significant unmet need exists for novel HBV therapy which will result in “functional cure”
- Investigational RNAi therapeutic offers significant promise for treatment of HBV
  - Novel mechanism for inhibiting all steps of HBV life cycle
  - Decreases viral proteins including highly abundant non-infective HBsAg particles
- Proof of concept data in naturally HBV-infected chimps suggests robust efficacy profile
- ASGPR-mediated delivery de-risked in Hepatitis
  - Regulus RG-101 in HCV employing Alnylam’s GalNAc-conjugate platform
- ALN-HBV Development Candidate (DC) selected and on track for CTA in late ’15
  - Best-in-class potential with subcutaneous, qM profile and wide therapeutic index
- ALN-PDL program initiated, DC planned to be selected in early ’16
  - Multi-pronged strategy for HBV and other hepatic infectious diseases
Upcoming ALN-HBV Events

Upcoming presentations
- American Association for the Study of Liver Diseases (AASLD, The Liver Meeting®)
  - November 13-17, San Francisco, CA

Upcoming planned milestones
- ALN-HBV CTA (late 2015)
- ALN-PDL DC selection (early 2016)
Agenda

Welcome
• Joshua Brodsky
  Senior Manager, Investor Relations and Corporate Communications

Introduction
• John Maraganore, Ph.D.
  Chief Executive Officer

Overview of Hepatitis B Virus Infection
• Edward Gane, MBChB, M.D., FRACP, MNZM, Professor of Medicine, University of Auckland, and Chief Hepatologist, Transplant Physician, Deputy Director of New Zealand Liver Transplant Unit, Auckland City Hospital

Patient Advocacy: The Changing Landscape of HBV
• Su Wang, M.D., MPH
  Board Member, World Hepatitis Alliance and Medical Director of Center for Asian Health at Saint Barnabas Medical Center

Q&A Session
• With Dr. Gane and Dr. Wang

ALN-HBV Program
• Laura Sepp-Lorenzino, Ph.D.
  Vice President, Entrepreneur-in-Residence

Q&A Session
Upcoming RNAi Roundtables

**ALN-AAT for the treatment of AAT Deficiency-associated liver disease**
*Friday, August 14, 2:00 – 3:00 p.m. ET*
- Alfica Sehgal, Ph.D., Principal Scientist, Research
- Moderator: Akshay Vaishnav, M.D., Ph.D., Executive Vice President of R&D, Chief Medical Officer
- Guest Speaker: Jeffrey Teckman, M.D., Professor, Department of Pediatrics, St. Louis University School of Medicine

**Patisiran and Revusiran for the treatment of Transthyretin (TTR)-Mediated Amyloidosis**
*Thursday, August 20, 9:00 – 10:30 a.m. ET*
- Eric Green, Vice President, General Manager, TTR Program
- Jared Gollob, M.D., Vice President, Clinical Research
- Moderator: Barry Greene, President and Chief Operating Officer
- Guest Speaker: Philip Hawkins, Ph.D., FRCP, FRCPath, FMedSci, Head, National Amyloidosis Centre, and Head, Periodic Fever Syndrome Service/Honorary consultant physician

Replays, presentations, transcripts of all RNAi Roundtables available at www.alnylam.com/capella
Speaker Biographies

John Maraganore, Ph.D.
Chief Executive Officer, Alnylam

Since 2002, John Maraganore has served as the CEO and a Director of Alnylam. Prior to Alnylam he served as an officer and a member of the management team for Millennium Pharmaceuticals, Inc. As Senior Vice President, Strategic Product Development for Millennium, he was responsible for the company’s product franchises in oncology, cardiovascular, inflammatory, and metabolic diseases. He was previously Vice President, Strategic Planning and M&A and prior to that he was General Manager of Millennium BioTherapeutics, Inc., a former subsidiary of Millennium. Before Millennium he served as Director of Molecular Biology and Director of Market and Business Development at Biogen, Inc. At Biogen, Dr. Maraganore invented and led the discovery and development of Angiomax™ (bivalirudin for injection, formerly Hirulog™) currently marketed by The Medicines Company. Prior to Biogen, Dr. Maraganore was a scientist at ZymoGenetics, Inc., and the Upjohn Company. Dr. Maraganore received his M.S. and Ph.D. in biochemistry and molecular biology at the University of Chicago. Dr. Maraganore is a Director for Agios Pharmaceuticals and bluebird bio. He also serves as a Venture Partner with Third Rock Ventures. Dr. Maraganore is a member of the Biotechnology Industry Organization (BIO) Board and the BIO Executive Committee, and serves as the chair of the Emerging Company Section and as co-chair of the Regulatory Environment Committee.

Edward Gane, MBChB, M.D., FRACP, MNZM
Professor of Medicine, University of Auckland (NZ), and Chief Hepatologist, Transplant Physician, Deputy Director of New Zealand Liver Transplant Unit, Auckland City Hospital

Dr. Gane trained in hepatology at the Institute of Liver Studies, King’s College School of Medicine, London, where he completed his MD on the pathogenesis of hepatitis C-related liver allograft injury following transplantation for HCV-cirrhosis. In 1998, Dr. Gane was appointed as Chief Transplant Physician for the first New Zealand Liver Transplant programme at Auckland City Hospital. In addition, Dr. Gane runs large Hepatitis Clinics in Auckland and GreenlaneHospitals for patients and a large tertiary Liver Cancer Clinic. In 2000, Dr. Gane became the Ministry of Health Clinical Advisor for the National Hepatitis B Screening and Follow-up Programme. In 2013, Dr. Gane was appointed as Hepatitis C Champion for the Ministry of Health National Hepatitis C Project. Dr. Gane is an Investigator for many international clinical trials of therapies for chronic viral hepatitis with particular interest in early phase development of new direct acting antiviral therapies against hepatitis C and hepatitis B. Dr. Gane has published almost 150 papers in peer-reviewed journals including The Lancet and The New England Journal of Medicine and serves on the editorial committee for several journals. Dr. Gane serves on the Executive Committee of the NZ Society of Gastroenterology and is a member of several international organisations including APASL, AASLD, ILCA and ILTS. In May 2011, Dr. Gane was awarded Member of the Order of New Zealand for Services to Medicine.
Speaker Biographies

Su Wang, M.D., MPH
Board Member, World Hepatitis Alliance and Medical Director, Saint Barnabas Medical Center
Su Wang, MD, MPH, is an executive Board Member of the World Hepatitis Alliance and the Medical Director of the Center for Asian Health at Saint Barnabas Medical Center. A practicing internist, she was the Assistant Director of Medical Affairs at the Charles B. Wang Community Health Center (CBWCHC), a large multidisciplinary health center dedicated to serving Asian-Americans in the greater New York City area. Dr. Wang directed the Hepatitis B programs at CBWCHC and led community outreach, clinical care initiatives, and community-based research. Dr. Wang was invited to be in a White House panel for World Hepatitis Day and spoke at the Department of Health and Human Service press conference for the release of the National Viral Hepatitis Action Plan. Dr. Wang received her medical degree from the University of Miami and a Master's Degree in Public Health from Johns Hopkins School of Public Health. She completed a combined internal medicine and pediatric residency at Georgetown University Hospital where she served as chief resident.

Laura Sepp-Lorenzino, Ph.D.
Entrepreneur-in-Residence, Alnylam
Dr. Sepp-Lorenzino joined Alnylam in 2014. Before joining Alnylam, Dr. Sepp-Lorenzino spent 14 years at Merck & Co., having most recently served as Executive Director and Department Head, RNA Therapeutics Discovery Biology. In this role, she was responsible for identification and optimization of siRNAs and delivery vehicles, advancement of pre-clinical candidates, and development of an siRNA-conjugate platform to expand the repertoire of tissues accessible to in vivo siRNA delivery. Prior to RNAi, Laura worked in oncology drug discovery and development, having led the Cancer Research Department at Merck West Point, and having been an Assistant Lab Member at Memorial Sloan-Kettering Cancer Center. Laura received her Professional Degree in Biochemistry from the University of Buenos Aires, and her M.S. and Ph.D. in Biochemistry from New York University.
Thank You

www.alnylam.com