RNAi Therapeutic Development for the Treatment of TTR Amyloidosis

October 15, 2014
Transthyretin (TTR)-Mediated Amyloidosis (ATTR) Program

Unmet Medical Need

- ATTR is a rare disease
  » ~50,000 patients worldwide
- Autosomal dominant, hereditary disease with >100 defined mutations\(^1\)
  » TTR is synthesized primarily in the liver
  » Mutant TTR protein misfolds and forms amyloid deposits
  » Two predominant forms:
    - Familial amyloidotic polyneuropathy (FAP)*
    - Familial amyloidotic cardiomyopathy (FAC)\(^\dagger\)
- Significant morbidity and mortality associated with the disease
- Unmet medical need remains

*Patisiran is being developed for the treatment of FAP
\(^\dagger\)ALN-TTRsc is being developed for the treatment of FAC

Transthyretin (TTR) Amyloidosis

TTR Protein

>100 defined mutations

Sensorimotor Polyneuropathy

Familial Amyloid Polyneuropathy (FAP)
- Age of onset 30-50
- V30M major variant

Restrictive Cardiomyopathy

Familial Amyloid Cardiomyopathy (FAC)
- Age of onset > 60
- V122I major variant

Senile Cardiac Amyloidosis
- Age of onset > 70
- WT TTR
RNAi Therapeutic Hypothesis for Treatment of ATTR

- **Production of mutant and wild type TTR**
- **Reduction of unstable circulating TTR tetramers**
- **Prevention** of organ deposition of TTR monomers and amyloid fibrils (and potential clearance)
- **Stabilization** of neuropathy/ cardiomyopathy (and potential recovery)

Patisiran (ALN-TTR02) and ALN-TTRsc act to knock down both mutant and wild-type TTR production.
hTTR V30M Transgenic Mice
Dose Dependent Regression of Tissue Deposits with siTTRSC

Dorsal Root Ganglion
Sciatic Nerve
Esophagus
Stomach
Duodenum
Colon

- PBS
- 1 mg/kg
- 2.5 mg/kg
- 25 mg/kg

Butler Saraiva Presentation at ISA (2014)
Patisiran in clinical development

- International Nonproprietary Name designation for ALN-TTR02 = Patisiran (Pa-TEE-sa-ran)
- Orphan drug status in US/EU
- Fast track designation by FDA
- Administered by IV infusion
- Positive Phase 1 results in human volunteers
  » Data published in *New England Journal of Medicine*
- Positive multi-dose Phase 2 results in FAP patients
- Phase 2 Open-Label Extension (OLE) study ongoing
  » Includes clinical endpoints measured every 6 months
  » Positive initial data reported at ISA, April 2014
- APOLLO Phase 3 trial ongoing
Patisiran Open-Label Extension (OLE) Study

FAP patients dosed in Phase 2 trial eligible for Phase 2 OLE study

- Clinical endpoints evaluated every 6 months for up to 2 years
  - Clinical endpoints same as APOLLO Phase 3 study
  - Dosing at 0.30 mg/kg IV every 3 weeks
- Study objectives
  - Primary: Safety and tolerability of long-term dosing with patisiran
  - Secondary: Effects on neurologic impairment (mNIS+7 and NIS), quality of life, mBMI, disability, mobility, grip strength, autonomic symptoms, nerve fiber density in skin biopsies, cardiac involvement (in cardiac subgroup), serum TTR levels

Status
- Ongoing; enrollment completed (N=27)
- Additional data in late ’14, to include 6 mo mNIS+7 data from ~20 patients
  - Presentation at ANA, October 12-14, 2014
- Report data at least once annually
## Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>N=27 (includes 11 patients in cardiac subgroup)</td>
</tr>
<tr>
<td>Median age</td>
<td>64.0 years (range 29-77)</td>
</tr>
<tr>
<td>Gender</td>
<td>18 males, 9 females</td>
</tr>
</tbody>
</table>
| TTR genotype                                        | • Val30Met (V30M) = 20  
• Ser77Tyr (S77Y) = 2  
• Ser77Phe (S77F) = 2  
• Tyr116Ser (Y116S) = 1  
• Phe64Leu (F64L) = 1  
• Arg54Thr (R54T) = 1                                                                 |
| FAP stage/PND score                                 | • Stage 1: 24  
• Stage 2: 3                                                                                                                          |
| Concurrent tetramer stabilizer use at baseline       | 13 tafamidis, 7 diflunisal, 7 none                                                                                                    |
| Current tetramer stabilizer use^                    | 12 tafamidis, 6 diflunisal, 9 none                                                                                                   |
| Total doses administered                            | 282                                                                                                                                    |
| Median doses/patient to date                        | 11 (range 4-16 doses)                                                                                                                  |
| Mean Treatment Duration*                            | 7 months (range 3-12)                                                                                                                  |

^2 subjects (1 – diflunisal, 1 - tafamidis) reported stabilizer use at the time of first dose but subsequently stopped using stabilizer

*As of September 8, 2014
Adams et al., ANA, Oct. 2014
### Patisiran Phase 2 OLE Preliminary Study Results

#### Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>Mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum TTR (µg/mL)</td>
<td>27</td>
<td>245.6 (154.6 – 339.9)</td>
</tr>
<tr>
<td>NIS (max impairment: 244)</td>
<td>27</td>
<td>34.8 (4.0 - 93.4)</td>
</tr>
<tr>
<td>mNIS+7 (max impairment: 304)</td>
<td>26</td>
<td>52.1 (2.0-122.5)</td>
</tr>
<tr>
<td>10-meter walk test (sec)</td>
<td>22</td>
<td>10.1 (4.6-22.0)</td>
</tr>
<tr>
<td>Hand grip strength (kg)</td>
<td>27</td>
<td>25.8 (3.2-49.3)</td>
</tr>
<tr>
<td>mBMI (kg/m² x albumin [g/L])</td>
<td>27</td>
<td>1031.6 (728.6-1379.6)</td>
</tr>
<tr>
<td>EQ-5D-5L QOL (max impairment: 0)</td>
<td>27</td>
<td>0.8 (0.3-1.0)</td>
</tr>
<tr>
<td>R-ODS a (no limitations: 48)</td>
<td>24</td>
<td>38.2 (15.0-48.0)</td>
</tr>
<tr>
<td>COMPASS-31 b (max impairment: 100)</td>
<td>26</td>
<td>16.2 (0.0 - 46.1)</td>
</tr>
</tbody>
</table>

#### Cardiac subgroup: N = 11

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>Mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP (ng/L)</td>
<td>8</td>
<td>823.3 (105.0 -2070.0)</td>
</tr>
<tr>
<td>Troponin I c (ng/mL)</td>
<td>8</td>
<td>0.14 (0.02–0.7)</td>
</tr>
<tr>
<td>LV wall thickness (cm)</td>
<td>7</td>
<td>1.6 (1.3-1.9)</td>
</tr>
<tr>
<td>V30M/non-V30M (N)</td>
<td>11</td>
<td>8/3</td>
</tr>
</tbody>
</table>

---

<table>
<thead>
<tr>
<th>Notes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>a R-ODS: Rasch-built Overall Disability Score, a 24-item questionnaire used to capture activity and social participation (Van Nes SI et al., Neurology 2011); raw scores are presented.</td>
</tr>
<tr>
<td>b COMPASS-31: 31-item questionnaire used to evaluate 6 autonomic domains (orthostatic intolerance, vasomotor, secretomotor, gastrointestinal, bladder and pupillomotor) (Sletten et al., Mayo Clin Proc. 2012)</td>
</tr>
<tr>
<td>c Values recorded as ‘&lt; LLOQ’ were imputed to be LLOQ/2</td>
</tr>
<tr>
<td>Adams et al., ANA, Oct. 2014</td>
</tr>
</tbody>
</table>
### Patisiran Phase 2 OLE Preliminary Study Results

#### Safety and Tolerability - TEAEs Related or Possibly Related

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>N (%)</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion-related reaction (IRR)</td>
<td>4 (14.8%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Flushing</td>
<td>4 (14.8%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (7.4%)</td>
<td>Mild-Moderate</td>
</tr>
<tr>
<td>Peripheral Edema</td>
<td>2 (7.4%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Ectropion</td>
<td>1 (3.7%)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1 (3.7%)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Infusion site irritation</td>
<td>1 (3.7%)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Neuralgia</td>
<td>1 (3.7%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Impairment of taste</td>
<td>1 (3.7%)</td>
<td>Mild</td>
</tr>
<tr>
<td>Insomnia</td>
<td>1 (3.7%)</td>
<td>Mild</td>
</tr>
</tbody>
</table>

- All TEAEs mild to moderate in severity
- No clinically significant changes in liver function tests, renal function, or hematologic parameters
- 2 subjects with SAEs (unrelated to study drug); both subjects had severe sensory deficit in the legs and feet; one subject with distal femur/proximal tibia fracture and resultant osteonecrosis and one subject with ankle/foot fracture with resultant osteonecrosis which occurred after running a marathon

Both patients have continued on study drug

Adams et al., ANA, Oct. 2014
Similar TTR knockdown in patients on patisiran alone or on patisiran + TTR tetramer stabilizers
Patisiran Phase 2 OLE Preliminary Study Results
Change in mNIS+7 at 6 Months (N=19)

Change from Baseline to Month 6

<table>
<thead>
<tr>
<th>Category</th>
<th>Mean Δ</th>
<th>Median Δ</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>-0.95</td>
<td>0.00</td>
<td>2.59</td>
</tr>
<tr>
<td>NIS-weakness</td>
<td>0.08</td>
<td>0.00</td>
<td>1.53</td>
</tr>
<tr>
<td>NIS-reflexes</td>
<td>-0.39</td>
<td>0.00</td>
<td>0.43</td>
</tr>
<tr>
<td>QST</td>
<td>-0.68</td>
<td>-2.00</td>
<td>1.82</td>
</tr>
<tr>
<td>NCS Σ5</td>
<td>0.11</td>
<td>0.00</td>
<td>0.15</td>
</tr>
<tr>
<td>Postural BP</td>
<td>-0.05</td>
<td>0.00</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Each line represents individual patient

SEM: Standard Error of the Mean
Adams et al., ANA, Oct. 2014
# Patisiran Phase 2 OLE Preliminary Study Results
## Comparison of ΔNIS and ΔmNIS+7 Across FAP Studies

<table>
<thead>
<tr>
<th></th>
<th>Natural History (linear)~</th>
<th>Natural History (nonlinear)#</th>
<th>Tafamidis Fx1A-201*</th>
<th>Diflunisal Phase 3+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SEM) ( \Delta ) mNIS+7 at 6 mos. ^</td>
<td>8.9 ± 5.7</td>
<td>10.3 ± 5.7</td>
<td>PBO: 8.7 ± 2.0</td>
<td>PBO: 7.4 ± 6.9</td>
</tr>
<tr>
<td>Mean (SEM) ( \Delta ) NIS at 6 mos.</td>
<td>7.2 ± 4.6</td>
<td>8.3 ± 4.6</td>
<td>Drug: 2.5 ± 2.9</td>
<td>Drug: 2.3 ± 6.0</td>
</tr>
</tbody>
</table>

## Patisiran Phase 2 OLE

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Patisiran Phase 2 OLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SEM) ( \Delta ) mNIS+7 at 6 mos.</td>
<td></td>
<td>-0.95 ± 2.59 †</td>
</tr>
<tr>
<td>Mean (SEM) ( \Delta ) NIS at 6 mos.</td>
<td></td>
<td>0.22 ± 1.39</td>
</tr>
</tbody>
</table>

^ Translated algebraically from NIS (Natural History study, Tafamidis study) or NIS+7 (Diflunisal study)
~ Linear interpolation between 0 and 12 month progression for median NIS value (from Gompertz curve fit)
# Predicted progression of median NIS value from Gompertz curve fit
PBO (Placebo) rate estimated from pre-study rate of change; drug rate as reported
† Estimated from 2-year NIS progression measurement in longitudinal analysis set
SEM: Standard Error of the Mean
Patisiran Phase 2 OLE Preliminary Study Results

Summary

- Chronic dosing with q3 weekly patisiran well tolerated in FAP patients, including patients on concurrent tetramer stabilizers
  - 282 doses administered to date, median of 11 doses/patient
  - Mean treatment duration of 7 months, longest treatment duration out to 1 year
  - IRRs infrequent (~15% incidence), mild in severity, did not result in any discontinuations
  - No significant LFT or renal function changes
  - No drug-related SAEs

- Patisiran achieves sustained serum TTR lowering of at least 80%, with further nadir of up to 89.6% between doses
  - Based on serial TTR measurements for over 9 months
  - Pharmacodynamic activity similar in patients with or without concurrent tetramer stabilizers

- Neuropathy impairment scores stable after 6 months of treatment with patisiran
  - Similar results for QOL and multiple additional neurologic and cardiac measures
  - Similar outcome in patients with or without concurrent tetramer stabilizers
  - Mean decrease in mNIS+7 of 0.95 points compares favorably to the rapid increase in mNIS+7 estimated at 6 months from prior FAP studies in a patient population with similar baseline NIS

Adams et al., ANA, Oct. 2014
Phase 3 Trial of Patisiran in FAP
Study Ongoing

Randomized, double-blind, placebo-controlled, global study

- Sample size and randomization
  » N=200
  » 2:1, Patisiran vs. placebo

- Key eligibility criteria
  » V30M and non-V30M FAP
  » Baseline FAP stages 1 and 2

- Treatment regimen
  » Patisiran 0.30 mg/kg vs. placebo IV q3w for 18 months
  » All completers eligible for patisiran treatment on Phase 3 OLE study

Primary Endpoint
- mNIS+7 at 18 months

Secondary Endpoints
- Norfolk QOL-DN, NIS-weakness, mBMI, timed 10-meter walk, COMPASS-31 autonomic symptom score

Statistical Considerations
- Placebo mNIS+7 progression rate of 17.8 points/yr derived from natural history study of 283 FAP patients
- Study with 90% power to detect as little as 37.5% difference in ΔmNIS+7 between treatment groups with 2-sided alpha=0.05
- Blinded interim analysis of variability planned for potential sample size re-estimation
Familial Amyloidotic Cardiomyopathy

- Epidemiology
  - Orphan disease
  - >40,000 symptomatic FAC patients WW
  - Cardiac-predominant TTR genotypes in US and EU
  - FAC currently underdiagnosed

- Clinical pathology
  - Onset >65 yrs
  - Amyloid deposition leads to cardiac wall thickening and HF
  - Fatal within 2.5-5 years of diagnosis depending on TTR variant

- Limited treatment options
  - Medical management of heart failure symptoms
  - Heart transplant or combined heart/liver transplant performed in small number of patients young enough (<70 yrs) to undergo procedure

ALN-TTRsc
- siRNA conjugated to N-acetylgalactosamine (GalNAc) ligand targeting wild-type and all mutant forms of TTR mRNA
- Efficient delivery to hepatocytes following subcutaneous administration
- Potent suppression of serum TTR demonstrated in rodents, non-human primates, and human volunteers
ALN-TTRsc Non-clinical Safety Summary

Rat
- IND enabling tox (6-weeks, 10 doses)
  - Liver was the only target organ of toxicity (dose-dependent minimal to moderate hepatocellular vacuolation)
  - Non-adverse basophilic granules in proximal kidney tubules at ≥ 30 mg/kg
  - NOAEL set conservatively at 30 mg/kg; based on liver pathology associated with reversible minor increase in liver transaminases at ≥ 100 mg/kg ALN-TTRsc
- Chronic 6-month tox
  - No new target organ pathologies identified
  - Liver and kidney findings did not progress in severity or incidence with chronic dosing
  - Same NOAEL as 6-week study: 30 mg/kg

NHP
- IND enabling tox (6-weeks, 10 doses)
  - No target organs of toxicity were identified
  - NOAEL in NHP (pharmacologically relevant species) was ≥ the highest dose tested (> 300 mg/kg)
- Chronic 9-month tox (dosing completed; histopathology pending)
  - Expected pharmacology at ≥ 15 mg/kg ALN-TTRsc
  - No meaningful changes in hematology, coagulation, serum chemistry or urinalysis
  - Doses ≤ 200 mg/kg ALN-TTRsc were well-tolerated
- CV/Respiratory Safety Pharmacology Study
  - NOEL > 100 mg/kg

Genotoxicity
- Negative in bacterial mutagenesis and chromosomal aberration assays
- Negative in in vivo rat bone marrow micronucleus study
ALN-TTRsc Phase 1 Study

Study Design

- Randomized, double-blinded, placebo-controlled SAD and MAD study in healthy volunteers
  - 3:1 randomization (ALN-TTRSC:Placebo)
  - 4 subjects/cohort
  - Cohort 1-4: single doses of 1.25, 2.5, 5.0 and 10 mg/kg
  - Cohort 5-10: multiple doses of 2.5, 5.0, 7.5 and 10 mg/kg
    - Multi-dose schedule: Daily x 5, followed by weekly x 5

Primary Objective

- Evaluate safety and tolerability of subcutaneously administered single and multiple doses of ALN-TTRsc

Secondary Objectives

- Assess clinical activity
  - Serum TTR, retinol binding protein (RBP), Vitamin A levels
Rapid, dose-dependent, consistent, and durable knockdown of serum TTR

- Maximum knockdown of serum TTR up to 95%; mean knockdown up to 92.4%
- Doses of ≥ 5 mg/kg: > 85% mean TTR knockdown

### Table: Mean % Serum TTR Knockdown Relative to Baseline

<table>
<thead>
<tr>
<th>Dose Level [mg/kg]</th>
<th>Mean Max % kd (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>58.2 (11.1)</td>
</tr>
<tr>
<td>5</td>
<td>87.5 (7.2)</td>
</tr>
<tr>
<td>7.5</td>
<td>87.9 (1.2)</td>
</tr>
<tr>
<td>10</td>
<td>92.4 (1.5)</td>
</tr>
</tbody>
</table>

**ALN-TTRsc Phase 1 Study**

**Serum TTR Lowering in Multi-dose Cohorts**

**ALN-TTRsc qd x5; qw x5**
ALN-TTRsc Phase 1 Study

RBP/Vitamin Reduction Highly Correlated with TTR Lowering

RBP: $R^2 = 0.87$, $P < 10^{-15}$
Vit. A: $R^2 = 0.94$, $P < 10^{-15}$
ALN-TTRsc Phase 1 Study
Consistent Plasma PK with Multiple Doses of ALN-TTRsc

ALN-TTRsc Dose Groups
- Dose 1 - 2.5 mg/kg
- Dose 5 - 2.5 mg/kg
- Dose 10 - 2.5 mg/kg
- Dose 1 - 5 mg/kg
- Dose 5 - 5 mg/kg
- Dose 10 - 5 mg/kg
- Dose 1 - 7.5 mg/kg
- Dose 5 - 7.5 mg/kg
- Dose 10 - 7.5 mg/kg
- Dose 1 - 10 mg/kg
- Dose 5 - 10 mg/kg
- Dose 10 - 10 mg/kg
Comparison of ALN-TTRsc in Human and NHP

- Excellent correlation of human to non-human primate TTR knockdown on mg/kg basis
  - Confirmation of human translation of GalNAc-siRNA conjugate platform
  - Extended durability in human vs. NHP due to attenuated nuclease environment

Zimmerman, Heart Failure Society of America 2013
Manoharan, TIDES 2014
### ALN-TTRSC Phase 1 Study
#### Related TEAES (≥ 10% Incidence) Cohort 1-10

- TEAEs mostly mild or moderate in severity, comprised of short-lived erythema and pain
- No study discontinuations, flu-like symptoms, or significant lab abnormalities

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Single Dose [mg/kg]</th>
<th>Multiple Doses [mg/kg]</th>
<th>Total TTRSC (n=31)</th>
<th>PBO (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection Site Reactions</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>13 (42%)</td>
</tr>
<tr>
<td>Injection Site Erythema</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>9 (29%)</td>
</tr>
<tr>
<td>Injection Site Pain</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>0 (0%)</td>
<td>5 (16%)</td>
</tr>
<tr>
<td>Headache</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>0 (0%)</td>
<td>2 (13%)</td>
</tr>
</tbody>
</table>

n = number of patients; % = percentage of patients

Related = Definitely Related, Possibly Related. Final AEs for cohorts 1-10.
ISR is defined as ≥2 mild or 1 moderate or severe IS sign or symptom.
Multiple doses of ALN-TTRsc generally well tolerated
• No serious AEs associated with ALN-TTRsc through 10 mg/kg
  » No discontinuations, flu-like symptoms, or significant lab abnormalities
  » Most common adverse events are ISRs that are mostly mild to moderate in severity

ALN-TTRsc achieved potent, rapid, dose-dependent, consistent, and durable knockdown of serum TTR
• Statistically significant (p<0.01), dose-dependent knockdown of serum TTR at doses of ≥ 2.5 mg/kg
• Consistent level of TTR knockdown achieved with weekly SC dosing; durable for at least 14 days after last dose
• Confirms human translation of GalNAc-siRNA conjugate platform
• Excellent correlation of secondary PD markers RBP/ vitamin A with TTR lowering
ALN-TTRsc Phase 2 Study

Study Design
- Open-label, multi-dose study in TTR cardiac amyloidosis
  - Includes patients with FAC and senile systemic amyloidosis (SSA)
- 25 Patients
- 5 mg/kg SC dose (qd x5 load, qw x5 maintenance)

Primary Objective
- Assess safety and tolerability

Secondary Objective
- Obtain preliminary evidence for clinical activity
  - Serum TTR knockdown of wild-type and mutant protein
  - Additional exploratory clinical endpoints: Cardiac imaging (echo and MRI), cardiac biomarkers (BNP, troponins), 6 minute walk, NYHC, and QOL

Status
- Ongoing; expanded target enrollment to 25
- Initial data November ’14
- Initiate open-label extension (OLE) in mid ’14
Patisiran and ALN-TTRsc Programs
Summary

Patisiran for FAP
- Phase 2 extension study fully enrolled
  - Chronic dosing with q3 weekly patisiran generally well tolerated in FAP patients
  - Sustained serum TTR lowering of at least 80%, with further nadir of up to 89.6% between doses
  - Neuropathy impairment scores stable after 6 months of treatment
- Apollo Phase 3 study in FAP ongoing

ALN-TTRsc for FAC
- Positive data from Phase 1 trial in healthy volunteers
  - Assessment of fixed dose cohorts ongoing
- Phase 2 trial in TTR cardiac amyloidsis patients ongoing; data to be presented in Nov ’14
- Phase 2 OLE to be initiated in coming weeks
- Initiated DISCOVERY screening study to identify FAC patients
- Phase 3 trial to start in 2014
Patisiran Phase 2 Investigators

- David Adams
  » Hospital de Bicetre, Le Kremlin-Bicetre, France
- Teresa Coelho, Ana Silva
  » Hospital de Santo Antonio, Porto, Portugal
- Ole Suhr
  » Umea University Hospital, Umea, Sweden
- Isabel Conceicao
  » Centro Hospitalar Lisboa Norte-Hospital de Santa Maria, Lisboa, Portugal
- Juan Buades
  » Hospital Son Llatzer, Palma de Mallorca, Spain
- Josep Campistol
  » Hospital Clinic Barcelona Instituto, Barcelona, Spain
- Jean Pouget
  » Hôpital de La Timone, Marseille, France
- Hartmut Schmidt
  » University Hospital of Muenster, Muenster, Germany
- Marcia Waddington-Cruz
  » Hospital Universitário, Rio de Janeiro, Brazil
- John Berk
  » Boston University, Boston, MA USA

TTR Program - Scientific Collaborators

- Maria Saraiva
  » Institute of Cellular and Molecular Biology, Porto, Portugal

ALN-TTRsc Phase I Investigators

- Joseph Chiesa
  » Covance Clinical Research Unit, Leeds, UK
- Malcolm Boyce
  » Hammersmith Medicines Research, London, UK

Alnylam Pharmaceuticals
Patisiran and ALN-TTRsc program teams