NASHTherapeutics

• Non-alcoholic steatohepatitis (NASH) is the most common liver disease in the US and has no approved therapy
• Market size is projected to reach $25.3B by 2026
• We are developing a novel compound, NT 7314, as a single first-line treatment for NASH

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**Sterile Inflammation (SI)**

- A ubiquitous response
- Due to cell death and **stress**
- Mediated by TLRs
- Very high amplitude in the liver
- Hepatic SI is very malleable

**SI in NASH**

- NAFLD occurs due to metabolic stress
- SI exacerbates metabolic stress and leads to NASH, and if untreated to fibrosis, cirrhosis and liver cancer
- TLR KO mice are protected from liver injury in HFD model of NASH
NASH Pathogenesis and Our Differentiation

Phase 3 NASH Programs

- Ocaliva
- Elafibranor
- Cenicriviroc
- Selonsterib

NT 7314 Differentiation

- Unique mode of action
- Blocking SI stops fibrosis
- Blocking SI reduces steatosis
- NT 7314 preferentially:
  - Accumulates in the liver
  - Is taken up into endosomes
  - Does not need to enter cytosol to be efficacious
About NT 7314 Program

- A large molecule inhibitor of toll-like receptors (TLRs)
- Receptor for NT 7314 is required for SI in NASH
- Therapeutic modality of NT 7314 is uniquely suited for NASH indication, as it preferentially concentrates in the liver cells
- Excellent in-vivo efficacy data in HFD mouse model of NASH
- NOAEL in rats and cynomolgus monkeys over 8 week dosing
NT 7314 Reduces Hallmarks of NASH in the HFD* Mouse Model

**ALT**

- Chow Saline
- HFD Saline
- Chow Drug
- HFD Drug

*** (P<0.01) *** (P<0.01)

**Steatosis**

- Chow Saline
- HFD Saline
- Chow Drug
- HFD Drug

*** (P<0.01) *** (P<0.01)

**Inflammation**

- Chow Saline
- HFD Saline
- Chow Drug
- HFD Drug

*** (P=0.01) ** (P=0.01)

* HFD: High Fat Diet for 12 weeks
## NT 7314: Target Product Profile

### Target Annotations

<table>
<thead>
<tr>
<th>Target</th>
<th>Annotations</th>
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<tbody>
<tr>
<td>Primary Indication</td>
<td>NASH. Single/Primary treatment as a first-line therapy. Potential combination with other NASH drugs.</td>
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<tr>
<td>Patient Population</td>
<td>Adults of all ages, with moderate to severe form of NASH. Pediatric population (11 years old and up) with NASH.</td>
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<td>Usage</td>
<td>Single/Primary treatment as first line therapy. Potential combination with other NASH drugs.</td>
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<td>Dose (TBD)</td>
<td>Tentative dose below 1 mg/kg/week. Lower dose likely due to preferential accumulation in liver.</td>
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## Long-Term Development Plan

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**NASHTherapeutics**
Summary

• NASH: New disease of epidemic proportions with no current therapy
• NT 7314 is a promising drug candidate for NASH
• NASHTherapeutics is on a straight path to success with
  • Efficacy data in disease models
  • Safety data in humans
  • Clear set of steps to IND submission

Development of this Drug will Provide Therapy to Large Numbers of Patients who are Developing Liver Cirrhosis and Liver Cancer