ASSIST Study Design:
A Randomized, Double-blind, Placebo-controlled, Crossover Study of Atrasentan* in Patients with IgA Nephropathy on SGLT2i

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*Atrasentan is an investigational drug that has not been approved by regulatory authorities.
I have the following relationships to disclose any COI for this research presentation within the period of 36 months:

<table>
<thead>
<tr>
<th>Employment/Leadership position/Advisory role:</th>
<th>Chinook Therapeutics; Novartis</th>
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</thead>
<tbody>
<tr>
<td>Research funding:</td>
<td>Chinook Therapeutics; Novartis</td>
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<tr>
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<td>None</td>
</tr>
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Endothelin-A Receptor Activation Drives the Hallmarks of IgA Nephropathy Progression through Multiple Mechanisms$^{1,2}$


ET-1, endothelin-1; ET$_A$, endothelin-A; Gd-IgA1, galactose deficient IgA1; IgA, immunoglobulin A
Atrasanen*

Atrasentan is a potent and selective ET$_A$ antagonist that has potential to reduce proteinuria and preserve kidney function in IgAN

- Interim results of a phase 2, open-label study in patients with IgAN (AFFINITY, NCT04573920) demonstrated that atrasentan was generally well tolerated and resulted in clinically meaningful and sustained proteinuria reductions in patients receiving a maximally tolerated and optimized dose of a RAS inhibitor (Rastogi et al, 2022, ASN Kidney Week).

* Atrasanen is an investigational drug that has not been approved by regulatory authorities. Efficacy and safety have not been established. There is no guarantee that it will become commercially available for the use(s) under investigation.
Sodium glucose cotransporter-2 inhibitors (SGLT2is)

SGLT2is are approved in the U.S. for use in adults with CKD at risk of kidney disease progression, including IgAN.¹,²

- In a post-hoc analysis of the global phase 3 SONAR study in patients with type 2 diabetes and CKD, 6-week treatment with atrasentan and SGLT2i in a small number of patients (n=14) further decreased albuminuria and decreased body weight, a surrogate for fluid retention, vs. atrasentan alone.³

ASSIST Study Design

ASSIST™ (NCT05834738) is a randomized, double-blind, placebo-controlled, crossover study to evaluate the safety and efficacy of atrasentan vs. placebo in adults with IgAN on stable SGLT2i and RASi with persistent proteinuria.

Study Objective

ASSIST™ (NCT05834738) is a randomized, double-blind, placebo-controlled, crossover study to evaluate the safety and efficacy of atrasentan vs. placebo in adults with IgAN on stable SGLT2i and RASi with persistent proteinuria.

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**ASSIST Key Inclusion Criteria**

<table>
<thead>
<tr>
<th>All patients</th>
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<tr>
<td>• Adults with biopsy-proven IgAN, not due to secondary causes</td>
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<tr>
<td>• Receiving max tolerated and stable RASi ≥ 12 weeks prior to screening</td>
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<tr>
<td>• eGFR ≥ 30 mL/min/1.73 m² (CKD-EPI) at screening</td>
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<tr>
<td><strong>SGLT2i stable</strong></td>
<td>Receiving SGLT2i at stable dose ≥ 8 weeks prior to screening</td>
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<td>• 24-hour total urine protein &gt; 0.5 g/d at screening</td>
<td></td>
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<tr>
<td><strong>SGLT2i naïve or non-stable</strong></td>
<td>24-hour total urine protein &gt; 0.85 g/d at screening</td>
</tr>
<tr>
<td>• 24-hour total urine protein &gt; 0.85 g/d at screening</td>
<td>Complete 8-week run-in period on a stable and well tolerated dose of an SGLT2i</td>
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<tr>
<td>• After run-in:</td>
<td>24-hour total urine protein &gt; 0.5 g/d confirmed at end of run-in</td>
</tr>
<tr>
<td> 24-hour total urine protein &gt; 0.5 g/d confirmed at end of run-in</td>
<td>eGFR of ≥ 30 mL/min/1.73 m² (CKD-EPI) at end of run-in</td>
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### ASSIST Study Endpoints

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<tr>
<th>Category</th>
<th>Description</th>
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<tr>
<td><strong>Primary</strong></td>
<td>Change in proteinuria (UPCR from a 24-hour urine collection) from baseline to week 12</td>
</tr>
<tr>
<td><strong>Key secondary</strong></td>
<td>In Treatment Period 2, the change in proteinuria (UPCR from a 24 hr urine collection) from baseline to week 24</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td>Type, incidence, severity and relatedness of adverse events (AEs) and serious AEs</td>
</tr>
<tr>
<td><strong>Exploratory</strong></td>
<td>In Treatment Period 2, change in eGFR from baseline to week 24</td>
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Atrasentan, a potent and selective ET$_A$ antagonist, has potential to reduce proteinuria and preserve kidney function in IgAN

The ASSIST crossover study will evaluate the safety and efficacy of atrasentan in combination with SGLT2i in patients with IgAN with persistent proteinuria despite maximized RASi

The ASSIST study is currently enrolling
For more information, scan QR or visit https://clinicaltrials.gov/ct2/show/NCT05834738