NUC-1031 in combination with cisplatin for first-line treatment of patients with advanced biliary tract cancer (NuTide:121)

**Background**
- No approved agents exist for the treatment of locally advanced/metastatic (LAM) biliary tract cancer (BTC).
- Current standard of care remains gemcitabine + cisplatin: overall survival (OS) 10.7 months (ARC-02).
- Resistance to chemotherapy is associated with poor survival.
- Effective new agents and combinations are required.

**Objective Response Rates in ARC-08 and ARC-02**

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<tr>
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<th>ARC-08</th>
<th>ARC-02</th>
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<tbody>
<tr>
<td></td>
<td>NUC-1031 + cisplatin</td>
<td>gemcitabine + cisplatin</td>
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<tr>
<td><strong>Complete Response</strong></td>
<td>75.0% (1/4)</td>
<td>0.0% (0/4)</td>
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<td><strong>Partial Response</strong></td>
<td>43.5% (2/4)</td>
<td>25.0% (1/4)</td>
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<tr>
<td><strong>Objective Response Rate</strong></td>
<td>50.0% (1/2)</td>
<td>25.0% (1/4)</td>
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**Treatment duration and best overall response by BTC anatomic site of origin (Evaluable population)**

**Safety profile**
- NUC-1031 + cisplatin was well tolerated.
- Multiple cycles administered (median 8 range 1-14).
- No unexpected adverse events (AEs).
- No dose-limiting toxicities (DLT).
- Grade 3 AEs included: fatigue (4%), neutropenia (14%), pyrexia (14%), anemia (1%), and increased liver function enzymes (1%, 14%).
- No Grade 4 treatment-related AEs.
- No patients discontinued due to NUC-1031 + cisplatin.

**Study design**

**Enrollment**
- Eligible patients: locally advanced/metastatic BTC.
- Osso study design: dose finding.

**Primary Objectives**
- OS
- OS in spheroendothelial BTC

**Secondary Objectives**
- Overall response rate (ORR)
- Tumor burden during treatment

**International multi-center study (15 countries ~120 sites)**

**Summary**
- NUC-1031 + cisplatin shows encouraging efficacy compared to standard of care.
- ARCTIC (ARC-08) is an open-label study.
- NUC-1031 + cisplatin is well tolerated over multiple cycles.
- **NuTide:121** is a Phase 3 study that will be conducted at ~120 sites across North America, Europe, and Asia-Pacific.
- **NuTide:121** has the potential to improve survival outcomes in patients with BTC.
- Further study information: NuTide:121@maccallum.com.