A first-in-human study of NUC-7738, a ProTide transformation of 3'-deoxyadenosine, in patients with advanced solid tumors (NuTide:701)

**BACKGROUND**

- Nucleoside analogs form the backbone therapy for solid and hematological malignancies
- 3'-deoxyadenosine (3'-dA, cordycepin) isolated from Cordyceps sinensis
- 3'-deoxyadenosine triphosphate (3'-dATP) believed to cause cell death by inhibiting DNA and RNA replication

**STUDY DESIGN - NuTide:701**

- **Primary objectives**
  - Safety
  - PK
  - Efficacy (BoR, ORR, DoR, PFS)
- **Secondary objectives**
  - PK
  - Efficacy (BoR, ORR, DoR, PFS)
- **Patient population**
  - Aged ≥ 18 years, ECOG PS 0 or 1
  - Advanced solid tumors not amenable to standard therapy

**RESULTS (interim)**

- **Patient Characteristics**
  - 29 patients treated; age 39-77 (median: 63)
  - Median prior lines therapy: 2.5 (1-7)
- **Primary tumor types**
  - Melanoma (5 cutaneous, 3 ocular)
  - Colorectal (3), Cervical (2), Lung (2)
  - Breast (2), Ovarian (2), Pancreatic (2)
  - Gastric (2), Oesophageal (1), Biliary tract (1)
  - Leiomyosarcoma (1), Mesothelioma (1)
  - Jejunal (1), Endometrial (1)

- **NUC-7738 Dosing**
  - Completed dose 14-900 mg/m² Q1W (IV infusion 30-120 mins)
  - Current dose 1350 mg/m² Q1W
  - Dose escalation ongoing

- **Safety profile**
  - NUC-7738 is well tolerated
  - No Grade 3 or 4 treatment-related AEs
  - No DLTs

- **CONCLUSION**
  - NUC-7738 is a novel ProTide with multiple potential anti-cancer mechanisms of action
  - NUC-7738 is designed to overcome key cancer resistance mechanisms of 3'-dA (cordycepin)
  - NuTide:701 study will establish the RP2D of NUC-7738 in patients with solid tumors
  - Interim data from NuTide:701 study demonstrate
    - Anti-cancer activity and prolonged disease control
    - Favorable tolerability profile
    - Efficient intracellular conversion to active metabolite, 3'-dATP
  - NuTide:701 study recruitment ongoing