PROGEMI: A Phase I/II study of a first-in-class nucleotide analogue Acelarin (NUC-1031) in patients with advanced solid tumours

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BACKGROUND

ProTides: Nucleotide Analogues
- New generation of anticancer agents
- Innovative phosphoramidate technology
- Overcome key cancer resistance mechanisms
- Broader utility to benefit a wide range of cancer patients
- Promising efficacy and safety profile

NUC-1031: The First Anti-Cancer ProTide
- Designed to overcome all the key resistant mechanisms associated with gemcitabine:
  - Cellular uptake independent of nucleoside transporters
  - Activation independent of deoxycytidine kinase
  - Avoids cyclotidase deaminase inactivation

Objectives
- Avoids cytidine deaminase inactivation
- Activation independent of deoxycytidine kinase
- Promising efficacy and safety profile
- Broader utility to benefit a wide range of cancer patients
- Overcome key cancer resistance mechanisms
- Innovative phosphoramidate technology

ProTides: Nucleotide Analogues

RESULTS

Patients Characteristics
- 36 patients at submission date
- 26 female, 10 male
- Mean age 56 years (range 20-74)
- Average number of previous chemotherapy regimens 2.4 (range 1-6)
- Primary tumour site:
  - Ovary 10; Pancreas 6; Biliary 4;
  - Lung 6; Breast 2; Oesophagus 2
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Pharmacokinetics
- NUC-1031 plasma half life is more favourable than gemcitabine (~3 hours versus 1.5 hours respectively)

Efficacy
- Recurrent adenocarcinoma of unknown origin (2.3 cycles over 12 months)
- Partial response: Best Overall Response
- RECIST defined % change in tumour measurement

CONCLUSIONS
- Innovative and durable disease control in a high proportion of evaluable patients
- Active in a broad range of cancers
- Disease control in patients refractory to/hospitalized on prior chemotherapy, including gemcitabine
- Well tolerated with no unexpected AEs
- Generates high intracellular levels of the active agent dFdCTP
- Overcomes key cancer resistance mechanisms
- Molecular profiling studies ongoing to characterise target patient population
- Phase II global studies planned in pancreatic, biliary, ovarian and NSCLC cancers

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