Oxford BioTherapeutics and ImmunoGen Partner to Develop Multiple First-in Class Antibody-Drug Conjugates in Cancer Indications with High Unmet Clinical Need

Abigail Houghton[1], Olga Ab[3], Sribalaji Lakshmikanthan[3], Somdatta Basu[1], Stephen Blance[1], Belinda Cairns[2], Ali Chesney[3], Lindsey Hudson[1], Matthew Metzger[2], Daniel Milano[3], Javier Morales[2], Callum M. Sloss[3], Yu-Tzu Tai[2], Ben Thomas[1], Madeline Tran[2], Carl Waiter[3], Alan Zulick[3], Eric Westin[3], Christian Rohlff[1]. [1]*Oxford BioTherapeutics Ltd;* [2]*Oxford BioTherapeutics Inc;* [3]*ImmunoGen Ltd*

Poster No. 14

OXFORD BioTherapeutics

Oxford BioTherapeutics (OBT) is a clinical-stage oncology company founded in 2004, specializing in the identification, validation and development of novel, first-in-class antibody-based therapeutics. Through 19 years' experience of target to monoclonal antibody (mAb) therapeutics, OBT have developed a broad internal clinical and pre-clinical pipeline with a major focus on antibody-drug conjugates (ADCs). OBT's pipeline and development capabilities has also been validated through multiple strategic partnerships. The externally partnered pipeline includes out-licenced oncology drug candidates identified using OBTs' OGAP® discovery platform. OBT facilitates its partnerships between its strategically placed head office in Oxford (Target Discovery), mAb research and development (R&D) site in San Francisco and clinical and regulatory base in New Jersey.

immunogen

ImmunoGen (IMGN), is a leader in the expanding field of antibody-drug conjugates (ADCs), developing next generation ADCs with 40 years of innovation in the ADC field. IMGN's ADC technology is clinically validated with ELAHERE and recently granted accelerated approval for ovarian carcinoma patients, and three other ADCs in various stages of clinical development. IMGN's ADC platform comprises a suite of proprietary, next generation payloads and linkers, built with both tolerability and efficacy in mind. IMGN is headquartered in Waltham, Massachusetts.

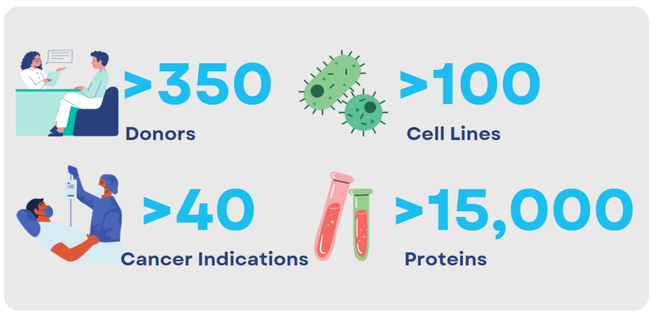
**** ELAHERE™ is a prescription medicine used to treat adults with folate receptor-alpha positive ovarian cancer, fallopian tubes cancer, or primary peritoneal cancer who have not responded to or are no longer responding to treatment with platinum-based chemotherapy and have received 1 to 3 prior types of chemotherapy. For full prescription information refer to www.elahere.com***

OBT and IMGN will collaborate through a strategic ADC development partnership to address cancer indications of high unmet clinical need. The collaboration utilises IMGN's proprietary linker-payload technologies together with OBT's capabilities to identify novel, tumour-specific, antibody-targetable proteins. Under the collaboration, IMGN and OBT jointly selected 'early-stage' and 'advanced-stage' assets from OBT's portfolio. Once therapeutic antibodies, generated by OBT, are optimized with IMGN's proprietary linker-payload technology, each company will select multiple development programs to pursue. Both companies share the intention to produce and advance successful, well-tolerated, first-in-class ADC oncology therapeutics. Together with OBT's novel, first-in-class programs, a key strength of this partnership is that multiple linker-toxin combinations will be tested which enables an individual, target-optimized approach to ADC selection without the constraints of a single ADC platform. This poster summarises the collaboration, from OGAP® target identification and validation, to therapeutic antibody generation, lead selection, ADC selection, optimization, and functional and preclinical testing.

Early-Stage Assets

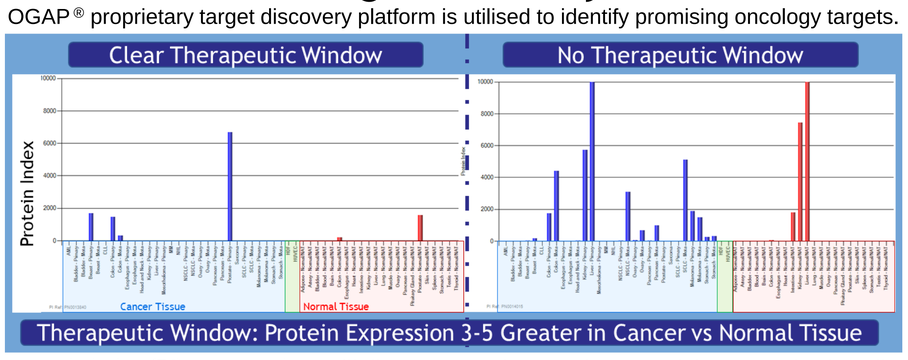
The 'Early-Stage' assets were identified during target discovery and are set to progress through a series of milestones. Here we highlight the high-level workflow beginning with Target Discovery and Target Validation.

The Oxford Genome Anatomy Project (OGAP®)



Target Discovery

OGAP® proprietary target discovery platform is utilised to identify promising oncology targets.



The protein index (PI) plots semi quantitatively summarise membrane protein expression in patient's cancers and normal tissue adjacent to the tumor (NATs)/normal tissues, using mass spectrometry data. The PI metric is a composite of protein abundance and prevalence enabling target selection. The blue bars represent protein expression in cancer tissues, the red bars represent target expression in normal/NAT tissues.

Discovery

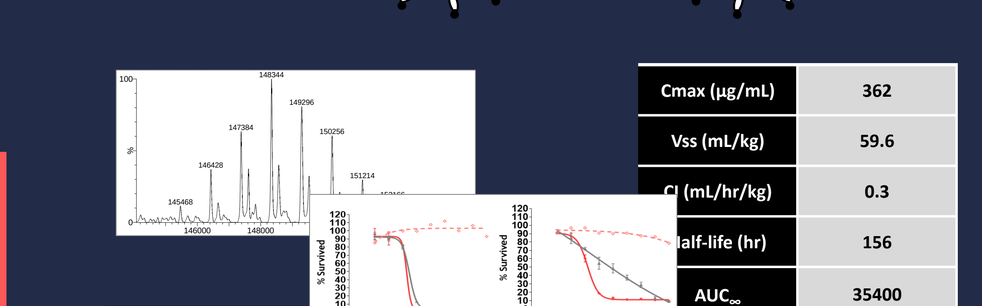
- OGAP® Target Identification and Data Package Generation
- Target Validation
- Generation and Validation of Tool Reagents
- Generation of Therapeutic Antibodies
- Antibody Screening & Lead Selection for ADC Development

Validation

Target Validation and Therapeutic Antibody Generation

- The target must be validated to establish presence of a targetable, extracellular epitope, confirmed by FACS and IHC
- Tool antibodies are generated and validated for use in FACS, IHC, ELISA & WB. Validated commercially available antibodies are also utilised were available.
- Target expression is determined in cell lines, healthy tissues and cancer tissues by FACs, ISH and IHC

Generation of The Therapeutic Antibody

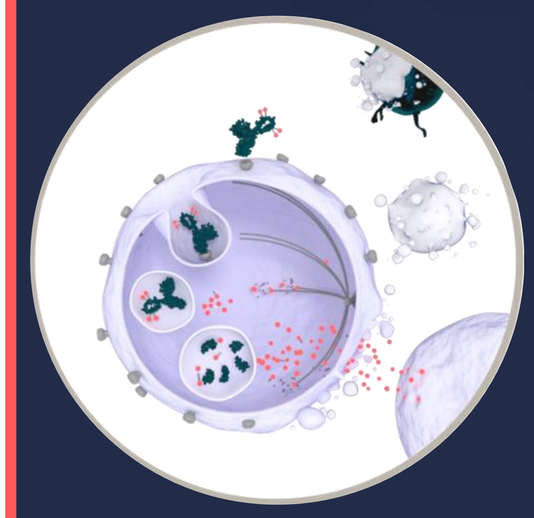


- Immunogens are generated and characterized in-house
- Therapeutic antibody campaigns utilise a variety of platforms at CROs
- Antibody characterization and lead selection for ADC development is carried out in-house

Advanced-Stage Assets

The Advanced-Stage assets enter the collaboration here, OBT have generated validated therapeutic antibodies ready for conjugation to IMGN's linkers and payloads. The early-stage assets will also progress through the following milestones.

Selection of Linker, Payload Technology



ImmunoGen technology has produced three approved products:

KADCYLA® (Roche/Genentech), SARCLISA® (Sanofi), and ELAHERE™ (ImmunoGen)

Payloads

- Multiple mechanisms of action:
  - Tubulin-acting maytansinoids
  - DNA-acting IGNs
  - Topoisomerase I inhibiting camptothecins
- Bystander activity for heterogeneously expressed targets

Linkers

- Cleavable
- Non-cleavable
- Multiple methods of conjugation, including site-specific technology

ADC Design

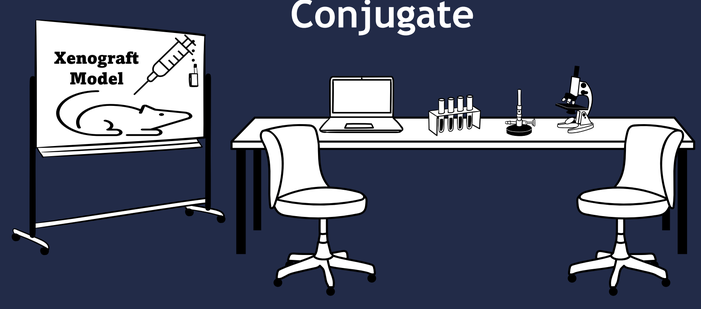
- Customized ADC composition for optimized efficacy/ tolerability

Lead selection

- Conjugation to multiple IMGN Linker-Payloads
- In Vitro and In Vivo Efficacy
- PK, mouse and NHP
- Tox Study, NHP

Lead evaluation

In Vitro, In Vivo Testing of the Antibody-Drug Conjugate



Cmax (µg/mL)	362
Vss (mL/kg)	59.6
Cl (mL/hr/kg)	0.3
Half-life (hr)	156
AUC_{∞}	35400

Both Parties Select Assets for IND

OXFORD BioTherapeutics

immunogen