Company overview

- Specialist pharma in peptides
- Listed on AIM 2006 (LSE:IMM)
- Research subsidiaries in France through CNRS collaboration
  - Elro Pharma, Nucant (cancer)
  - Ureka Sarl, novel peptide platform technology
- Lead drug Lupuzor™ (forigerimod) for Lupus
  - Phase III program ongoing
ImmuPharma Group
R&D Subsidiary Companies in France

ImmuPharma France
Autoimmune Diseases
Lupuzor™
Late clinical stage

ELRO Pharma (France)
Cancer & Ophthalmology
Nucant
Early clinical stage

Ureka
Platform Technology
Urelix™
Preclinical stage
A year of progress

- Forigerimod / Lupuzor™
  - Insights into last phase III reveal the way forward
  - New optimized Lupus phase III design in progress
  - PC experiments show potential in other autoimmune diseases
  - Open label extension study meets primary endpoint of safety & tolerability
- Nucant
  - MOA and target oncology indications becoming clearer
  - Drug combination potential attractive
- UreKa
  - Novel attractive peptide-platform technology
  - Peptides that last significantly longer with superior PK and PD profiles
  - Metabolic disease is 1st in the pipeline
**Key progress 2018 to 2019**

- **Lupuzor™ Ph III trial top line data announced – April 2018**
- **Lupuzor™ Ph III further analysis reveal a way forward – May 2018**
- **Lupuzor™ Ph III extension study meets primary endpoint of safety & tolerability – June 2019**
- **UreKa Nature Comms paper published. Superior GLP-1 analogues pave way for many peptide types across many therapy areas – Feb 2019**
- **New lupus phase III protocol in progress. Positive impact from improbable expectations from Ph III 2018. Routes for international trial now under consideration**
Pipeline status

Forigerimod
- ADs: Autoimmune diseases
- PC
- I
- II
- Lupus

Nucant
- Cancer
- MDs: Metabolic diseases
- I
- II
- Cancer

UREkA*
- MDs: Metabolic diseases
- Cancer
- I
- II

ADs = Autoimmune diseases, MDs = Metabolic diseases, *505 B(2) route for lead requires PK study only
ImmuPharma

Lupuzor™
forigerimod

Significant evidence in support of Lupuzor™
SPA & Fast-Track designation for Lupuzor™
Phase III top line data announced
What is Lupus?

- Lupus is an autoimmune chronic inflammatory disease, sometimes fatal, associated with disorders of the immune system.
- Unmet market need, due to the lack of safe and effective treatments.
- Multi-billion sales potential.
- Varying patient estimates*:
  - an estimated 5 million people globally suffer from lupus.
  - 1.5 million lupus sufferers in Europe/US/Japan.
- Current drugs have serious side-effects and limited effectiveness.
- GSK’s approval of Benlysta paves the path to market.

* source: Lupus Foundation of America ‘www.lupus.org’ (2017)
Lupuzor™ Key USP's

- Novel mechanism that modulates *not blocks* the immune system
- Outstanding safety profile

Attractive economics
- Lupus patients are treated by specialists, not GPs = low marketing costs
- Long term treatment creates high costs to the community
- Benlysta priced at approx. US$25,000 / per patient / per year
- Lupuzor™ anticipated to have lower pricing
- High margin
Lupuzor™ - mechanism of action

First line of defence

Antigen presenting cell

Lupuzor™ / Forigerimod
1st in class autophagy modulator

(New) therapeutics: most if not all target B cells
Phase III now completed – 28 investigator sites
- 11 centres in the US
- 16 centres in Europe
- 1 centre in Mauritius
- Simbec-Orion (CRO) experts in Lupus trials

Protocol agreed with the FDA
- One year dosing
- Protocol similar to that of Phase IIb
- n = 200 patients/study
- Double-blind, Randomised, Placebo controlled; once a month (dose 0.2mg)

Find more information on: www.ClinicalTrials.gov (Search: ‘Lupuzor’)
**Lupuzor™ top line data**
- announced 17 April 2018 & 29 May 2018

- Lupuzor™ demonstrated a superior response rate over placebo (52.5% vs 44.6% “responders”) in the primary analysis on the Full Analysis Set of all 202 patients

- Due to the high response rate in the placebo group, this superior response did not allow statistical significance to be reached (p = 0.2631) and the trial's primary end point was not met

- Across the whole study population, in those patients who had anti-dsDNA autoantibodies, Lupuzor™ demonstrated a superior response rate over placebo (61.5% vs 47.3%, p = 0.0967)

- Further data analysis demonstrated that in the Europe cohort (130 patients) Lupuzor™ plus standard of care showed statistically significant reductions in disease activity compared to placebo plus standard of care in 79 patients who were anti-dsDNA autoantibody positive (71.1% vs 48.8%, p = 0.0218)

- The study confirmed the outstanding safety profile of Lupuzor™, with no serious adverse events reported

- 62 patient open label extension study completed with data announced June 2019 –primary endpoint of safety & tolerability met – further analysis to follow
Forigerimod

A first in-class autophagy modulator for Autoimmune Diseases
ImmuPharma together with Professor Sylviane Muller, Lupuzor’s inventor, have presented new evidence supporting Lupuzor’s™ P140 peptide activity in several other major autoimmune disease indications outside of Lupus.

- Based on P140 strong efficacy and safety profile and mechanism of action.

- This includes Rheumatoid Arthritis, Crohn’s Disease, and Asthma - the peptide appears to have general effects against chronic inflammatory indications.

- Other pre-clinical evidence supports the molecule’s use in: Neuropsychiatric lupus (NPSLE); Gougerot-Sjögren syndrome (GSS); and Guillain-Barre disease (chronic/CIDP).

- Further preclinical work continues with Prof. Muller at the CNRS with the objective of further indications moving into the clinic in due course.

For more information go to: http://www.immupharma.co.uk/media/events/
A multi-faceted product

- SLE (Systemic Lupus Erythematosus) Phase 3 trial completed in patients
- NPSLE (Neuro Psychiatric SLE) Preclinical results published
- RA (Rheumatoid Arthritis) Preclinical studies planned
- Asthma (Preclinical studies ongoing)
- IBD (Inflammatory Bowel Disease) Preclinical studies ongoing
- Sjögren’s Syndrome Preclinical results published
- CIDP (Chronic Inflammatory Demyelinating Polyneuropathy) Preclinical results published
- Other
  - Lupuzor™ IPP-201101 P140
  - Further Preclinical studies planned in other AI indications
New lupus phase III design - path to success

- Understanding the unexpected – intensive learning process over the last year
- Analysis of Lupuzor™ clinical data and clinical strategy support from leading healthcare organisation
- Identified key elements to optimise success
  - Selection on the basis of ds-DNA antibody positive status
  - Selection of more severe SLE patients
  - Increased sample size
  - Assess steroid use over time – steroid sparing potential
Potential breakthrough cancer drug in clinical trials in cancer patients.

Dual mechanism of action - normalises angiogenesis and inhibits proliferation.

 Novel target – binds to nucleolin on the surface of cells and inhibits its action.

Major funding grant received from prestigious French state organisations.
• ImmuPharma is developing as combination therapy with cytotoxics such as Gemcitabine

• Gemcitabine alone doesn’t penetrate efficiently enough cancer tissues to be effective
  • (e.g. as treatment of choice of Pancreatic cancer, it only increases life expectancy by few months)

• This is in part because tumours have abnormal vessels which:
  • Prevent drugs to penetrate them (so called ‘EPR effect’ is overated for small molecule)
  • ‘Abnormal’ tumour vessels are in fact helping the tumour (hypoxia helps tumour growth as it promotes the expression of growth factors!)

• Our strategy is to normalise blood vessels WHILST administering a potent cytotoxic such as Gemcitabine
Urelix™
Generating new molecules

A Company within the Company...
Examples of approved & natural peptides

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<th>Cancer</th>
<th>Metabolic</th>
<th>Infection</th>
<th>Pain</th>
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<th>GI</th>
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- Challenges in peptide drug development are:
  - to slow down metabolism of the drug
  - improve PK profile – reduced frequency of dosing
  - improve route of administration, preferably oral
  - achieve lowest dose
  - Ease of manufacture at cost effective levels

Source: ImmuPharma Research
Current peptide technologies

- Amino acid (AA) sequence remodeling & extension
- Lipidation and Pegylation
- Macrocyclisation
- Fusion to large proteins

UREkA foldamer technology

- Proprietary oligoureia “foldamers” based technology
- α-helix biomimetics – mimics the structural conformation of the target peptide
- Significant stabilization of peptide
- Peptide looks the same but lasts significantly longer without loss of efficacy
- Very safe and well tolerated in animals
- Lower doses and less frequent dosing
- Oral potential has been identified
Evidence for UREkA technology

- Paper published in Nature Communications in February 2019
- Improved pharmaceutical properties of GLP-1 in animals
- GLP-1 a critical hormone in metabolism & glycemic control
- 4 consecutive amino acids of GLP-1 replaced by 3 ureido residues
- GLP-1-oligourea hybrids superior PK profile - potential for once monthly dosing?
- Technology can be easily adapted to many peptides
- Doses are significantly lower than conventional approaches
- Solid phase synthesis

Source: Nature Communications volume 10, Article number: 924 (2019)
Oligoureas: $\alpha$-helix Biomimetics

Oligoureas | Hybrids | Peptide
---|---|---

$\alpha$-helix

$N$-term

Peptide

Fremaux & Guichard AICE
2015
**Financial status**

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£10 million (gross) fundraising completed in January 2018

Acquired a 15% stake (and warrants) in Incanthera in September 2018

Post balance sheet event: Lanstead financing of £2.7 million in June 2019
Investment rationale

- Confident of Lupuzor™’s future as a blockbuster asset still 100% owned by ImmuPharma
- Competitive efficacy & safety profile
- P140 platform has potential to expand into other autoimmune diseases
- Partnering discussions continue

- Ongoing activities continue to create value within Elro & UreKa including:
  - Merging the two subsidiaries
  - Securing external investment from private equity
  - Public listing on a European stock exchange

- Robust financial position balance
- Continued transparency with news-flow
- Proactive IR strategy ongoing
ImmuPharma plc
50 Broadway
Westminster
London SW1H 0RG
U.K.

Tel: +44 20 7152 4080
www.immupharma.co.uk

Contact
tim.mcarthy@immupharma.com
dimitri.dimitriou@immupharma.com
lisa.baderoon@immupharma.com

Twitter : @immupharma

UK Advisers

Nominated Advisor & Joint Broker
SPARK Advisory Partners Limited

Joint Brokers
Stanford Capital Partners
SI Capital

Public Relations & Investor Relations
lisa.baderoon@immupharma.com
Capital Access Group

Auditors
Nexia Smith & Williamson

Solicitors
Bircham Dyson Bell