developing science delivering therapies
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The Microbiome
FROM COMPLEX MIXTURES TO NEW THERAPEUTIC CLASSES

- Serum therapy
- Fungal broths
- Plant extracts
- Blood transfusions
- Antibodies
- Vaccines
- Cytotoxic small molecules
- Targeted small molecules
- Therapeutic proteins
THE MICROBIOME – THE POTENTIAL

Microbiome

- Trillions of bacteria which colonise the human gut
- More gut bacteria than host cells
- $100x$ as many genes as the human genome
- Crucial in shaping the host immune system & metabolism

Live Biotherapeutics

- Breakthrough class of medicines
- Myriad therapeutic areas
- Potential to change the way we treat disease
Pharma
- Recognising the ability for microbiome to increase response rates
- Product deals currently target gastrointestinal disease

Bacterial components
- Small molecule approach
- No advantages over existing traditional approaches
- Enterome, Second Genome, Synthetic Biologics

Microbiome: consortia
- Ecological approach
- Based on FMT/reseeding gut
- Clinical trials based on repackaged human material
- Seres, Vedanta, Rebiotix

Microbiome: single strain
- Mechanistic approach
- Target and address same pathways as traditional drugs
- Only 4D in clinic across multiple disease areas
- 4D, Evelo, OxThera
4D PHARMA – ADDRESSING THE CHALLENGES

Moving beyond gastrointestinal disease

- Commencing a clinical trial in asthma in 2019
- Superior efficacy to biologics
- 4D is the only company developing microbiome therapeutics for asthma

Delivering large and robust clinical studies

- US and European Phase 2 IBS study is underway
- 500 patients - the largest LBP trial to date
- Novel MoA, potentially treating the underlying cause of disease
- A disruptive new therapy, addressing significant unmet patients needs

Integrating LBPs into biopharma pipelines

- Clinical collaboration with Merck investigating combination of Keytruda and MRx0518
- In renal, bladder, melanoma and NSCLC
- Significant pre-clinical data and detailed MoA (Cowie et al., in press)
- Trial conducted at MD Anderson

The Microbiome

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World leader in the development of live biotherapeutics

Pipeline of 17 clinical and preclinical programmes, covering disease areas such as IBS, cancer, poorly controlled asthma, autoimmune and CNS disease

- Founded: 2014
- Shares Listed: AIM (DDDD)
- Market Cap: £100M\(^1\)
- Cash: £37M\(^2\)
- Headquarters: Leeds UK
- Employees: 120+
The Company

Research

MicroRx platform
Focus on functionality
Well understood pathways

Development + Manufacturing

Glass to stainless steel in-house
Stable, repeatable processes
GMP certified

Clinical

Phase II IBS open for enrolment
Phase Ib CD complete
Up to 4 clinical studies by end 2018

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**4D PHARMA - PIPELINE ADDRESSING KEY GLOBAL DISEASES**

<table>
<thead>
<tr>
<th>DISCOVERY</th>
<th>PRECLINICAL</th>
<th>DEVELOPMENT</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
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</thead>
<tbody>
<tr>
<td><strong>Gastro-intestinal</strong></td>
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<tr>
<td>Blautix <em>Irritable Bowel Syndrome</em></td>
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<td><strong>Phase II open for enrolment</strong></td>
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<td>Thetanix <em>Crohn’s Disease</em></td>
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<td><strong>Phase II opening 2019</strong></td>
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<td>Rosburix <em>Ulcerative Colitis</em></td>
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<td><strong>Immuno-oncology</strong></td>
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<td>MRx0518 <em>Solid tumours</em></td>
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<td><strong>Monotherapy and combo trials open Q4 2018</strong></td>
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<td><strong>Respiratory</strong></td>
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<tr>
<td>MRx0004 <em>Asthma</em></td>
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<td><strong>Phase I opening 2019</strong></td>
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<tr>
<td>MRx0001 <em>Allergic Asthma</em></td>
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<td><strong>Autoimmune</strong></td>
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<td>MRx0002 <em>Multiple Sclerosis</em></td>
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<tr>
<td>MRx0006 <em>Rheumatoid Arthritis</em></td>
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<tr>
<td>Others</td>
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<tr>
<td><strong>CNS</strong></td>
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<td><em>Neurodegeneration</em></td>
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<td><em>Autism</em></td>
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</table>
Shubham Pant, MD

Associate Professor, Department of Investigational Cancer Therapeutics, University of Texas MD Anderson Cancer Center

Previously Director of Clinical Trials, Section of Hematology - and as Associate Director of the TSET Phase I Program at the University of Oklahoma.

Recipient of Mai Eager Anderson Endowed Chair in Cancer Clinical Trials

Selected for ASCO Leadership Development Program, serves on the ASCO Quality of Care Committee and ASCO's International Quality Task Force

Key opinion leader in Phase 1 drug development and GI cancer including pancreatic, biliary, gall bladder and colorectal cancer

Expertise in targeted therapy and immunotherapy

Completed fellowship at James Cancer Hospital/Solove Research Institute at the Ohio State University (elected Chief Fellow)
Microbiome and Cancer

Presented by: Shubham Pant, MD
Key Topics Covered in Today’s Talk

• The functional diversity of the gut microbiome and its impact on cancer therapy
• Role of the microbiome in influencing response to checkpoint inhibitors
• Clinical studies demonstrating microbiome as driver of anti-PD-1 efficacy
• Evidence for key role of specific Enterococcus organisms in response to anti-PD-1 therapy
• Impact of the microbiome across other cancer settings
The Microbiome by Numbers

Microbiome in Numbers

100 Trillion
symbiotic microbes live in and on every person and make up the human microbiota.

95%
of our microbiota is located in the GI tract.

150:1
The genes in your microbiome outnumber the genes in our genome by about 150 to one.

The surface area of the GI tract is the same size as 2 tennis courts.

You have
1.3X
more microbes than human cells.

>10,000
Number of different microbial species that researchers have identified living in and on the human body.

The gut microbiota can weigh up to 2Kg.

90%
of disease can be linked in some way back to the gut and health of the microbiome.

5:1
Viruses:Bacteria in the gut microbiota.

2.5
The number of times your body’s microbes would circle the earth if positioned end to end.

Each individual has a unique gut microbiota, as personal as a fingerprint.

The human body has more microbes than there are stars in the milky way.

It is thought that
90%
the microbiome is more medically accessible and manipulable than the human genome.
The Microbiome is Functionally and Phylogenetically Diverse
Duodenal Infusion of Donor Feces for Recurrent Clostridium difficile

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D., Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.
a) Sample preparation

- Stool sample from healthy donor
- Homogenized and liquidised with sterile saline
- Filter out residual solid faeces with metal sieve
- Homogenous liquid sample ready for transplantation

b) Delivery method

- Delivered via duodenal tube
- Colonoscopy

c) Microbiome diversity increases

- FMT
102 patients were assessed for eligibility or their treating physician contacted the study center

49 were excluded
- 2 pregnant
- 2 admitted to intensive care unit
- 2 had life expectancy <3 months
- 3 immunocompromised
- 8 unable to give informed consent
- 1 allergic to vancomycin
- 31 did not meet criteria of both diarrhoea and positive stool toxin for C. difficile
- 10 declined to participate

43 underwent randomisation

17 assigned to receive donor faeces infusion
- 1 excluded
- 16 completed evaluation

13 assigned to receive vancomycin
- 1 death
- 12 completed evaluation

13 assigned to receive vancomycin and bowel lavage
- 13 completed evaluation

**Figure 1. Enrolment and Outcomes**

After randomisation, one patient in the infusion group required high-dose prednisolone because of a rapid decrease in renal-graft function that was noted immediately after randomization but before the study treatment was initiated. This patient was excluded from the analysis. One patient in the vancomycin-only group died before the first stool sample could be tested for the presence of *Clostridium difficile* toxin.
Figure 2. Rates of Cure without Relapse for Recurrent *Clostridium difficile* Infection.

Shown are the proportions of patients who were cured by the infusion of donor feces (first infusion and overall results), by standard vancomycin therapy, and by standard vancomycin therapy plus bowel lavage.
# Approved Checkpoint Inhibitors

By Tumour Type in US and EU

<table>
<thead>
<tr>
<th>Name</th>
<th>Target</th>
<th>Company</th>
<th>FDA-Approved indications</th>
<th>EU-Approved Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pembrolizumab</strong></td>
<td>PD-1</td>
<td>Merck &amp; Co. (MSD)</td>
<td>• Inoperable or metastatic melanoma; • Metastatic NSCLC with PDL-1 expression; • Metastatic non-squamous NSCLC; • Metastatic NSCLC with high PD-L1 expression; • Recurrent or metastatic HNSCC; • Refractory classical Hodgkin lymphoma; • Locally advanced or metastatic urothelial carcinoma; • MSI-H cancers; &amp; rmetastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma</td>
<td>• Inoperable or metastatic melanoma; • Metastatic non-squamous NSCLC</td>
</tr>
<tr>
<td><strong>Nivolumab</strong></td>
<td>PD-1</td>
<td>Bristol-Myers Squibb</td>
<td>• Inoperable or metastatic melanoma; • Metastatic NSCLC; • Advanced renal cell carcinoma; • Classical Hodgkin lymphoma; • Recurrent or metastatic HNSCC; • Locally advanced or metastatic urothelial carcinoma; • MSI-H or dMMR cancers; • Hepatocarcinoma</td>
<td>• Inoperable or metastatic melanoma; • Metastatic NSCLC; • Advanced renal cell carcinoma; • Classical Hodgkin lymphoma</td>
</tr>
<tr>
<td><strong>Ipilimumab</strong></td>
<td>CTLA-4</td>
<td>Bristol-Myers Squibb</td>
<td>• Inoperable or metastatic melanoma</td>
<td>• Inoperable or metastatic melanoma</td>
</tr>
<tr>
<td><strong>Atezolizumab</strong></td>
<td>PD-L1</td>
<td>Genentech (Roche)</td>
<td>• Locally advanced or metastatic urothelial carcinoma; • Metastatic NSCLC</td>
<td>-</td>
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<tr>
<td><strong>Avelumab</strong></td>
<td>PD-L1</td>
<td>EMD Serono (Merck KGaA) - Pfizer</td>
<td>• Metastatic Merkel cell carcinoma (MCC); • Locally advanced or metastatic urothelial carcinoma</td>
<td>-</td>
</tr>
<tr>
<td><strong>Durvalumab</strong></td>
<td>PD-L1</td>
<td>AstraZeneca</td>
<td>• Locally advanced or metastatic urothelial carcinoma</td>
<td>-</td>
</tr>
<tr>
<td><strong>Cemiplimab</strong></td>
<td>PD-1</td>
<td>Regeneron/Sanofi</td>
<td>• Locally advanced or metastatic cutaneous squamous cell carcinoma</td>
<td>-</td>
</tr>
</tbody>
</table>

*Cook et al., Current Strategies to Enhance Anti-Tumour Immunity. Biomedicines 2018, 6. 37*
Factors Contributing
To Primary Resistance to Immune Checkpoint Therapy

- Low TILs
- Low non-synonymous mutation burden
- Low expression of immune signalling molecules
- Epigenetic silencing of chemokines & type 1 immunity
- Increased immunoregulatory signalling
- Oncogene signalling pathways

Tumour microenvironment

- Older age
- Background infection or chronic disease
- Immuno-suppression
- Smoking
- Effects of other drug interventions
- Host genetics or HLA
- Poor induction of ICD hallmarks (e.g. post chemotherapy)

Environmental factors

- Diet (e.g. vitamin deficiency, undesired metabolites)
- Microbiota

Other factors

- Hormone levels and endocrine disturbances
- Stress response
- Obesity?
- Diabetes?
- Biological interference (e.g. host-to-host variability in PK)

Increased chance of host resistance to checkpoint blockade

The Gut Microbiome Influences Efficacy of Anti-PD-1 Immunotherapies

Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors

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Gladys Ferrere,1,2,3 Céline Clémenson,1,13 Laura Mezquita,1,14 Jordi Remon Masip,1,14 Charles Naltet,1,5
Solen Brossae,1,15 Coureche Kaderbhai,16 Corentin Richard,16 Hira Rizvi,17 Florence Levenez,4
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Gérard Zalcman,15 François Goldwasser,9,21,22 Bernard Escudier,1,14,23 Matthew D. Hellmann,24,25
Alexander Eggermont,1,2,14 Didier Raoult,26 Laurence Albige,1,3,14 Guido Kroemer,8,9,10,11,12,27,28*
Laurence Zitvogel1,2,3,5*
Patients Receiving Antibiotics Have Significantly Lower Progression-Free Survival on Anti-PD-1

- **Median PFS**
  - No ATB: 4.1 mo
  - ATB: 3.5 mo
  - $p=0.017$

- **Median OS**
  - No ATB: 20.6 mo
  - ATB: 11.5 mo
  - $p<0.001$

- **Median OS**
  - No ATB: 15.3 mo
  - ATB: 8.3 mo
  - $p=0.001$

- **Median PFS**
  - No ATB: 7.4 mo
  - ATB: 4.3 mo
  - $p=0.012$
Strains of Enterococcus are Enriched
In Patients with NSCLC who Respond to Anti-PD-1
The Gut Microbiome Influences Efficacy of Anti-PD-1 Immunotherapies

Gut microbiome modulates response to anti-PD-1 immunotherapy in melanoma patients

The Gut Microbiome Influences Efficacy of Anti-PD-1 Immunotherapies

- Initial microbiome sampling (oral & fecal)
- Tumor biopsy
- Start of therapy
- Clinical assessment and imaging
- Repeat microbiome sampling (oral & fecal)
- 16S sequencing
- Metagenomic whole genome shotgun sequencing
  - WES
  - IHC
  - Flow cytometry
  - Cytokine analysis

E:

- Inverse Simpson
  - High
  - Intermediated
  - Low
- Proportion surviving progression-free
  - R
  - NR

** Science 359 (6371). 97-103.**
The Gut Microbiome Influences Efficacy of Anti-PD-1 Immunotherapies

D-14 → D-7 → D0 → D21 → D28

FMT from R/NR human donor

BP melanoma cell injection (s.c.)

anti-PD-L1 (IP)

germ-free mice → colonised by donor microbiota

250-500 mm$^3$ tumor

I

J

K

Tumor size

Tumor volume (mm$^3$)

CD8 (density/field of view)

CD8 (density/field of view)

NR FMT source

Time from injection (days)

C R NR

Science 359 (6371). 97-103.
The Gut Microbiome Influences Efficacy of Anti-PD-1 Immunotherapies

The intestinal microbiota influences the efficacy of PD-1 blockade

The enrichment of specific microbial taxa in intestines correlates with response to PD-1 blockade in cancer patients. FMT from responders into tumor-bearing mice improved responses to anti–PD-1 therapy and correlated with increased antitumor CD8⁺ T cells in the tumors. Mice receiving FMT from nonresponders did not respond to anti–PD-1 therapy, and tumors had a high density of immunosuppressive CD4⁺ Tregs cells.
The Microbiome has the Potential To Impact Across a Range of Cancer Settings

Biomarkers
Sequencing stool samples

Microbiome therapy
Fecal microbial transplantation

Precision medicine
Computational biologist

Therapy optimization
Immunotherapeutic effects

Toxicity
Efficacy

Drug discovery
Microbiome-derived compounds or microbiome-targeted drugs

KEEP CALM AND BOLDLY GO
Programmes:
MRx0518 – Immuno-oncology

© 4D pharma plc
MRx0518

- Gram-positive, motile, anaerobic bacterium of the *Enterococcus* genus
- Selected for immunostimulatory host response profile, unique within the 4D strain library

**Efficacy in vivo**

- Monotherapy: reduction of tumour volume in three syngeneic cancer models
- Combination: boosts efficacy of checkpoint inhibition *in vivo*

**Mechanism of action**

- Increases tumour CD8+/Treg ratio
- Immune stimulation through action of bacterial flagellin on TLR5

**Upcoming clinical studies**

- Phase Ib neoadjuvant biomarker study (UK)
- Combination study with anti-PD-1 (US)
Microbiome impacts efficacy of checkpoint inhibition in patients

- Anti-PD-1-responsive patients have significantly increased microbiome diversity compared with non-responders (Gopalakrishnan et al., Routy et al.)

This effect is causative, not just a correlation

- Animals humanised with ‘responder’ microbiota have delayed tumour growth and enhanced response to anti-PD-L1 therapy (Gopalakrishnan et al.)

Single-strain LBPs inhibit tumour growth in vivo

- Single-strain live biotherapeutics are effective in reducing tumour growth in vivo (Sivan et al., Vetizou et al., 4D pharma data)

Clinical data supports MRx0518 intervention

- NSCLC patients who respond to checkpoint inhibition have an increased abundance of MRx0518 in their microbiome (Routy et al.)
Caco-2 response

- Strong upregulation of a number of immunostimulatory transcripts:
  - TNFα, CXCL1, CXCL3, CXCL10, CCL20, IL-8

THP-1 response

- Strong and significant increases in:
  - TNF-α, IL-1β and IL-23, CXCL9 and IP10 (CXCL10)
- Very large induction of IL-8 beyond detection limit

PBMC response

- Strong and significant induction of pro-inflammatory cytokines:
  - IL-6, IL-8, TNF-α
MRX0518 MONOTHERAPY INHIBITS TUMOUR GROWTH IN DIFFERENT CANCER TYPES

**Efficacy in multiple tumour types**
- Inhibition of tumour growth in different preclinical models
  - Breast cancer (EMT6)
  - Lung cancer (LLC1)
- Increased survival in EMT6 model

**Complementary efficacy profile**
- Efficacy in models not responsive to monotherapy checkpoint blockade

**Benchmark**
- MRx0518 outperforms *Bifidobacterium* and *Bacteroides* – reported to have anti-tumour effects (Sivan et al., 2015; Vetizou et al., 2015)
- The effect of MRx0518 is not genus-specific

Cowie et al., in submission
MRX0518 AFFECTS CD8+ CELL POPULATIONS

**Effect of MRx0518 on CD8+/FoxP3+ ratio**

- MRx0518 and anti-CTLA-4 increase the ratio CD8+/FoxP3+ cells
- MRx0518 increases CD8α cells in the crypt region of the ileum

**Effect of MRx0518 on ileal CD8α cells**

Terminal ileum sections

Ileum cryosections immunolabelled with antibodies against CD8α (green) and DAPI (blue)

MRx0518 – Immuno-oncology

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MRX0518 BOOSTS THE EFFICACY OF CHECKPOINT BLOCKADE – ANTI-CTLA-4

**EMT6 Breast Carcinoma Model**

**Mice:** Balb/c  
**Tumour induction:** $10^6$ EMT6 cells SC  
**MRx0518 dosing:** D-14 to D24  
**Anti-CTLA-4 dosing:** TWx2 from D10  
**Readouts:** Tumour volume; tumour, spleen, serum, MLN, intestinal immunology; microbiome analysis; others

**Anti-CTLA-4 combination flatlines tumours**

- MRx0518 and anti-CTLA-4 combination therapy assessed in EMT6 breast carcinoma model
- MRx0518 monotherapy reduced tumour volumes comparably to anti-CTLA-4 treatment
- MRx0518 + anti-CTLA-4 combination virtually eradicated mouse tumours
- Immunology, microbiome, metabolomics, statistical analysis currently ongoing
MRx0518 PUTATIVE EFFECTOR MOLECULES

Transcriptomics
- Whole genome sequencing and genome mining
- Targeted bacterial effector and host response
- Mono-colonised mice (dual RNASeq)

Surfacome/secretome
- ID of MRx0518 MAMPS
- Multiple targets of interest related to host signalling

Flagellin
- Flagellin identified as potential contributing molecule
- Activation of TLR5 by flagellin known to inhibit tumour proliferation in vivo
- In depth investigation of MRx0518 flagellin has identified strain-specific signalling effects
Flagellin in MRx0518 culture activates NF-κB and TLR5 signalling

- Little to no NF-κB/TLR5 activation when flagellin is knocked out
- Supernatant of the reference strain does not activate TLR5
- Effects of MRx0518 were exacerbated by higher abundance of flagellin in the supernatant

Dose-response with recombinant flagellins

- Purified recombinant flagellins activate TLR5
- MRx0518 flagellin is more potent than the reference flagellin at low concentrations
**Inactivation of MRx0518 flagellin gene abolishes immunostimulatory effects**

- No stimulation of immune response gene expression in comparison with MRx0518 when flagellin gene is inactivated.
- Stimulatory effect of MRx0518 recombinant flagellin.
- IL-8 stimulation abolished by flagellin gene inactivation.
- Stimulatory effect of MRx0518 recombinant flagellin.
MOA: MRX0518 ACTS VIA FLAGELLIN-INDUCED TLR5 SIGNALLING

Increased immunostimulatory effects of MRx0518 translates into increased performance in preclinical cancer models

- MRx0518 is a flagellated bacterium and host TLR5 signalling contributes to its immuno-stimulatory effects
- The active flagellin protein, FliC, is produced by the bacterium
- The MRx0518 FliC is a more potent TLR5 agonist than homologous flagella from other strains of the same species
- MRx0518 outperforms reference strain in in vivo syngeneic tumour models
UK neoadjuvant monotherapy study

- Window study: dosing between diagnosis and surgery
- Up to 120 patients; multiple solid tumour types
- Placebo-controlled
- Clean background: treatment naïve patients

Primary endpoint: safety and tolerability
- Suite of immunological biomarkers
- Full MicroDx microbiome analysis
- MHRA have cleared CTA; commences Q4 2018

Neoadjuvant study design:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Surgery</th>
<th>Long term follow-up</th>
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<tbody>
<tr>
<td>- Immunological markers</td>
<td>- Immunological markers</td>
<td>- Safety and survival</td>
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<tr>
<td>- MicroDx microbiome analysis</td>
<td>- MicroDx microbiome analysis</td>
<td>- Up to 60 months post-surgery</td>
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<td>- Metabolomics</td>
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Combination study with Keytruda®

- Assessing ability of MRx0518 to re-engage immune system to respond to checkpoint blockade

- Up to 132 patients who have progressed on prior anti-PD-1 therapy

- Four different solid tumour types (melanoma, bladder, renal and NSCLC)

- Primary outcome measure: Safety & tolerability

- Secondary outcome measure: Tumour response based on RECIST

- Exploratory outcome measures: immunological markers, microbiome profile, overall survival up to two years

- Commences Q4 2018
MRX0518 – SUMMARY

• Gut commensal bacterium with highly immuno-stimulatory host-response profile, unique in the 4D strain library

• Efficacy in three different syngeneic tumour models as a monotherapy and outperforms other LBPs in the IO space in reduction of tumour growth

• Combination therapy with anti-CTLA-4 flatlines tumours in breast cancer model

• Increases tumour CD8+ : Treg ratio

• TLR5 signalling via bacterial flagellin contributes to immunological effects; MRx0518 has more potent flagellin than reference strains

• UK monotherapy study: window study and biomarker play in treatment naïve background; Commences 2018

• US combination study: Clinical collaboration with Merck and Co.; combination with Keytruda® in patients who have failed prior anti-PD-1 therapy
<table>
<thead>
<tr>
<th>2018</th>
<th>Q4</th>
<th>2019</th>
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<tr>
<td><strong>June</strong></td>
<td><strong>August ✓</strong></td>
<td><strong>Asthma Phase Ib study opening</strong></td>
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<tr>
<td>Presentation Blautix Phase Ib data at DDW 2018 ✓</td>
<td>Publication preclinical asthma data</td>
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<td><strong>September ✓</strong></td>
<td><strong>Publication IBS clinical observational study</strong></td>
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<tr>
<td>Readout Phase Ib Crohn’s disease</td>
<td>Initiate immuno-oncology monotherapy trial</td>
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<td><strong>September ✓</strong></td>
<td><strong>Initiation immuno-oncology combination trial</strong></td>
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<td>IBS Phase II study opening</td>
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• Deep, broad pipeline across multiple therapeutic areas
• Largest intellectual property estate in microbiome space
• Only microbiome company with true ‘end-to-end’ capability
• In patient data with IBS and Crohn’s; first mover in cancer and asthma
• Targeting four clinical programmes by end 2018