Enabling scientific advances to positively impact human health

Your genes. Your health.

Yourgene Health plc
Capital Markets Day

5 November 2019
Strategic Update
Lyn Rees, CEO
Yourgene Health
Key commentary

• **International molecular diagnostics group** which develops and commercialises genetic screening products and services in **over 60 territories**
  - First forays into US market via new Yourgene Health Inc entity

• **Proprietary DNA analysis technology** used to develop safer and improved non-invasive screening tests

• **Acquired Elucigene Diagnostics** in April 2019 for an enterprise value of £8.8m
  - Integration proceeding very well, strong cultural alignment and synergy savings >£0.5m

• **Group now has a suite of leading CE-IVD NGS & PCR products** focused on **reproductive health** including non-invasive prenatal screening (NIPT), Cystic Fibrosis and invasive prenatal aneuploidy screening

• Technology agreements with **Thermo Fisher** and **Illumina**, market leaders in NGS and PCR instrumentation

• **Pipeline of new innovative diagnostic solutions** in development for reproductive health and **oncology** clinical segments including DPYD - the **Group’s first oncology product**

• **Positive H1 trading update**
Yourgene Health

By numbers

A leading NIPT test over 99% accurate(1)

67% volume growth year on year

£8.9 million for year ending 2018/19 revenue (45% growth)

£12.5 million pro-forma revenue (2)

Revenues £7.8 million for the six months to 30 September 2019, up 98% from previous year

Sales in over 60 countries

Global partners

(1) Relating to Down’s syndrome, Edwards syndrome and Patau’s syndrome (2) Pro-forma revenue calculated as £8.9m revenue calculated for 12 months to 31 March 2019 for Yourgene Health and £3.6m to 31 December 2018 for Elucigene Diagnostics
Key investment highlights

1. A leading next generation portfolio of NIPT and PCR solutions in large, fast growing markets with quantitative benefits versus standard of care

2. Blue-chip industry partnerships including leading NGS players, Thermo Fisher and Illumina

3. Real commercial momentum 98% revenue growth with clean balance sheet

4. In-house development expertise with pipeline of additional complementary products

5. Elucigene is Yourgene’s latest acquisition in a fragmented market that presents opportunity for further consolidation

6. Experienced management team with combined c.20% shareholding and track-record of executing a commercialisation strategy
Integration highlights

• Integrated marketing and range-selling now effective
• Global sales team conference held in July
• £0.5m annualised integration cost synergies identified and implementation underway
• Head office UK property consolidation well advanced
• Registered office changed to Citylabs 1.0
• All departments combined into single management structure
• Process, systems and regulatory harmonisation plan developed for implementation by mid 2020
• First IVD product launched post acquisition (DPYD)
• Integrated manufacturing operations
• Strong cultural alignment
**Transformational 24 months**
**Foundation for future growth**

*Elucigene Diagnostics acquisition offers an opportunity to accelerate Yourgene’s future growth strategy*

<table>
<thead>
<tr>
<th>2017</th>
<th>2018</th>
<th>2019+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Building a Global Platform</strong></td>
<td><strong>Positioning for Accelerated Growth</strong></td>
<td><strong>Accelerating Ahead</strong></td>
</tr>
<tr>
<td>✓ Completion of Yourgene Biosciences acquisition</td>
<td>✓ NGS collaborations agreed with Abnova and Coastal Genomics</td>
<td>✓ Major capital and commercial agreement with Thermo Fisher, writing off £12.7m of loans for 9% shareholding in Company</td>
</tr>
<tr>
<td>✓ Increased access to Asia, the world's fastest growing NIPT market</td>
<td>✓ Lyn Rees appointed CEO</td>
<td>✓ High throughput product launched (Sage 32 plex)</td>
</tr>
<tr>
<td>✓ IONA® test validated for Thermo Fisher’s Ion S5 instrument range</td>
<td>✓ Final litigation settlement with Illumina ended three and a half year IP dispute</td>
<td>✓ 82,000 NIPT tests completed in year ended 31 March 2019</td>
</tr>
<tr>
<td>✓ New laboratory partnerships established in Europe, Middle East and Asia</td>
<td>✓ Entered into licence and supply partnership agreement with Illumina</td>
<td>✓ Transformational acquisition</td>
</tr>
<tr>
<td>✓ 24,000 NIPT tests completed in the year ended 31 March 2017</td>
<td>✓ 50,000 NIPT tests completed in the year ended 31 March 2018</td>
<td>✓ Product line expansion with DPYD launched</td>
</tr>
<tr>
<td></td>
<td>✓ Changed name to Yourgene Health</td>
<td>✓ Deliver US market entry</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Regulatory submission for NIPT on Illumina platform</td>
</tr>
<tr>
<td>Strategic priorities for growth</td>
<td></td>
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<td>--------------------------------</td>
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**Organic**

<table>
<thead>
<tr>
<th>Product penetration</th>
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<tbody>
<tr>
<td><strong>Sell More in Existing Channels</strong></td>
</tr>
<tr>
<td>Drive worldwide sales of NIPT, Cystic Fibrosis and other Reproductive Health products and services by targeting further expansion through direct and key distribution channels</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Geographic expansion</th>
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</thead>
<tbody>
<tr>
<td><strong>Sell into New Territories</strong></td>
</tr>
<tr>
<td>Expand directly and through distributors into new geographies, including those opened up by Illumina licence agreement</td>
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<table>
<thead>
<tr>
<th>Product expansion</th>
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</thead>
<tbody>
<tr>
<td><strong>New Product Lines and Content</strong></td>
</tr>
<tr>
<td>Leverage our technical and regulatory expertise and partnerships to extend our genetic testing offering</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>M&amp;A</th>
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<tbody>
<tr>
<td><strong>Consolidator in the Market</strong></td>
</tr>
<tr>
<td>Delivering integration benefits of the Elucigene acquisition, creating a strong platform for future M&amp;A activity</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Inorganic</th>
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<tbody>
<tr>
<td><strong>Fragmented market with minimal medium-sized entities, presents opportunity for consolidation</strong></td>
</tr>
<tr>
<td>Considering additional selective synergistic M&amp;A opportunities</td>
</tr>
</tbody>
</table>
Commercial Strategy
Hayden Jeffreys, COO
Commercial Strategy
Strategic priorities for growth

Principals of current and future growth

Product penetration

*Sell More in Existing Channels*

- Range selling - expanded product offering through existing sales channels
- Increasing income per customer
- Expanded commercial partnerships with *Blue Chip* diagnostic companies
- Comprehensive support packages to drive sales & volume: marketing, sales support, clinical education

Geographic expansion

*Sell into New Territories*

- Expanding into new markets such as US, Australia
- New customers in existing markets – multiple routes to customers
- Increase global sales coverage
- Doubled customer base >300 customers

Product expansion

*New Product Lines and Content*

- Launching new services through our own laboratories
- Launch new products to our customers i.e. DPYD
- Providing bespoke solutions on commercial basis for key partners such as bioinformatics and software development
Expanded Global Coverage

Expanding reach
Yourgene coverage
Extra Elucigene coverage
Development markets

YH Inc
Comprehensive Portfolio of Reproductive Health Solutions

Carrier screening for Cystic Fibrosis

Newborn screening for Cystic Fibrosis

Pre-conception:
- Male Factor Infertility

Prenatal:
- QST*R Recurrent Pregnancy Loss
- Genetic Thrombosis Risk Test
- Non-invasive prenatal testing (NIPT): IONA test and Sage prenatal screen
- QST*R Rapid Aneuploidy Analysis
Future solutions across the Reproductive Health pathway

New Product Roadmap
- Apply successful existing model to additional tests
- Partnering across the value chain
- Diversify into gene analysis
- Inorganic product acquisition

Potential Future Products
- CF US version
- PCR development capability
- NGS variants of Elucigene products

<table>
<thead>
<tr>
<th>Year</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
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<tbody>
<tr>
<td>NIPT on New Platforms</td>
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</table>
cfDNA enables screening for Reproductive Health & Oncology

Reproductive Health and Cancer are the Largest Segments

- Reproductive Health (NIPT, IVF, Newborn Screening) - 54%
- Cancer (Risk Prediction, Therapy selection & Response) - 27%
- Medelian Disorders (Rare Disease Diagnostics)
- Metabolic Immune (Diagnostic)
- Cardiovascular (Risk Prediction, Diagnostic)
- Other

Our extensive successful commercial experience in using cell-free DNA (cfDNA) in Reproductive Health screening has a strong foundation for transition to Oncology screening where the same sample type and technology is deployed.
Current offering and future expansion into Oncology

cfDNA enables screening for current and future oncology products and services

New Product Roadmap
- Apply successful existing model to additional tests
- Partnering across the value chain
- Diversify into gene analysis
- Inorganic product acquisition

Potential Future Products
- Additional
- PCR development capability for oncology
- NGS oncology products for partners

<table>
<thead>
<tr>
<th>Year</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
<th>2023</th>
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</thead>
<tbody>
<tr>
<td>DPYD Launch</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Extended Oncology Service Menu</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Additional Oncology Menu</td>
<td></td>
<td></td>
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</tbody>
</table>
DPYD Deficiency can cause severe and sometimes lethal side effects in patients receiving 5-Fluorouracil (5-FU) chemotherapy used to treat a range of cancers.

DPYD genotyping can identify these patients with DPD deficiency allowing an alternative treatment to be offered. Recommended by The Clinical Pharmacogenetics Consortium (CPIC) guidelines.

Estimated that 2 million people are treated with 5-FU every year.
- Prevents unnecessary deaths
- Reduces the incidence of hospital admissions
Product & service portfolio
Delivering world class solutions

**Reproductive Health**
- NIPT
- QST*R Rapid Aneuploidy Analysis
- QST*R Pregnancy Loss
- Male Factor Infertility
- Newborn screening: cystic fibrosis carrier screening

**Bioinformatics**
- Product development and consultation
- Yourgene *Flex* Analysis Software

**Oncology**
- DPYD pharmacogenetics test
- BRCA1 and BRCA2 screening
- cfDNA breast / colon / lung cancer screening
- Cancer Hotspot screening

**Research service**
- Whole genome sequencing
- Metagenomics for microbiome
Half year trading update
Barry Hextall, CFO
Revenue growth driven by global progress

Revenue progression

- Revenue has grown in each of the past six half year periods
- Six months to 30 September 2019 (H1 20) +98% vs equivalent prior year period
- Rapid organic growth plus accretive acquisitions driving momentum

Group segmental sales by geography

- Elucigene acquisition and NIPT reimbursement growing UK & Europe during Illumina transition
- Rapid international growth (+122%) due to NIPT progress and oncology services in Asia, plus first revenues in USA
- 2020 opportunity for geographic expansion opened up by September 18 Illumina licence agreement
## H1 Trading Update

### Segment analysis

#### Regional segments

<table>
<thead>
<tr>
<th>Region</th>
<th>6 months to 30 Sept 2019</th>
<th>6 months to 30 Sept 2018</th>
<th>Growth</th>
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<tbody>
<tr>
<td>UK</td>
<td>£1.1m</td>
<td>£0.8m</td>
<td>+35%</td>
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<tr>
<td>Europe ex-UK</td>
<td>£1.6m</td>
<td>£0.8m</td>
<td>+90%</td>
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<tr>
<td>International</td>
<td>£5.1m</td>
<td>£2.3m</td>
<td>+122%</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>£7.8m</strong></td>
<td><strong>£3.9m</strong></td>
<td><strong>+98%</strong></td>
</tr>
</tbody>
</table>

#### Product segments

<table>
<thead>
<tr>
<th>Segment</th>
<th>6 months to 30 Sept 2019</th>
<th>6 months to 30 Sept 2018</th>
<th>Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIPT</td>
<td>£4.8m</td>
<td>£3.6m</td>
<td>+34%</td>
</tr>
<tr>
<td>Reproductive health</td>
<td>£1.6m</td>
<td>£0.0m</td>
<td>n/a</td>
</tr>
<tr>
<td>Oncology &amp; research</td>
<td>£1.4m</td>
<td>£0.3m</td>
<td>+290%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>£7.8m</strong></td>
<td><strong>£3.9m</strong></td>
<td><strong>+98%</strong></td>
</tr>
</tbody>
</table>

- Elucigene acquisition focused on UK & Europe
- French reimbursement maintaining NIPT momentum during Illumina transition
- APAC and ME showing string momentum
- First US revenues

- NIPT remains the core revenue stream at 62% of H1 revenues
- 20% derived from reproductive health products generated by the acquired Elucigene
- 18% derived from oncology and research services activities in Asia, plus future DPYD revenues
DPYD Genotyping

5 November 2019

Dr Stephen Little
Founder & Vice Chair
Safety vs Efficacy in Drug Treatments

• All drugs balance dose vs side effects – over the past 20 years there has been increasing use of companion diagnostics (CDx) to personalise the medicine

• **Efficacy** - Some CDx markers identify individuals who have the right genetic profile to respond to a drug eg EGFR/Iressa

• **Safety** - Many CDx markers identify individuals who are likely to suffer side effects with a drug and should be offered a lower dose or an alternative

• In the published FDA list of 180 Rx/Dx combinations over half are safety related

• One of these is DPYD
DPD Deficiency and 5-FU treatment
Pharmacogenomic impact

• 5-FU (aka Efudex, Carac, Tolak, Fluoroplex, Xeloda) is a chemotherapeutic agent ($billions pa) used in the treatment of a range of cancers:
  • Colorectal
  • Gastric
  • Breast

• Estimated that 2 million people are treated with 5-FU every year.
  • 10-20% of these patients will be hospitalised because of 5-FU toxicity (200,000 - 400,000).
  • 0.1-1% of these patients will die as a result of 5-FU toxicity (2,000 – 20,000)

• DPYD genotyping can identify patients at risk of 5FU toxicity allowing an alternative treatment to be offered.
  • Prevents unnecessary deaths
  • Reduces the incidence of hospital admissions
  • Recommended by The Clinical Pharmacogenetics Consortium (CPIC) guidelines
How does the cancer drug 5-FU work?

5-FU inhibits Thymidylate Synthase leading to cell death in fast growing cancer cells.
Why is the DPYD gene important?

If DPD is functioning sub-optimally the drug is not removed from the body causing an effective overdose and severe side effects.
The Elucigene DPYD assay is a simple genotyping test that can identify patients with DPD deficiency allowing an alternative treatment to be offered.

- DPYD genotyping prior to treatment:
  - Prevents 5-FU associated toxicity:
    - Prevents unnecessary deaths
    - Reduces the incidence of hospital admissions
  - 6 SNPs covered that are recommended by Clinical Pharmacogenetics Consortium (CPIC) for DPYD genotyping
- Two tube PCR kit
- 100% accuracy
- 100% reproducibility and repeatability
- CE marked
<table>
<thead>
<tr>
<th>Type of Analysis</th>
<th>Amount of Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Genome Sequencing</td>
<td>3,300,000,000 base pairs</td>
</tr>
<tr>
<td>Whole Exome Sequencing</td>
<td>30,000,000 base pairs</td>
</tr>
<tr>
<td>Targeted Sequencing</td>
<td>100,000 base pairs</td>
</tr>
<tr>
<td>Multiplex PCR panels</td>
<td>10-100 base pairs</td>
</tr>
<tr>
<td>Single gene testing</td>
<td>1-10 base pairs</td>
</tr>
</tbody>
</table>
# Technology v Application

<table>
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<tr>
<td>Single gene testing</td>
<td>1-10 base pairs</td>
</tr>
</tbody>
</table>

**DNA Sequencing**

**PCR**

- **Cost**
- **Time**
- **Complexity**
Genetic variation in the activity of DPD

Clinical Guidelines

The Clinical Pharmacogenetics Consortium (CPIC) published a new guideline in 2017 for DPYD genotyping and they recommend testing for the 6 SNPs outlined.

- The CPIC guidelines also recommend 5-FU dose based on DPYD genotype.
- Elucigene DPYD assay tests for the most significant DYPD alleles.

https://cpicpgx.org/guidelines/guideline-for-fluoropyrimidines-and-dpyd/
DPYD Genotype and 5-FU Dose

- DPD Deficiency is an autosomal recessive condition.
- Each SNP has been given an activity score (CPIC, 2017).
- The total activity score determines the 5-FU dose.

<table>
<thead>
<tr>
<th>SNP</th>
<th>Activity Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>c.1905+1G&gt;A</td>
<td>0</td>
</tr>
<tr>
<td>c.1679T&gt;G</td>
<td>0</td>
</tr>
<tr>
<td>c.2846A&gt;T</td>
<td>0.5</td>
</tr>
<tr>
<td>Haplotype B3</td>
<td>0.5</td>
</tr>
<tr>
<td>Wildtype SNP</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Activity Score</th>
<th>DPD Function</th>
<th>5-FU Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No Function</td>
<td>Prescribe alternative</td>
</tr>
<tr>
<td>1</td>
<td>Decreased Function</td>
<td>Reduce dose by 50%</td>
</tr>
<tr>
<td>1.5</td>
<td>Decreased Function</td>
<td>Reduce dose by 25%</td>
</tr>
<tr>
<td>2</td>
<td>Normal Function</td>
<td>Normal dose</td>
</tr>
</tbody>
</table>
Positive Cancer Diagnosis

Blood Sample Taken and Transported to Lab

DNA Mutation Analysis

Results Reported

Commence 5-FU Chemotherapy

Adjust chemotherapy

<7 days
Early access programme ongoing
Clinical sites

**DPYD**

- Douglas Hanly Moir, Australia.
- Sahlgrenska University Hospital, Sweden.
- IMOMA, Spain.
- Southern General Hospital, Scotland.
- Leeds Teaching Hospital, England.
- St Mary’s Manchester, England.
- UCL, Belgium.
- UZ Gent, Belgium (TBC)
Prevention of 5-fluorouracil-induced early severe toxicity by pre-therapeutic dihydrouracil dehydrogenase deficiency screening: Assessment of a multiparametric approach

Michele Boisdron-Celle, Olivier Capitain, Roger Faroux, Christophe Borg, Jean Philippe Metges, Marie Pierre Galais, Mehdi Kaassis, Jaafar Bennouna, Karine Bouhier-Leporrier, Eric Francois, Isabelle Baumgaertner, Véronique Guerin-Meyer, Dana Cojocarasu, Celia Roemer-Becuwe, Claire Stampfl, Ludovic Rosenfeld, Thierry Lecompte, Virginie Berger, Alain Morel, Erick Gamelin

ARTICLE INFO

Keywords: 5-Fluorouracil, Lethal toxicity, DPD deficiency, Multiparametric approach

ABSTRACT

5-Fluorouracil (5-FU)-based treatments can lead to early-onset severe (4%-5%) even fatal (0.3%) toxicities in patients with dihydrouracil dehydrogenase (DPD) deficiency. This multicenter prospective cohort study aimed to assess the clinical benefit of pretherapeutic screening for DPD deficiency using a multiparametric approach. Two parallel cohorts of patients treated with 5-FU-based chemotherapy for colorectal carcinoma were compared in a prospective nonrandomized study. In arm A, patients had DPD deficiency screening before treatment, whereas in arm
Clinical Utility

- With DPYD genotyping
  - 11% early toxicity
  - 0 deaths/1000

- Without DPYD genotyping
  - 17% early toxicity
  - 2.5 deaths/1000

Trial stopped on ethical grounds
Clinical Utility in the News

**Daily Mail Online**

**Revealed: How hundreds are being killed by chemo meant to save them (it’s down to a little known side effect which can be avoided with a simple £60 blood test)**

- Some genetic disorders mean patients can’t process chemo drug capcitabine
- Dihydropyrimidine dehydrogenase (DPD) means the liver can’t process the drug
- The deficiency is shared by five to eight per cent of the population

By DAVID ROSE
PUBLISHED: 22:01, 6 October 2018 | UPDATED: 22:02, 6 October 2018

- Share 14k shares
- View comments

For West Sussex farmer Keith Gadd and his family, last year’s Father’s Day, June 18, was an unusually happy one. That April, he had undergone major surgery to remove a sizeable tumour from his bowel, but the operation had been a complete success: scans showed he was cancer-free, and he was rapidly regaining his physical fitness, able to walk miles and shift bales of hay.

He and his daughter Louise, son-in-law Martin and youngest granddaughter Daisy enjoyed a summer picnic on his land near Petworth. Afterwards, he hurried off to meet his wife Pamela and friends from their hiking group for afternoon tea and cakes.

**USA Today News**

**Her cancer surgery was a success. Then a genetic condition let a chemo drug ravage her body**

By Lindy Washburn | North Jersey Record
Published 11:44 AM EDT Nov 2, 2019

He knew the cure could be more painful than the disease, but his wife’s condition was worse than he could have imagined. Her first chemotherapy treatment after colon cancer surgery had flattened her.

Kerrie Frettitore was 42. She’d come through surgery well, but her oncologist had recommended chemo after cancer cells were detected in one of her lymph nodes.

The New Jersey couple had been upbeat, hoping to maintain a comfortable routine and a positive attitude for their three kids, the youngest of whom was 2. Kerrie’s good health and vitality would carry her through chemo’s side effects, they hoped.
Elucigene DPYD assay is a simple genotyping test that can identify patients with DPD deficiency allowing an alternative treatment to be offered.

The Elucigene DPYD assay will save lives and save money and supports our mission of enabling scientific advances to positively impact human health.
Enabling Development Partnerships with Yourgene Flex™ Analysis

Dr. Matthew C. Forman
Head of Bioinformatics & Software

5th November 2019
Overview

• NGS (Next Generation Sequencing) Analysis Software
  • Introduction: What does it do?
  • History and limitations

• Enabling new opportunities: Yourgene Flex™
  • What is Flex? Why is Flex?
  • Partnership, product and intrinsic benefits
  • Progress and benefits to date
NGS Analysis Software

Introduction & History
Processes NGS sequence data, combined with patient/sample information, into a clinical test report.

- Read and filter DNA sequence reads
- Map reads to genome
- Analyse DNA location data (statistical models/A.I.)
- Calculate test results and apply QC checks
- Generate test report
NGS Analysis Software

History

Evolution from research-grade bioinformatics pipelines

- Freely-available tools developed without commercial considerations.
- Created without medical-grade code or development processes.

Limited integration with lab systems

User experience not generally a focus

Limited clinical data entry/reporting capabilities
NGS Analysis Software

Yourgene approaches (to date)

• **IONA® Software** – *analysis solution for IONA® test*
  • Written ground-up as medical-grade software (market first).
  • Principles and process according to ISO/IEC 62304.
  • Fully catered for clinical user needs through a full requirements exercise.
  • Supports controlled end-to-end sample workflow

• **Sage™ Link** – *analysis solution for Sage™ prenatal screen*
  • Developed from Yourgene Bioscience code (Taiwan).
  • Platform for innovation in NGS bioinformatics algorithms.
  • Bespoke configuration to individual clinic workflows which is more flexible but less controlled
Enabling new opportunities:
Yourgene Flex™
Enabling new opportunities with software
Aligning with Business Goals

• Forge contract development partnerships
  • Need.. Reconfigurable analysis software to suit customer requirements

• Broaden in-house product development
  • Needs.. Ability to apply across diverse test portfolio
  • Needs.. Efficient software code re-use across products
  • Needs.. Development team/resource flexibility

A modular software system could meet all these needs
Introducing Yourgene Flex™

What is modular software?

Single software platform ...

NGS Sequence Data from lab workflow

GUI/Data entry: patient and sample info

Analysis Software Application

Clinical Report
Introducing Yourgene Flex™
A modular platform

Combining the best of IONA® and Sage™
...in modular form:

All blocks are re-usable
Introducing Yourgene Flex™
Strategic Partnership and Product benefits

- **Medical-grade software quality** across applications
  - Compatible with regulatory submissions for faster route-to-market

- **Enables contract development partnerships**
  - Re-use core modules
  - Develop custom modules as needed

- **Enables more efficient internal product development**
  - Tailored solutions for test applications

- **Potential partnerships with other software developers**
  - ...offering modules alone, with developer support
Conclusion

Key points

• A unique reconfigurable, medical-grade NGS IVD analysis software framework
• All code developed within fully validated, risk managed process
• Modular approach enables re-use of core, validated modules, and also design of completely bespoke routines as needed
• Supports ambition to develop strategic IVD product development partnerships
• Ability to broaden and accelerate in-house product development pipeline

Thank you!
NIPT: a clinical perspective
Prof Basky Thilaganathan
Our responsibility is to offer parents the option to accurately assess risks rather than to instruct or create arbitrary definitions of (high) risk.
Fetal trisomy
Current standard of care

- Combine scan and blood tests
- False positive rate of 3%
- Detection rate of >75%
## Analysis of cell-free DNA in maternal blood in screening for fetal aneuploidies: updated meta-analysis

M. M. GIL*, M. S. QUEZADA*, R. REVELLO*, R. AKOLEKAR*† and K. H. NICOLAIDES*†

### Table 2: Studies reporting on the application of cell-free DNA analysis of maternal blood in screening for trisomy 21 in singleton pregnancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>GA (weeks)</th>
<th>Trisomy 21</th>
<th>Non-trisomy 21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled analysis (% (95% CI))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed effects model</td>
<td></td>
<td></td>
<td>99.2 (98.5–99.6)</td>
<td>0.09 (0.05–0.13)</td>
</tr>
<tr>
<td>Random effects model</td>
<td></td>
<td></td>
<td>99.2 (98.5–99.6)</td>
<td>0.09 (0.05–0.14)</td>
</tr>
<tr>
<td>Cochran’s Q</td>
<td></td>
<td></td>
<td>10.7230 (P = 0.9858)</td>
<td>27.2044 (P = 0.244)</td>
</tr>
<tr>
<td>I² statistic (% (95% CI))</td>
<td></td>
<td></td>
<td>0.0 (0.0–39.6)</td>
<td>15.5 (0.0–48.6)</td>
</tr>
<tr>
<td>Egger bias</td>
<td></td>
<td></td>
<td>−0.0512 (P = 0.6525)</td>
<td>0.2367 (P = 0.2270)</td>
</tr>
</tbody>
</table>

*Data are presented as percentage (%) with 95% CI.
Communicating probability

0.3%  

99.7%
UK NSC Care Pathway

Combined or serum biochemistry test

Detailed scan

No anomalies

Fetal anomalies

Options

CVS/amnion (PCR only)

NIPT

Routine care

Offer CVS+ Array CGH

Chance >1:150

No anomalies

Offer CVS+ Array CGH

Routine care

NIPT

CVS/amnion (PCR only)
Clinical implementation of routine screening for fetal trisomies in the UK NHS: cell-free DNA test contingent on results from first-trimester combined test

M. M. GIL*, R. REVELLO*, L. C. POON*, R. AKOLEKAR*† and K. H. NICOLAIDES*

- 90% chose NIPT over CVS
- 32% T21 babies live born

Uptake, outcomes, and costs of implementing non-invasive prenatal testing for Down’s syndrome into NHS maternity care: prospective cohort study in eight diverse maternity units

Lyn S Chitty,1,2 David Wright,3 Melissa Hill,1 Talitha I Verhoef,4 Rebecca Daley,2 Celine Lewis,1,2
### NIPT REPORT

**Genetics - the SAFE test Laboratory**
Jenner Wing - Basement - Room 01.242
St George's University Hospitals NHS Foundation Trust
Blackshaw Road
London
SW17 0QT

**Rohan Taylor FRCPATH (Consultant Clinical Scientist)**
John Short (Technical and R&D Manager)
Tel: 020 725 5864
E-mail: theSAFEtest-report@nhs.net

### PATIENT DETAILS:

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>00175</th>
<th>Maternal Age (at test)</th>
<th>37 years 0 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Surname</td>
<td>Smith</td>
<td>Gestation Age (at test)</td>
<td>37 weeks 0 days</td>
</tr>
<tr>
<td>Patient Forename</td>
<td>Sharon</td>
<td>Multiple Pregnancy Status</td>
<td>Single</td>
</tr>
<tr>
<td>Clinician Name</td>
<td>David Dickinson</td>
<td>Patient Date of Birth</td>
<td>13th Dec 1977</td>
</tr>
<tr>
<td>Hospital/Clinic Name</td>
<td>Ambridge County Hospital</td>
<td>Date of Blood Draw</td>
<td>21st Oct 2014</td>
</tr>
</tbody>
</table>

### TEST RESULTS:

<table>
<thead>
<tr>
<th>Trisomy</th>
<th><em>BACKGROUND RISK (before the SAFE test)</em></th>
<th>SAFE TEST RISK SCORE</th>
<th>CLINICAL SUMMARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21</td>
<td>1 in 171</td>
<td>Greater than 99%</td>
<td>HIGH RISK – INVASIVE TEST RECOMMENDED</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>1 in 542</td>
<td>Less than 1 in 1,000,000 (&lt;0.00001%)</td>
<td>LOW RISK</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>1 in 1655</td>
<td>Less than 1 in 1,000,000 (&lt;0.00001%)</td>
<td>LOW RISK</td>
</tr>
</tbody>
</table>

The SAFE test is indicated for screening NOT diagnosis – (results should be reviewed and discussed with the healthcare provider).

### SUPPLEMENTARY INFORMATION FOR HEALTHCARE PROVIDERS:

- Originating sample ID: 500000175
- Sequencing run and sample validity checks passed: YES
- Sample notes (if entered): 
- Report generated: 09 Dec 2014 15:08
- IONAS® Software version: TDA: 1.0.4617.481; DAA: 1.0.4619.438

- The SAFE test detects trisomies by analysing placenta-derived cell-free DNA extracted from the mother’s plasma. The relative amount of chromosomes 13, 18 and 21 are used to calculate a likelihood ratio to predict the presence of a trisomy. This is then adjusted according to the prior risk of the mother at the time of sampling and an adjusted probability calculated for the fetus being affected.
- The SAFE test is a screening test and an increased risk result should be discussed with the healthcare provider and confirmed by an appropriate diagnostic test following an invasive procedure (e.g. amniocentesis).
- The age-adjusted probability (risk score) is capped. The cap is derived from an estimate of the predictive value of a high risk test result.
- in dichorionic twins, the detection rate is reduced from greater than 99% to about 95% (before age adjustment).
- *Background risk is conventionally based on maternal age. The prior screening test risk result will be used when samples are sent in high-risk women.*

Powered by the IONAS® test - a registered trademark of Premaitha Limited.
### Commercial justification for NOT measuring FF:

- **Unnecessary** (1:40,000 chance of T21 in routine pregnancy)
- **Cost** (laboratory versus bioinformatic methods)
- **Increases no-call rate** (for low FF)

### Table 1: Non-invasive prenatal test (NIPT) results for two non-pregnant women from five commercial laboratories

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Test result available</th>
<th>Details</th>
<th>Test result available</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab A</td>
<td>No</td>
<td>Insufficient fetal cfDNA for accurate NIPT evaluation</td>
<td>No</td>
<td>Insufficient fetal cfDNA for accurate NIPT evaluation</td>
</tr>
<tr>
<td>Lab B</td>
<td>No</td>
<td>Unable to report due to low fetal fraction (fetal fraction reported as 0.6%)</td>
<td>No</td>
<td>Unable to report due to low fetal fraction (fetal fraction reported as 0.6%)</td>
</tr>
<tr>
<td>Lab C</td>
<td>Yes</td>
<td>Negative, consistent with female fetus (fetal fraction 4.3% reported on request)</td>
<td>Yes</td>
<td>Negative, consistent with female fetus (fetal fraction 3.9% reported on request)</td>
</tr>
<tr>
<td>Lab D</td>
<td>Yes</td>
<td>No aneuploidy detected, two sex chromosomes (XX)</td>
<td>Yes</td>
<td>No aneuploidy detected, two sex chromosomes (XX)</td>
</tr>
<tr>
<td>Lab E</td>
<td>Yes</td>
<td>No aneuploidy detected, two sex chromosomes (XX)</td>
<td>Yes</td>
<td>No aneuploidy detected, two sex chromosomes (XX)</td>
</tr>
</tbody>
</table>
### Detection Rate vs False Positive Rate

<table>
<thead>
<tr>
<th>FF (%)</th>
<th>MA + cfDNA</th>
<th>CT + cfDNA</th>
<th>MA + cfDNA</th>
<th>CT + cfDNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1%</td>
<td>37%</td>
<td>86%</td>
<td>6.0%</td>
<td>2.6%</td>
</tr>
<tr>
<td>1%</td>
<td>44%</td>
<td>87%</td>
<td>6.0%</td>
<td>2.5%</td>
</tr>
<tr>
<td>2%</td>
<td>62%</td>
<td>90%</td>
<td>6.0%</td>
<td>2.1%</td>
</tr>
<tr>
<td><strong>3%</strong></td>
<td><strong>78%</strong></td>
<td><strong>94%</strong></td>
<td><strong>4.6%</strong></td>
<td><strong>1.5%</strong></td>
</tr>
<tr>
<td>4%</td>
<td>88%</td>
<td>96%</td>
<td>2.8%</td>
<td>1.0%</td>
</tr>
<tr>
<td>5%</td>
<td>94%</td>
<td>98%</td>
<td>1.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>6%</td>
<td>97%</td>
<td>99%</td>
<td>0.7%</td>
<td>0.2%</td>
</tr>
<tr>
<td>7%</td>
<td>&gt;99%</td>
<td>&gt;99%</td>
<td>0.3%</td>
<td>0.1%</td>
</tr>
<tr>
<td>8%</td>
<td>&gt;99%</td>
<td>&gt;99%</td>
<td>0.1%</td>
<td>&lt;0.1%</td>
</tr>
<tr>
<td>&gt;9%</td>
<td>&gt;99%</td>
<td>&gt;99%</td>
<td>&lt;0.1%</td>
<td>&lt;0.1%</td>
</tr>
</tbody>
</table>

**Optimising test performance**

**Use correct a-priori risk**

**FF integrated (dynamic FF)**
Over 300 tests/month and 10,000 tests overall

Number of samples/month
Turn-around time (TAT)

Median TAT 4 days
Scheduled downtime: 3 days
Performance

• T21 sensitivity 99.4%
• T21 PPV 98.8%
• No-call rate 0.39%

Clinical advantages

• No risk of miscarriage
• Results in 4-5 days
• Local test – no referral needed
• Cheaper than CVS
Opinion

Cell-free DNA testing for 22q11.2 deletion syndrome: appraising the viability, effectiveness and appropriateness of screening
Tell it Right, Start it Right™

These RCM accredited study days, provided by the Down’s Syndrome Association, are for all health professionals working in fetal medicine, maternity and neonatal services including midwives, screening co-ordinators, neonatal nurses, paediatricians, sonographers and health visitors.

About the day
Specific learning outcomes for the day ensure that delegates are best equipped to support parents, in-line with their professional guidelines (NICE, 2008) and care pathways.

Tell it Right™ aims to provide information about:
- Down’s syndrome that is balanced, accurate and up-to-date
- How best to support expectant parents through the screening process
- How best to impart information to parents and families, following a pre/post-natal diagnosis of Down’s syndrome
- Some common issues which may affect a baby with Down’s syndrome in the early weeks of life.

Tell it Right™ also aims to encourage delegates to reflect on:
- The decision making processes related to screening
- The parents’ perspective
- Life for a person with Down’s syndrome
- The training involves parents who will share their experiences and also a person with Down’s syndrome who will talk about their life.

training@downs-syndrome.org.uk or 0333 12 12 300

www.downs-syndrome.org.uk
Non-Invasive Prenatal Testing (NIPT): An Introduction for Healthcare Professionals

Get broad insight into the key issues surrounding Non-Invasive Prenatal Testing with this course for healthcare professionals.

www.futurelearn.com
NIPT MOOC