Delivery of Clinical Genomics

David Atkins
Chief Executive Officer
Congenica, a genomics business

Development of Clinical genomics in the UK: Genomics England

Routine use of Clinical Genomics in the National Provider system: The NHS
Congenica is making clinical genomics a reality

In commercial scale-up

In broad applications

In global markets
Congenica’s Mission

We are driven to empower Healthcare Professionals everywhere to transform health and wellness by converting genomic data into actionable information that provides life-changing answers.

We will develop software systems and services that makes the use of complex genomic data routine, accessible and ubiquitous.
Congenica Background

Founders
From Sanger Institute and Great Ormond St. Hospital

2014
Spin out from Sanger Institute

UK Locations
- Wellcome Genome Campus, Hinxton
- St. George’s Hospital, London

>70 Employees

Sapientia™
Commercialising lead genomic analysis platform

US, China
International staff

Venture funded
£22m series B round
Genetic variation is an important root-cause of disease.

Clinical Genomics is the analysis of a patient’s genome to enable diagnosis and treatment.

A genome is 3bn bases and disease is often caused by variance in a single base.

Congenica enables Clinical Genomics by rapidly identifying disease causing DNA variants.
Delivering Genomic Medicine

Cost effective genome sequencing

Data handling and analysis

100GB

Health economics and payment

Regulatory approval

Workforce development and education

Patient education
Delivering Clinical Genomics

Sample taken
Patient sample taken by doctor

Sequencing
Sample sequenced in a laboratory

Interpretation
Sequence data is processed by bioinformatic pipeline

Report
Doctor’s report identifies variants which may be disease-causing and gives a potential diagnosis

Diagnosis
Patient receives diagnosis, opening up possible treatments or ways of managing their condition
Congenica’s Clinical Genomics Pipeline

Delivered at Scale
Platform Evolution: Tertiary to Primary

Rare Disease Business
Tertiary Centre
Specialty Institution

Common Disease
Secondary Centre
Moderate Complexity

Risk Factors
Primary Physician/GP

No. of patients
One Platform Servicing Multiple Clinical Markets

- Prenatal Health
- Rare Disease Characterization
- Carrier Screening
- Disease Predisposition “Wellness”
- Pharmacogenomics
- Oncology
- Clinical Studies
Rare Disease, a Very Common Problem

1 in 17 people develop a rare disease at some point in their lives.

350 million people with rare diseases.

80% of rare diseases are genetic in origin.

75% children, 25% adults.

Impact:
Major social and financial impact.

>7000 different types of rare diseases.

30% of sick children never reach their 5th birthday.

5 years to diagnose.

350 million people with rare diseases.
Clinical Genomics and Rare Disease, Why?

- Improved diagnosis
- Improved therapeutic support
- Economically beneficial
### Comprehensive Deployment Modes

<table>
<thead>
<tr>
<th>National Health England</th>
<th>NYGC</th>
<th>IBR-DD</th>
<th>Children’s Hospital of Fudan University</th>
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<tbody>
<tr>
<td>✓ Rare disease diagnosis</td>
<td>✓ RD characterisation ✓ Genome Centre ✓ WGS &amp; WES ✓ Custom cloud</td>
<td>✓ Complex RD diagnosis ✓ NY State tertiary care ✓ WES ✓ SaaS</td>
<td>✓ Rare disease diagnosis ✓ Public Health ✓ WGS, WES &amp; Panel ✓ On Premise</td>
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<td>✓ Public Health</td>
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<tr>
<td>✓ Custom cloud</td>
<td>CLIA laboratory utilising Sapientia to interpret and report clinical findings for Rare Disease Diagnosis, Carrier and Pre-Disposition Screening and PGx.</td>
<td>Led by Gholson Lyon, a Proof of Concept project interpreting 200 WES with a view to an insurance funded service based on ROI &amp; Clinical Value.</td>
<td>Rapid Response NICU testing for over 10,000 babies per year, presenting with phenotypic issues at birth and re-analysis of previously unresolved cases.</td>
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- **Enabling diagnosis of Monogenic Germline disease as standard part of universal healthcare provision in UK.**
  - Enabling ~200 users to interpret >300k samples/year.
100,000 Genomes Project (2014-2018)

The Rt Hon David Cameron MP, The Prime Minister, 10 December 2012

“It is crucial that we continue to push the boundaries and this new plan will mean we are the first country in the world to use DNA codes in the mainstream of healthcare.”

To sequence 100,000 whole genomes with rare inherited disease, and cancers

To return new diagnoses to NHS patients

To build research infrastructure, capability and skills.

To generate inward investment

To lead the world in the application of Genomic Medicine

To bring benefit to patients

To enable biomedical research

To promote ethics and transparency

To stimulate the genomics industry
In numbers

100,000 genomes

70,000 patients and family members

21 Petabytes of data.
1 Petabyte of music would take 2,000 years to play on an MP3 player.

13 Genomic Medicine Centres, and
85 NHS Trusts within them are involved in recruiting participants

1,500 NHS staff
(doctors, nurses, pathologists, laboratory staff, genetic counsellors)

2,500 researchers and trainees from around the world

• Whole Genomes
• Multiple Users
• Routine clinical use
How Genomics England works

- Private company, 100% owned by the Department of Health
- Recruitment via NHS Genomic Medicine Centres covering over 85 hospitals and 50 million people
- Centralised sample storage and whole genome sequencing
- Industry and academic research collaboration in a single, safe environment
Academic: Genomics England Clinical Interpretation Partnership
(As of 13 September 2018)

GeCIP launched in June 2014
@ Wellcome Trust

3017 researchers world-wide

387 academic institutions

108 signed Participation Agreement

1646 researchers eligible for data access

33/42 ARC-approved domains
Genomics England and Congenica Partnership

- D. Cameron’s Statement
- GMCs Established
- Illumina selected
- Sequencing Centre
- Congenica Selected as CIP
- 100K “Completed”
- NHS “Live”

- GEL Founded
- CIP Competition
- Congenica, Fabric, Wuxi

- Year:
  - 2012
  - 2013
  - 2014
  - 2015
  - 2016
  - 2017
  - 2018
  - 2019
  - 2020
We have leveraged Sapientia to generate clinical reports faster and more accurately.

A key advantage is the ability to facilitate more effective multi-disciplinary team meetings.”

Angela Douglas, Clinical Programme Director, NW Coast Genomic Medicine Centre
Preparing for the NHS
Supporting Genomics England & the NHS

100k Genomes

Key milestones:
- Sept 2015 – Agreement complete
- June 2016 – 1st cases returned
- April 2018 – Ref38 live
- Sept 2018 – Backlog acceleration

Technical status:
- GeL UKCloud environment:
  - >40k WGS live
  - ~4.5k WGS added / month
  - All decisions returned to GeL via API

NGIS (Main Phase)
- Sept 2018 – Sole supplier award
- April 2019 – Testing commences
- May 2019 – 1st GLH WES & Panel agreement
- July 2019 – NGIS ‘Go live’

Congenica AWS environment:
- Test system live (April)
- Integration testing (May)
- End-to-end UAT commences (July)
**Improved Diagnostic Yield**
Significant increase in diagnosis, with a Diagnostic Yield of 43% across more than 25,000 cases.

**Efficient Workflow**
Supports user needs in routine practice through intuitive integrated visual interface.

**Increased Confidence**
Quality-certified with curated variants and a comprehensive audit trail to enhance diagnostic confidence.

43% diagnostic yield

30 minutes review to report

>60k variants unique curated
NGIS Services

The National Genomic Informatics Service (NGIS) will integrate existing and new services to provide a single national platform to support the GLH National Network. It will consist of the following elements:

1. A single National Genomic Test Ordering Service which will enable any authorised user to create a Test Request.
2. The National Genomic Test Directory Service will provide the approved list of Genomic Tests within the scope of the Services and will specify the required data for each test.
3. The NPEx (National Pathology Exchange) Service will enable the tracking of Genomic Test samples across the genomic laboratory network. It will facilitate connectivity between Ordering Entity LIMS and GLH LIMS subject to its adoption in an Ordering Entity.
4. The eConsent, Panel Assigner and Pedigree Tool Services are standalone services which will be called by the Test Ordering Service.
5. An Authentication Service will enable single sign-on across several elements of the service.
6. The Data Management Service for patients and samples will receive and distribute information about the status of each Genomic Test order, in progress or completed. It will manage clinical and sample data for each patient, and provide consolidated management information to all users of the NGIS, including the NHS England Genomics Unit. It will provide a view of the Genomic Health Record for each individual who has undergone a Genomic Test.
7. A National BioInformatics Service will provide an automated pipeline which will perform genomic checks and analysis of WGS data together with the clinical data associated with each WGS test order. This service will be ISO 15189 accredited. The Service will also manage the ingestion into the National Genomic Data Store of genomic sequence data for WES and complex NGS panel tests.
8. The Decision Support Service provides a set of services to clinicians, clinical scientists and others involved through MDTs, in the interpretation of Genomic Tests. The services will be provided to support WGS, WES and complex NGS panel tests.
9. Whole Genome Sequencing will be provided through a central service procured by Genomics England.
10. The National Genomic Data Store will hold all patient identifiable Genomic Test data and reports, together with clinical data provided with the Genomic Test order. It will also hold longitudinal clinical data from secondary sources, if appropriate consent has been obtained from the patient.
11. The Research Support Service enables clinical, academic and commercial researchers to access de-identified data from the National Genomic Data Store, subject to consent by each patient and to a strict set of security and privacy controls and contractual obligations.
Insights Gained
Lessons learned from Supporting GEL/NHS

• Partnership & planning is key
• Expect delays and build contingency
• Allocate sufficient resources – it’s complicated!
• Involve all stakeholders at every stage
• Develop test data as early as possible
• Training and re-training is essential
• Champions and sponsors are key – Government, KOL, Patients and Families
Congenica’s Customer Base Extends Beyond GEL/NHS
National Genomics Program Engagement

- Canada
- UK
- Netherlands
- Sweden
- Qatar
- Bahrain
- Oman
- KSA
- Taiwan
- Hong Kong
Welcome Trust
Sanger Institute

Great Ormond
Street Hospital

Team

David Atkins
CEO

Nick Lench
Chief Scientific Officer

Andy Richards
Chairman

Matt Hurles
Scientific Director

Wendy Britten
Chief Financial Officer

Richard Durbin
Informatics Director

Peter Fox
Chief Technical Officer

Phil Beales
Medical Director

Alistair Johnson
Chief Product Officer

Yvonne Larkin
Chief Organisational Development & Talent Officer