Oxford NANOPORE Technologies

“When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind.” Lord Kelvin

THE MINION MK1C: PORTABLE,
CONNECTED SEQUENCING + ANALYSIS + SCREEN

Disclaimer

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Introduction to Oxford Nanopore Technologies

1

Single molecule sensing platform

Building on DNA/RNA to enable the multi-omics world of tomorrow

2

DNA/RNA Sequencing market

$5.8* billion opportunity for sequencing in 2021 with potential $10s of billions in future applied markets

3

Growing user community

Customers in >100 countries doing ground-breaking science

4

Relentless, agile innovation

Delivering continuous improvement and intellectual property creation

5

Scaled operations

In-house manufacturing and global distribution

6

Our people

Experienced, driven leadership enabled by a highly ambitious and talented global team of >750

*DeciBio, est 2021 $5.8 billion manufacturers market size (devices, consumables, excludes services) in sequencing, Health Advances applied markets, Allied Market Research for other omics. See market slides for full details.

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A Novel, Electronic, Single Molecule Sensing Platform

Our goal: to enable the analysis of anything, by anyone, anywhere

Bioelectronics-based sensing technology platform

Broad range of analytes eg DNA/RNA, proteins, small molecules

First products: DNA/RNA sequencing

Differentiated: Fast, Flexible, Scalable, Data-Rich

Versatility: fit the tech to the biological question

Two pillars of innovation: R&D and manufacturing

Manufacturing processes at the heart of innovation

Platform can be manufactured at high volume, low cost

Differentiated Business Model

Accessible, plug and play devices for a one-to-many approach

Proprietary end to end process to participate in all parts of the value chain

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Innovation is driven by in-house R&D teams and extensive partnerships

Foundational academic partners: Professors	
Dan Branton	Hagan Bayley
Dave Deamer	Mark Akeson
Jene Golovchenko	Amit Meller

2022
License agreements/ research partnerships with academic groups at 28 institutions give breadth and global reach in fundamental nanopore science

>license agreements with 28 institutions

>2,000 issued patents* and patent applications

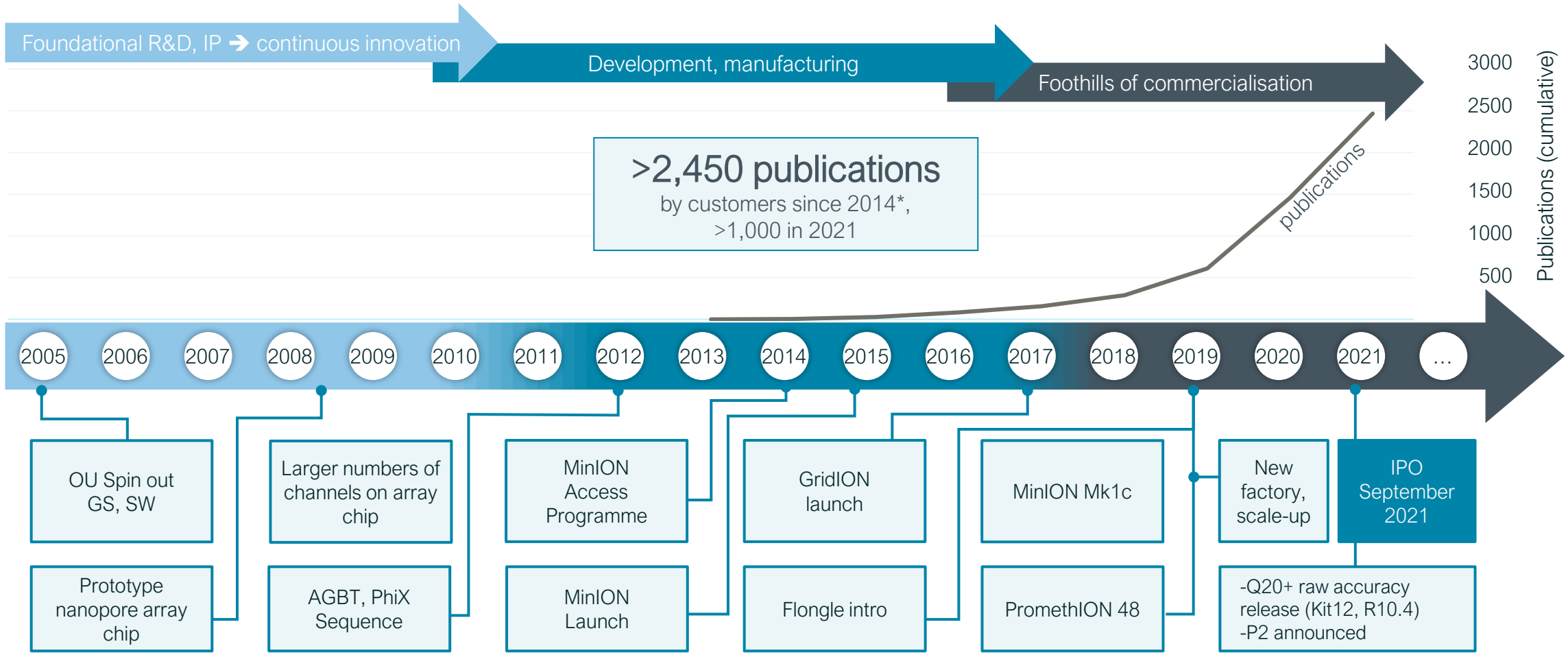
Of which >800 generated internally

>260 patent families* covering multiple elements of nanopore sensing technology.

**Nov 2021: numbers may change. Not all partnerships shown*

Journey to today

Investment in foundational IP, platform development, infrastructure, to prepare for rapid growth



*PubMed, and other sources of publications, includes peer review and preprints

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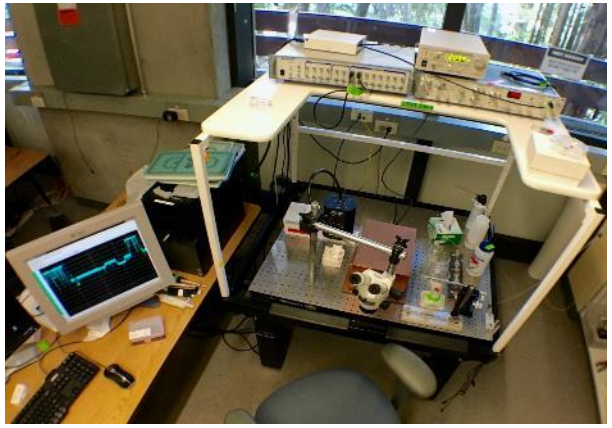
Proprietary electronic platform: the foundation for nanopore sensing

Adaptable for multiple analytes: native or amplified DNA/RNA, proteins, small molecules



MinION Flow Cell

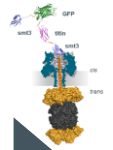
MinION device

PromethION Flow Cell

P48 device
Runs up to 48 Flow Cells

Pipeline of lower power and higher density flow cells

Protein and other molecule sensing on same hardware



2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 …

1 channel

Axopatch
1 Nanopore channel
~1 experiment per person per week

up to 512 channels

MinION
512 nanopore sequencing channels
Running in parallel

up to 128,400 channels

Range of devices
from 126 to 128,400 channels

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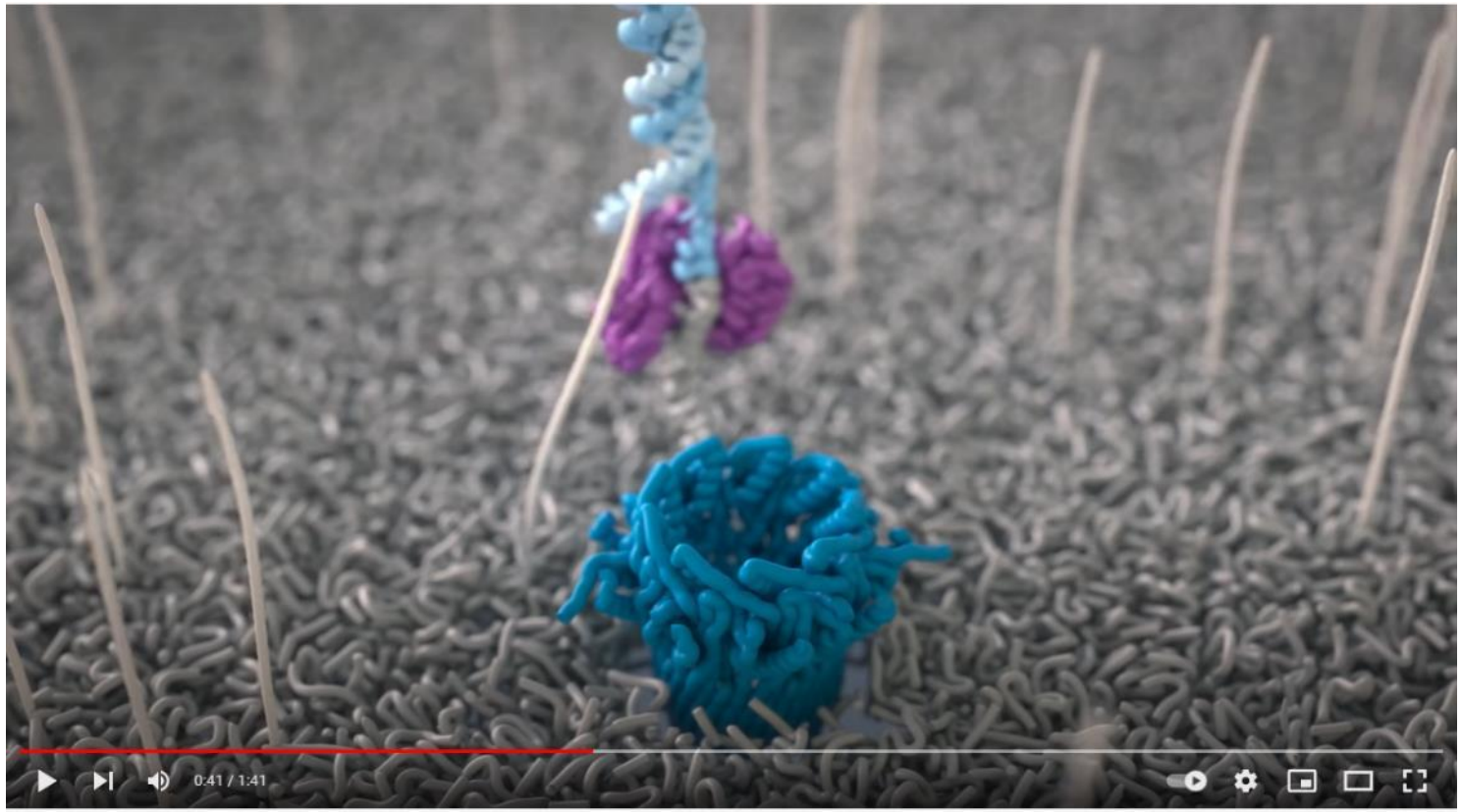
How nanopore sequencing works:

A novel, electronic, single molecule sensing technology



https://www.youtube.com/watch?v=RcP85JHLmnI

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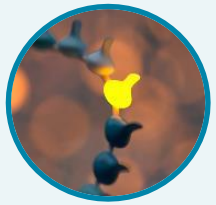
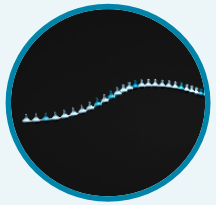
Information-rich: the most comprehensive genomes

Any-length fragments, native DNA/RNA and other features contribute to **telomere-to-telomere**, rich insights

Full biology from a single experiment


SNP detection


Methylation detection

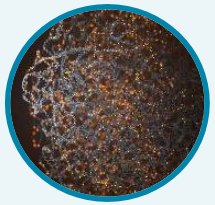

SV detection


Phasing


Assembly

Sequence *ANY* fragment length from:

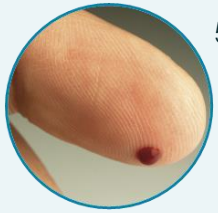

30 base pairs


to…4 Mb + “ultra-long”

With nanopore benefits:


Simple workflows


Scalability


Inputs as low as:

50 ng amp-free

10 ng amp

Picogram workflows avail

“We identified 2,855 dark CDS regions across 748 protein-coding genes that were dark

There are 76 dark genes with known mutations associated with 326 human diseases

Systematic analysis of dark and camouflaged genes reveals disease-relevant genes hiding in plain sight”

Mark Ebbert et al. (2019) Genome Biology 20:97

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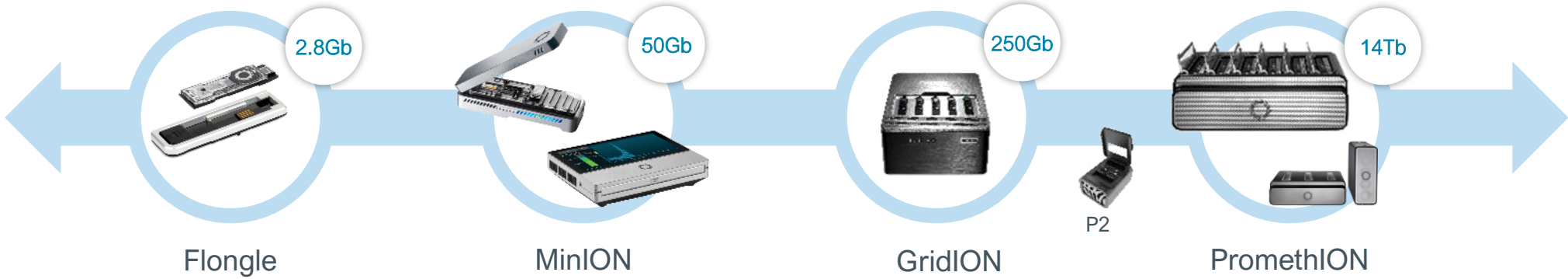
TMO Gb*

Theoretical maximum output, Gigabases. Assumes system is run for 72 h at 420 bases / second. Actual output varies according to library type, run conditions, etc. TMO noted may not be available for all applications or all chemistries.

Scalability: sequencing devices that fit the tech to the biological question

Versatility comes through both electronic scalability, and real-time workflows



Near user
High volume, rapid,
smaller tests/enquiries/tasks

Same nanopore platform, different scale

Central
High volume, discovery
Processing larger datasets

Small Genomes | Targeted Sequencing | Animal WGS | Human WGS | Plant WGS | Transcriptomics

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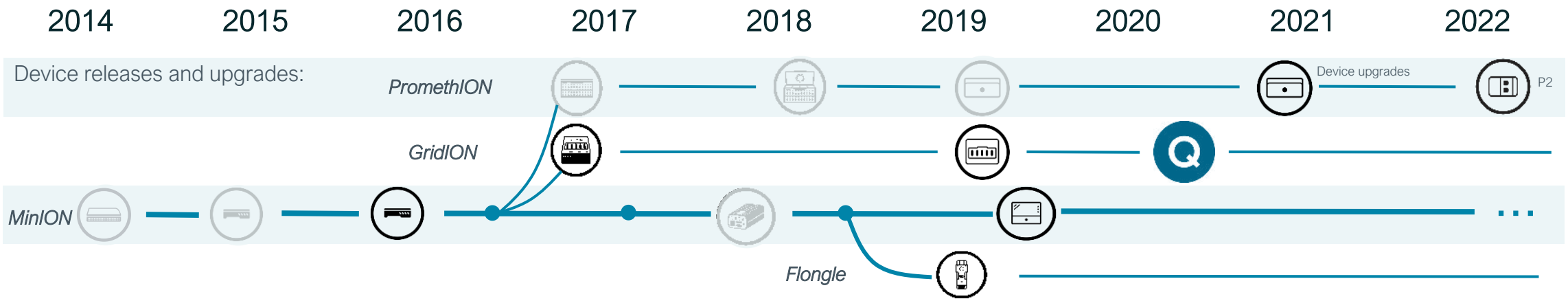
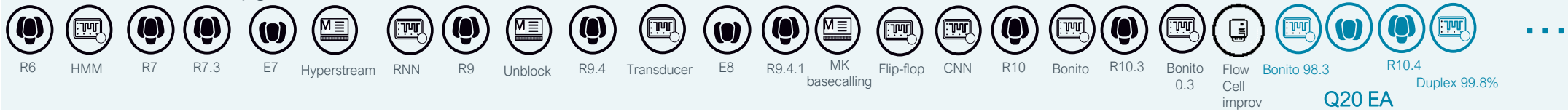
Upgrades drive performance enhancements, delivered through consumables

Continuous, simple upgrades for customers without needing to change device



Hardware *(ASIC)* is in consumable flow cell - upgrades mostly ship in kits, flow cells, algorithms and software - Same nanopore chemistry across all devices

Platform releases and upgrades



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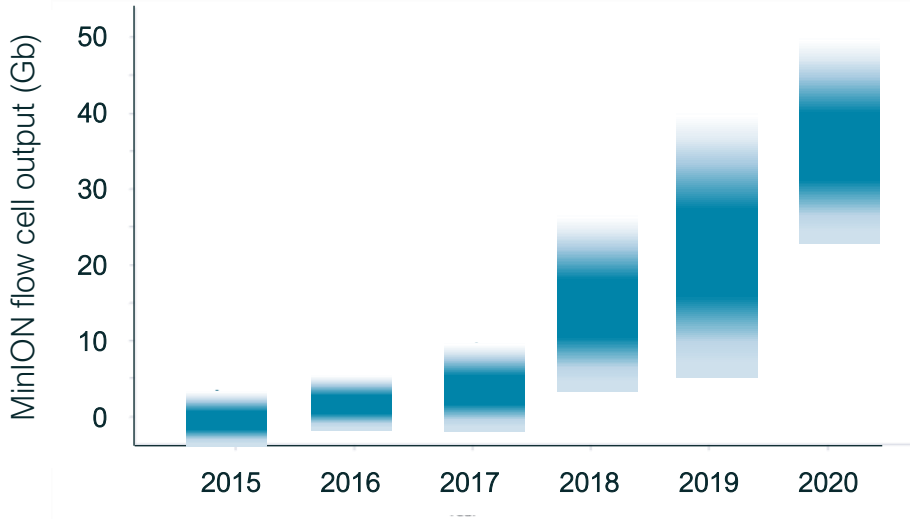
Upgrades drive performance enhancements

Sequencing data output per flow cell

Improvements to kits, flow cells and software have delivered rapid increases in platform output



Example customer data output shared in publications or social media

Flongle

Theoretical max. output	Cost per Gb at max output
2.8 Gb	~ $24

MinION

Theoretical max. output	Cost per Gb at max output
50 Gb	~ $9.5

PromethION

Theoretical max. output	Cost per Gb at max output
290 Gb	~ $2

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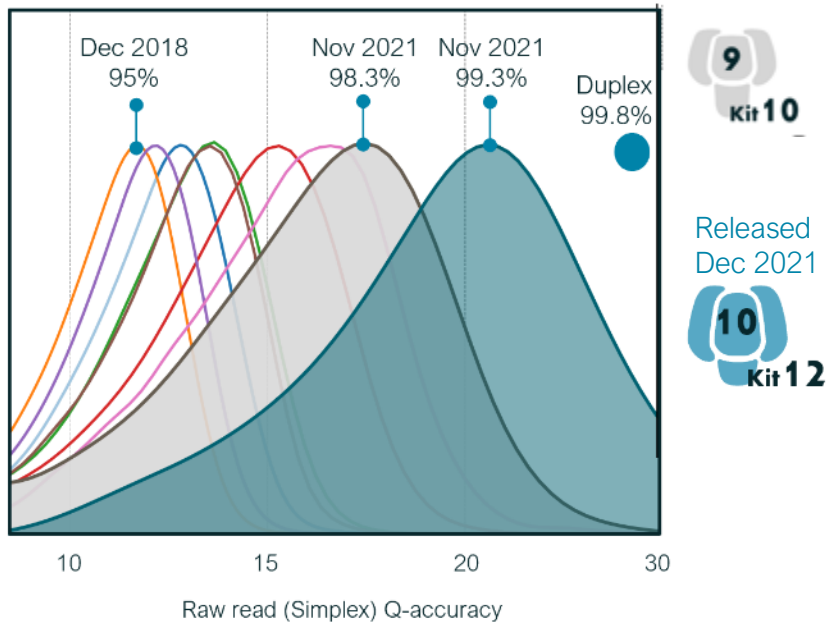
Upgrades drive performance enhancements

Accuracy

Chemistry and algorithm improvements: raw read accuracy

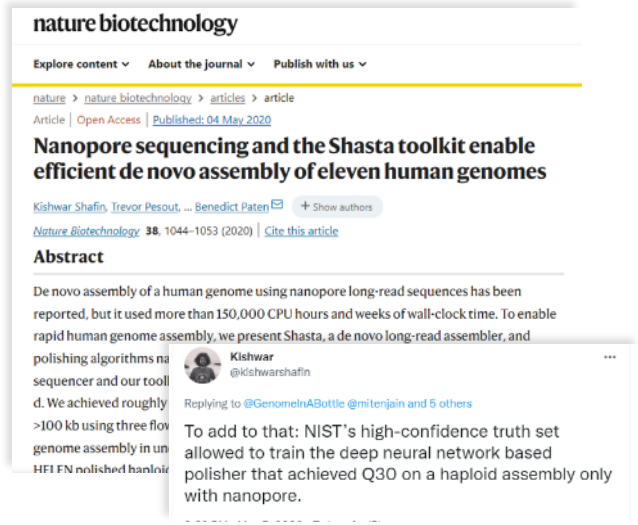


Current products enable:

Raw read accuracy	99.3%
Duplex accuracy	99.8%
Consensus accuracy	Q50+ genomes Bacteria, plants. Human at Q47
SNV detection | SV detection	99.9% (F1) | 96% (F1) Indel whole genome: 89%
Methylation detection	5mC, 5hmC, 6mA Outperforming bisulphite sequencing

High-accuracy nanopore sequence for comprehensive genomes: user data

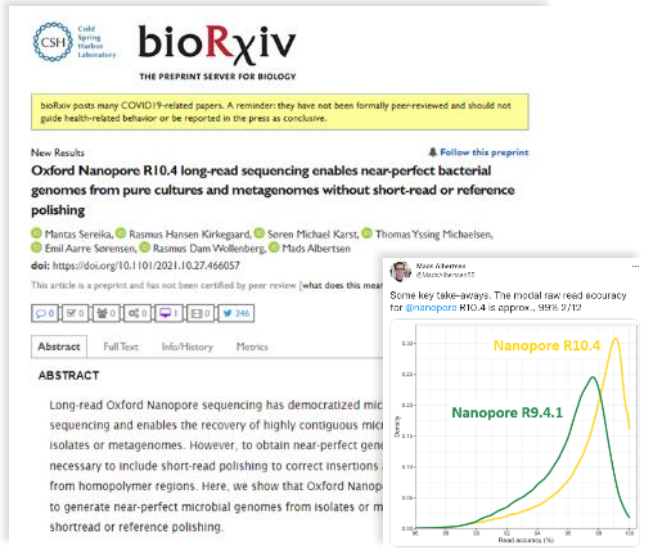
2020/2021: R9.4 already capable of high-throughput, high accuracy data



"NIST's high-confidence truth set allowed to train the deep neural network based polisher that achieved Q30 on a haploid assembly only with nanopore"

Kishwar Shafin, University of California, Santa Cruz, 2020

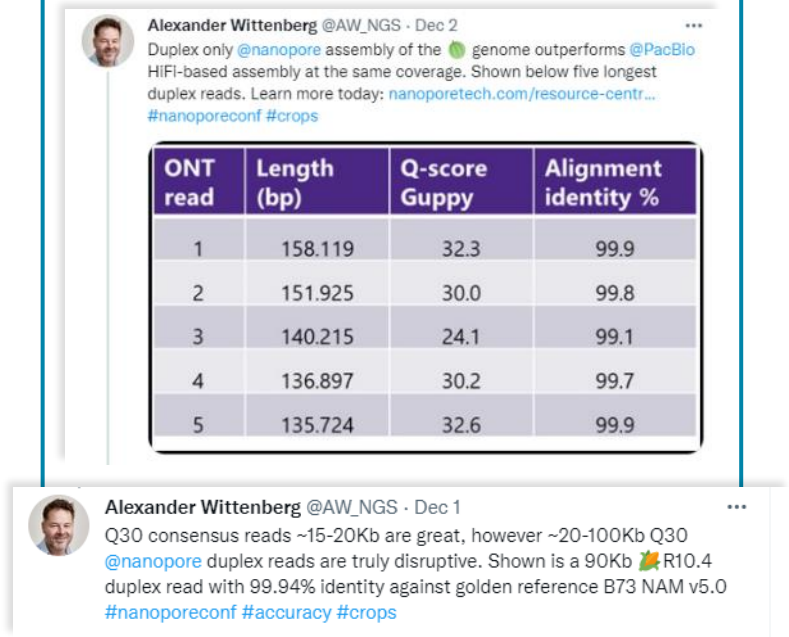
Early Access of Q20+ release (R10.4 & Kit 12) enables "near perfect assemblies"



"R10.4 long-read data enables near-perfect bacterial genomes from pure cultures and metagenomes without short-read or reference polishing"

Mads Albertsen, Aalborg University, November 2021

December 2021: Kit 12 & R10.4 for ultra-high accuracy



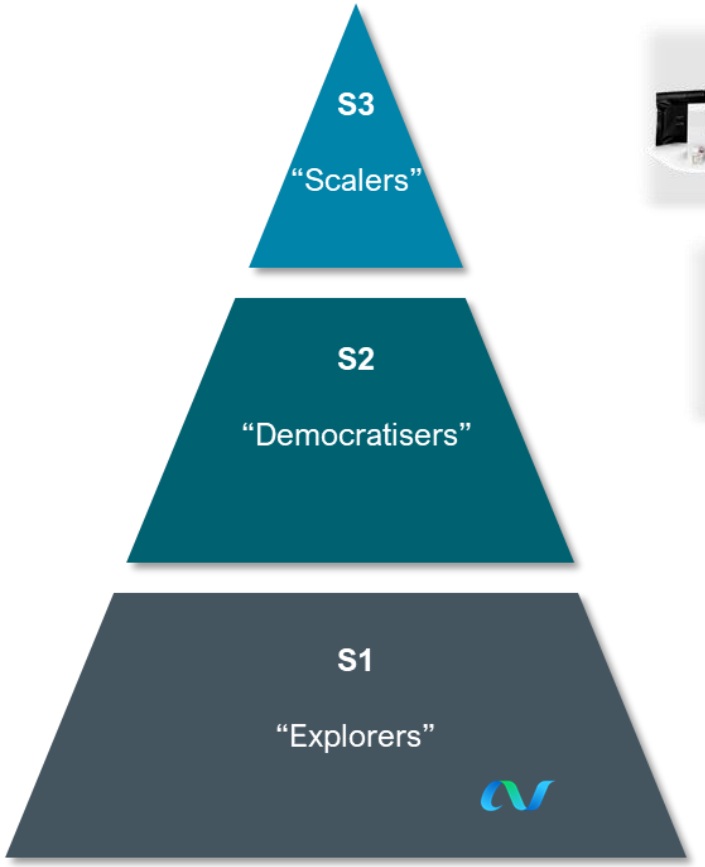
"…outperforms Pacbio Hifi at the same coverage"

Alexander Wittenberg, KeyGene, December 2021

Life sciences research: go-to-market approach

Customer categorisation determines opportunity, approach and mode of support

Customer Segment	Product



S3: Commercial approach: Sales teams and deeper technical/application support

- **Users seeking rich data, at scale, at a competitive price point**
- Example use cases: population sequencing, high throughput human genomics/ plant genomics
- Higher throughput transcriptomics projects
- Typically PromethION/ some GridION, but can include strategic MinION customers with particularly high impact application areas

S2: A blend of sales and support approaches, increasing focus on repeat analyses

- **Users seeking on-demand data at higher volumes, may be in regulated environment. Example use cases:**
  - larger sample numbers eg COVID-19 surveillance, food safety, pathogen analysis
  - Mid-high data requirements eg transcriptomics
  - Service providers

S1: Community-focused marketing, digital, inside sales, distribution partners

- **Users seeking: on-demand, accessible, rich sequencing data in a wide range of applications, and may be motivated to develop methods for future applied market uses**
- Long tail of use cases span targeted sequencing, metagenomics, smaller genome WGS, methylation analysis, everyday QC/plasmid/other sequencing

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Oxford Nanopore technology can address breadth of genomics applications

Sequencing market* continues to expand, expected to grow from $4.2 billion in 2020 to $5.8 billion in 2021, and potential for $10s of billions in future applied markets

Oxford Nanopore aims to penetrate, reshape, expand, and create new opportunities

Life science Predominantly Research setting	
Broad Genomics Research	>2,450 publications illustrate breadth and depth of usage across human genetics, plant, animal, pathogen.
Pathogens	Public health: international COVID surveillance, TB, Flu, Dengue, Zika, Ebola, Drug-resistant pathogens Emerging health eg metagenomics.
Human Genomics, at scale	Population-scale, and high-throughput human genomics. PromethION supports rich data, at scale
Translational, Cancer research	Rapidly emerging fields include rapid, comprehensive analysis of cancer samples or samples to understand variants that cause rare disease. Includes short to long fragments

From early "real world" uses to broader "applied markets"	
User-driven clinical genomics	Current lab-developed tests include methylation analysis of brain tumour, HLA, infectious disease
Broader clinical	Emerging: Oxford Nanopore establishing specific resource and strategies to address this potentially valuable segment
Applied: non-clinical	Emerging areas e.g. food safety, environmental analyses, are currently still in research phase but substantial opportunities for broader markets

Fit the tech to the biological question

*DeciBio market report 2020 **Allied Market Research: Proteomics estimated market size, revenue 2019 for instruments, reagents and services. Publications at end 2021

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TMO Gb* Theoretical maximum output, Gigabases. Assumes system is run for 72 h at 420 bases / second. Actual output varies according to library type, run conditions, etc. TMO noted may not be available for all applications or all chemistries.

Users: from genomic explorers to democratisers of sequencing

Accessible

- Entry point from $1,000
- Easy to use, plug and play enabling users new to sequencing to get started
- Used by many undergrad & PhD students

Scalable

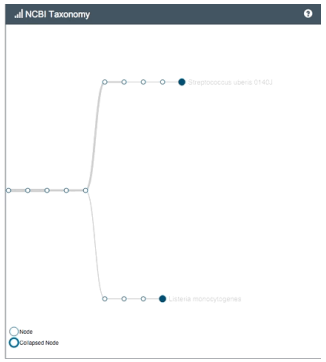
- MinION applications can scale up to GridION, PromethION or down to Flongle
- Multiple device installs are simple to do
- Fit the tech to the biological question

Information-rich

- More comprehensive complete genomes with SVs, repetitive regions, dark regions, methylation in one sequence

Real time insights

- DNA is read and immediately available for analysis on device or in cloud



Competitive

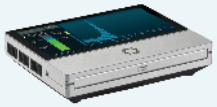
- Perform small single experiments on Flongle
- Multiplex on MinION flow cell for as low as $8 per sample

GridION
from $49,955
Consumable starter pack

250 Gb

MinION Mk 1c
from $4,900
Consumable starter pack

50Gb



MinION from $1,000
Consumable starter pack

50 Gb

Flongle flow cell
$90 each

2.8 Gb

Typically S2
Typically S1
Typically S1 customer

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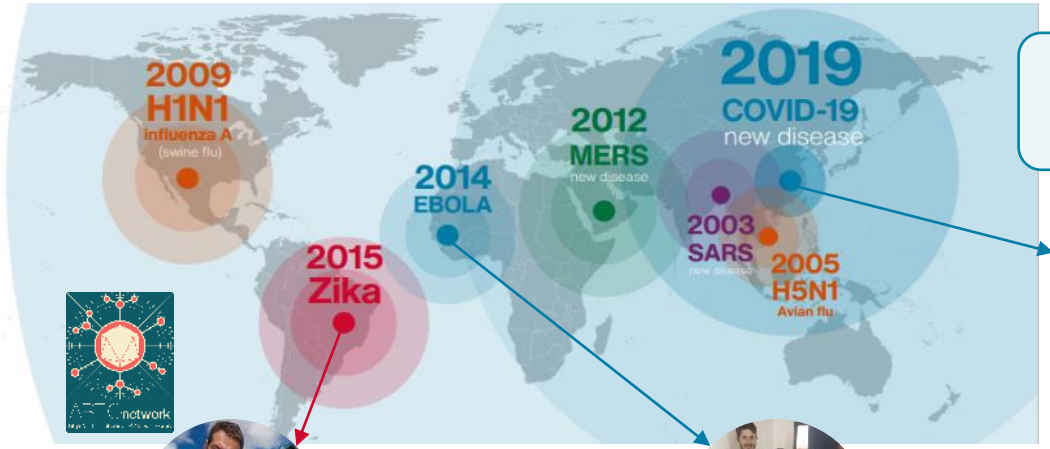
Rapid, distributed pathogen sequencing for public health decision making

…and beyond public health into potential management of infectious disease

Genomic Epidemiology: sequencing can inform public health decisions



200 MinIONs shipped to China CDC labs Jan 2020

"Despite there being probably millions of cases of the Zika virus in Brazil, there was only a handful of known virus genomes prior to our work."

Nuno Faria et. al. 2017

"I saw, first-hand, epidemiologists being able to accurately track transmission routes in real time and then intercept the chain to prevent further transmission of the virus."

Lauren Cowley et. al. 2015

COVID-19

- Nanopore sequencing used in >85 countries, providing >765k genomes into GISAID
- Rapid and flexible: Midnight protocol and kit sequences SARS-CoV-2 genomes in hours, multiplexing for costs below $10 per genome
- Scalable: Deployed on MinION and GridION depending on scale required

Rapid infection research & AMR detection

"We realised there would be a benefit to sequencing genomes of all bacteria and fungi causing infection in COVID-19 patients while on ICU. Within a few weeks we showed it can diagnose secondary infection, target antibiotic treatment and detect outbreaks much earlier than current technologies – all from a single sample. This will revolutionise our approach to prevention and treatment of serious infection on ICU."

Jonathan Edgeworth, GSTT 2021

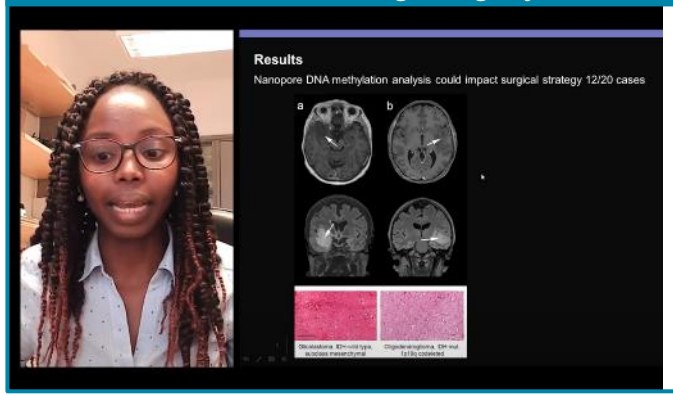
Fit the tech to the biological question

Examples of outbreaks; samples prior to 2014 not sequenced using nanopore

Real-time sequencing in cancer research

Real-time sequencing capability enables rapid, information-rich insights:

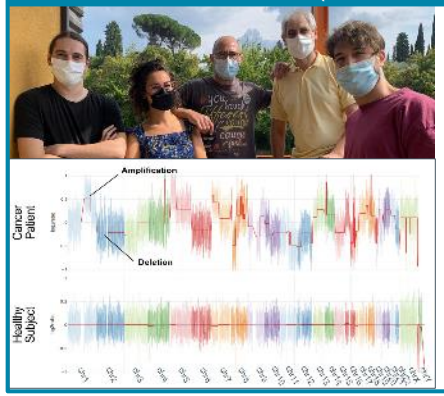
Real time brain tumour characterisation, during surgery: Oslo University



"Using nanopore would influence surgical strategy in 12/20 cases"

Luna Djirackor

Liquid Biopsy: cfDNA in lung cancer (short fragments): ISPRO, Italy

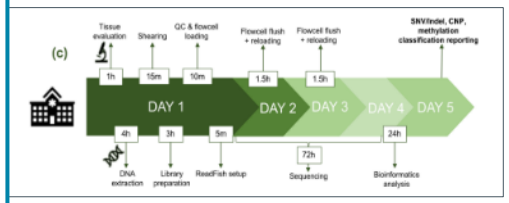


"sWGS is a read-count based approach able to detect CNVs from low-coverage whole genome sequencing (<1X)… In this context, Nanopore represents a reliable alternative to Illumina sequencing, with the advantages of minute instrumentation costs and extremely short analysis time."

Filippo Martignano et. al.

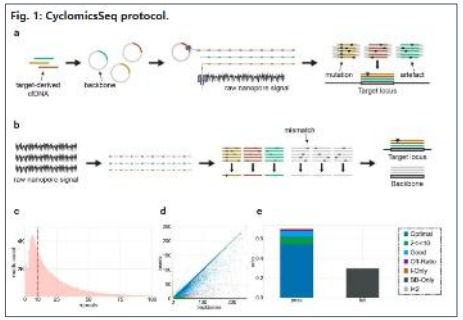
Comprehensive brain tumour profiling using "adaptive sampling"

German Cancer Research Center (DKFZ), University Hospital Heidelberg



In diffuse glioma samples*"…enables comprehensive **mutational**, **methylation and copy number** profiling of CNS tumours with a single, cost-effective sequencing assay. It can be run for single samples and offers highly flexible target selection that can be personalized per case with no additional library preparation"*

Liquid biopsy: TP53: cfDNA in head and neck cancer (short fragments): Cyclomics, Netherlands



"We demonstrate that a TP53-specific CyclomicsSeq assay can be successfully used to monitor tumor burden during treatment for head-and-neck cancer patients. CyclomicsSeq can be applied to any genomic locus and offers an accurate diagnostic liquid biopsy approach that can be implemented in clinical workflows."

Fit the tech to the biological question

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TMO Gb* Theoretical maximum output, Gigabases. Assumes system is run for 72 h at 420 bases / second. Actual output varies according to library type, run conditions, etc. TMO noted may not be available for all applications or all chemistries.

Human Genomics: Accessible, accurate, at scale, with richer content

Accessible

- Low barrier to entry: simple and low cost to get started
- Competitive cost per genome

Scalable

- Only way to scale long reads to 10,000s - 100,000s of genomes with reasonable infrastructure
- Fit the tech to the biological question

Information rich

- More comprehensive human genomes with SVs, repetitive regions, dark regions, methylation in one sequence

*In dev

# of genomes per PromethION flow cell (20 - 30X)	1	2	3*
# of genomes per device / year	~4, 600	~ 9,200	13,800
Nanopore cost per genome	~ $690	~ $345	~ $235

P48: from $285,955
Consumable starter pack

14Tb

P24: from $195,955
Consumable starter pack

7Tb

P2: from $10,455
In development

580Gb

Typically S3 customer

Likely to be S2 customer

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Generating a comprehensive view of the human genome: at scale

Genomics england

- Thousands of cancer samples
- Characterise SVs & methylation at scale
- Intention to integrate into rapid clinical care in UK

NIH

- 4,000 sample Alzheimer study
- Sequence through complex repeats

G42 | الجينوم الإماراتي لمستقبل أجيالنا | EMIRATI GENOME FUTURE OF OUR GENERATIONS

- Highly scaled operation, generating thousands of genomes per week
- Tens of thousands genomes sequenced
- New Arab reference genome in analysis

A population scale genomics programme designed to improve human health outcomes in the Gulf region

deCODE genetics

- First 3,600 genomes published
- ~ 22,000 SVs per genome characterised (*vs 8,000 on SBS*)
- Methylation characterisation underway

"Oxford Nanopore's long-read sequencing capability creates a window into parts of the genome that have been out of reach, as well as giving us a much better handle on structural variants that confer risk of a wide variety of diseases."

Kári Stefánsson
CEO, deCODE Genetics

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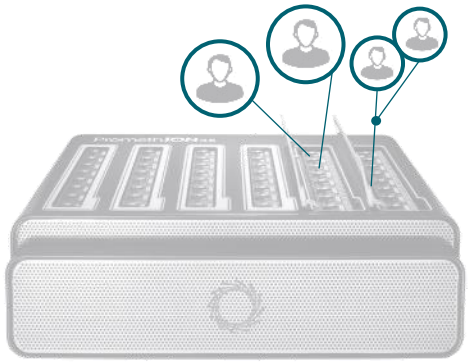
Translating high-throughput, real-time sequencing into *on-demand* applications

Exploring: operating mode

Users typically prepare samples, load flow cells and run for 72 hours

Flow cell independence enables users to run full or partial boxes so samples are run as they become available

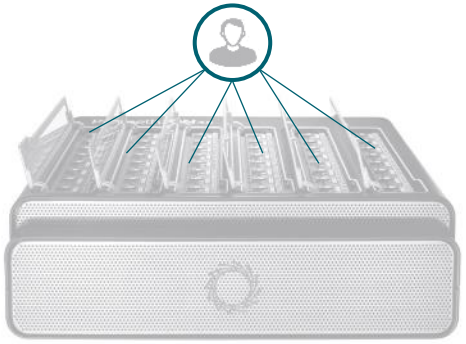


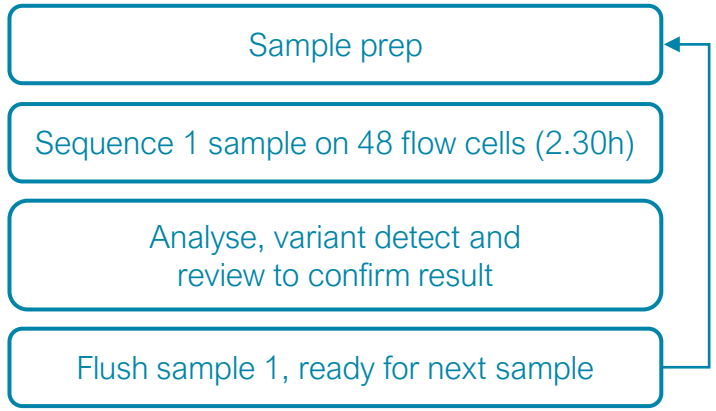
Translating: same day human WGS, potential for use in critical care

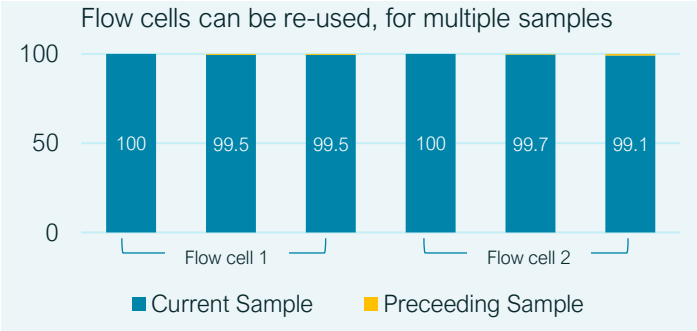
Users can load a single sample across all 48 PromethION flow cells

Sample to fully variant called and interpreted data can be delivered same-day

Method can be cost effective through flow cell re-calibration







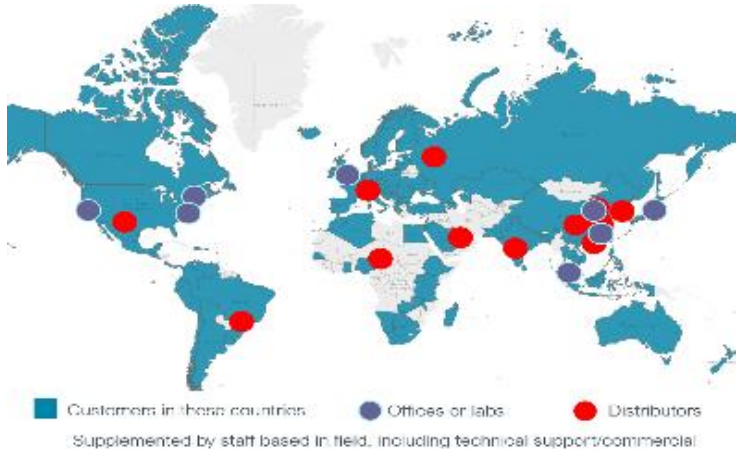
Commercial and Manufacturing Operations established for scale-up

Innovation is key to scaling up manufacturing

Selling to and supporting customers in > 100 countries

Global customer support team

Active digital community supporting each other



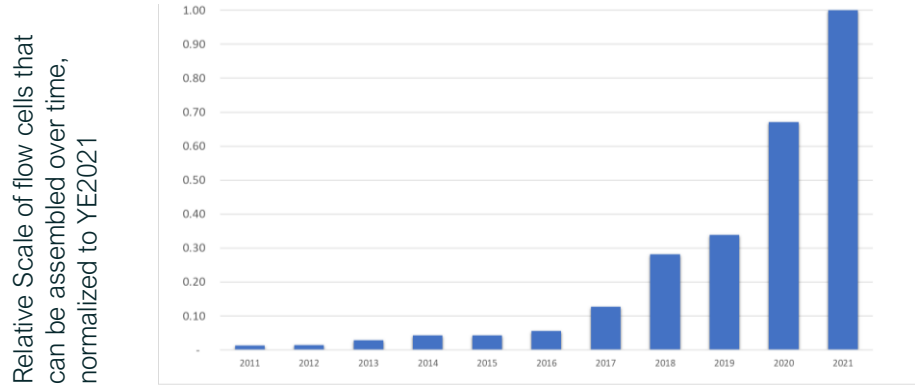
Enhanced through distribution partners including:

avantor

MinION Building: flow cell manufacture, operational 2019

OXSP - Dedicated vialing & kitting labs and box build & test labs, H1 2020

Manufacturing established, with flexible scale-up capacity to 2025 built-in



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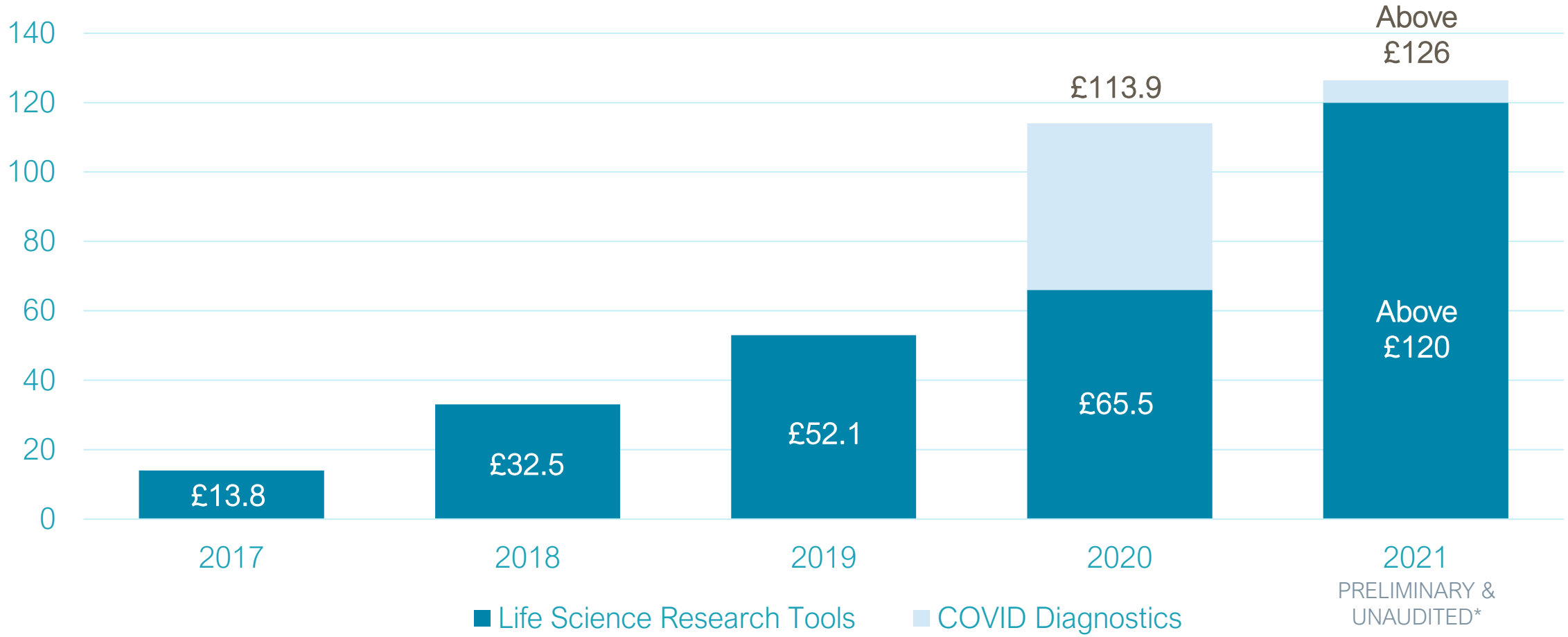
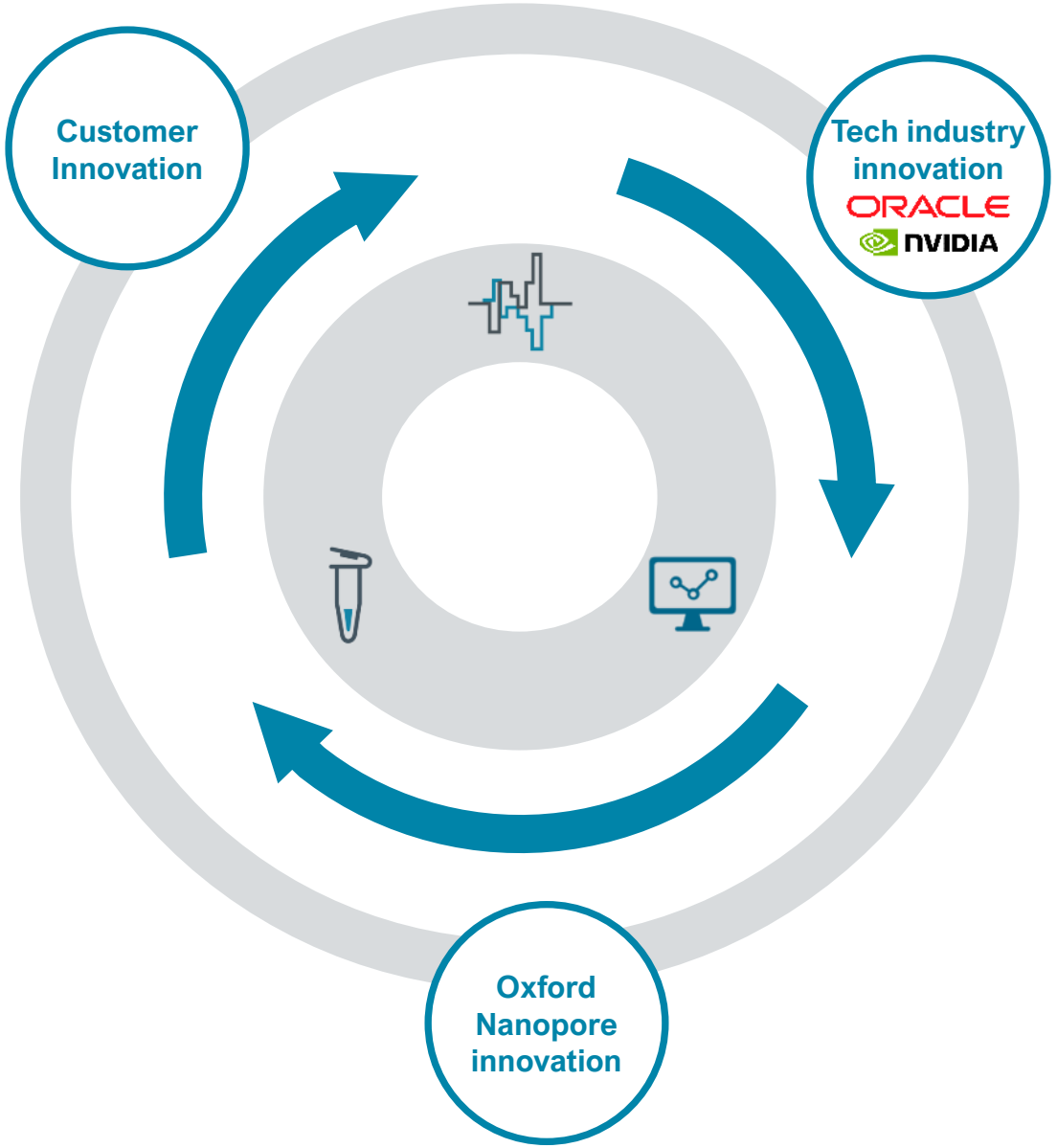
Revenue growth reflects adoption of nanopore sequencing

Revenue for fiscal year ended 31 December (£ millions)



* Please refer to 7 January 2022 RNS announcement for additional information

Innovation strategy for long term growth




Human health

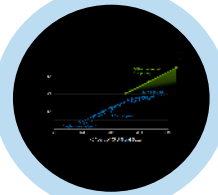

Pathogens

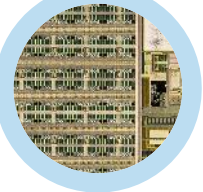

Food sustainability

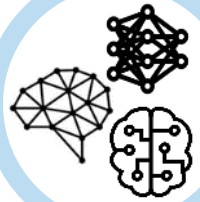

Environmental

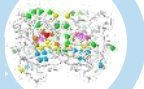

Data digitisation


Cloud connectivity


Compute acceleration


Mixed mode electronics


Algorithms, ML, AI


Directed evolution

Analysis of anything by anyone anywhere… towards:

Thank you

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