

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



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

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“

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”

2021 Highlights & Business Review

Gordon Sanghera, CEO

Introduction to Oxford Nanopore Technologies

1

Single molecule sensing platform

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

2

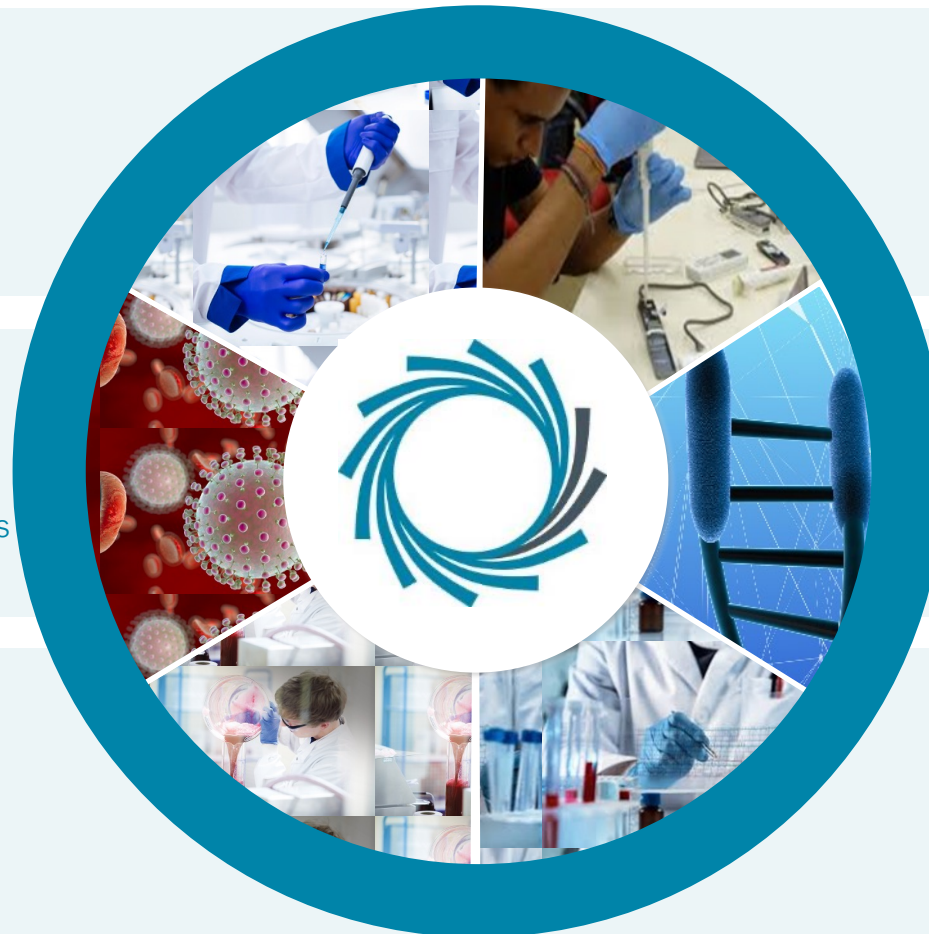
DNA/RNA Sequencing market

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

3

Growing user community

Customers in >120 countries doing ground-breaking science



Relentless, agile innovation

Delivering continuous improvement and intellectual property creation

4

Scaled operations

In-house manufacturing and global distribution

5

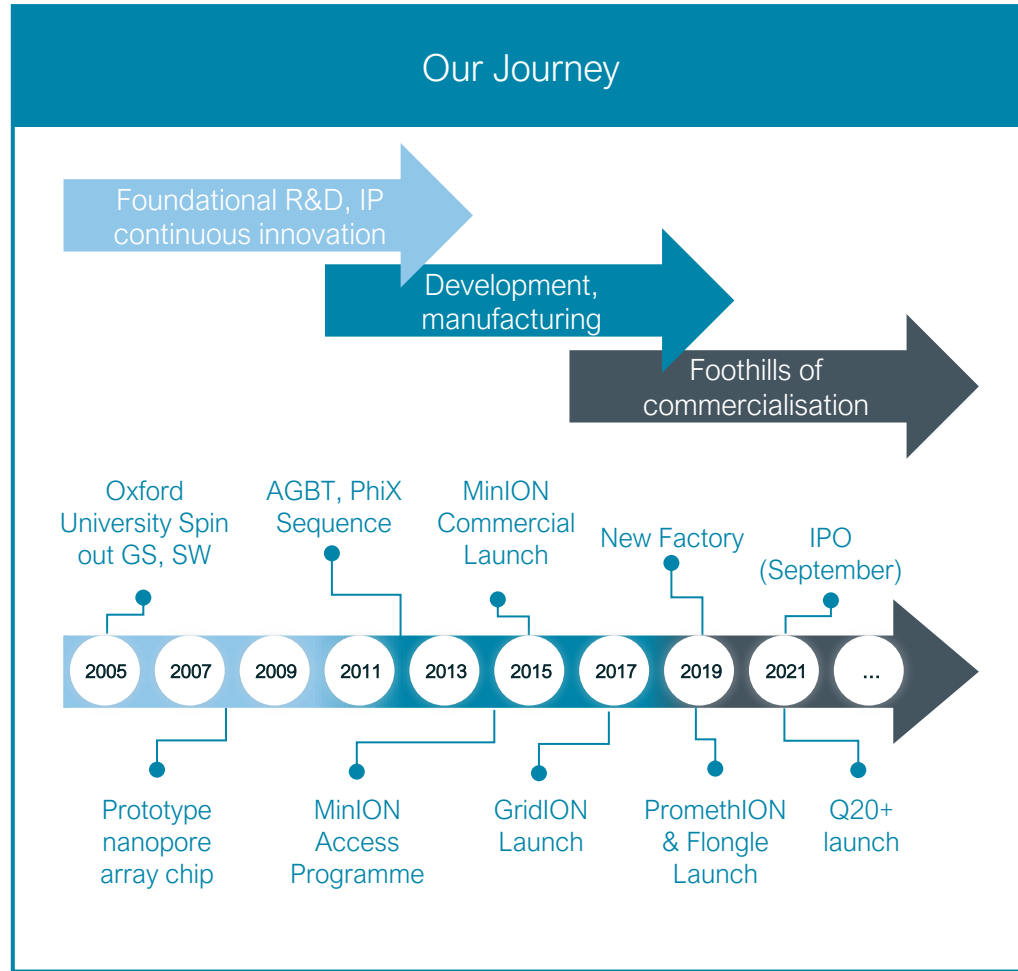
Our people

Experienced, driven leadership enabled by a highly ambitious and talented global team of >800

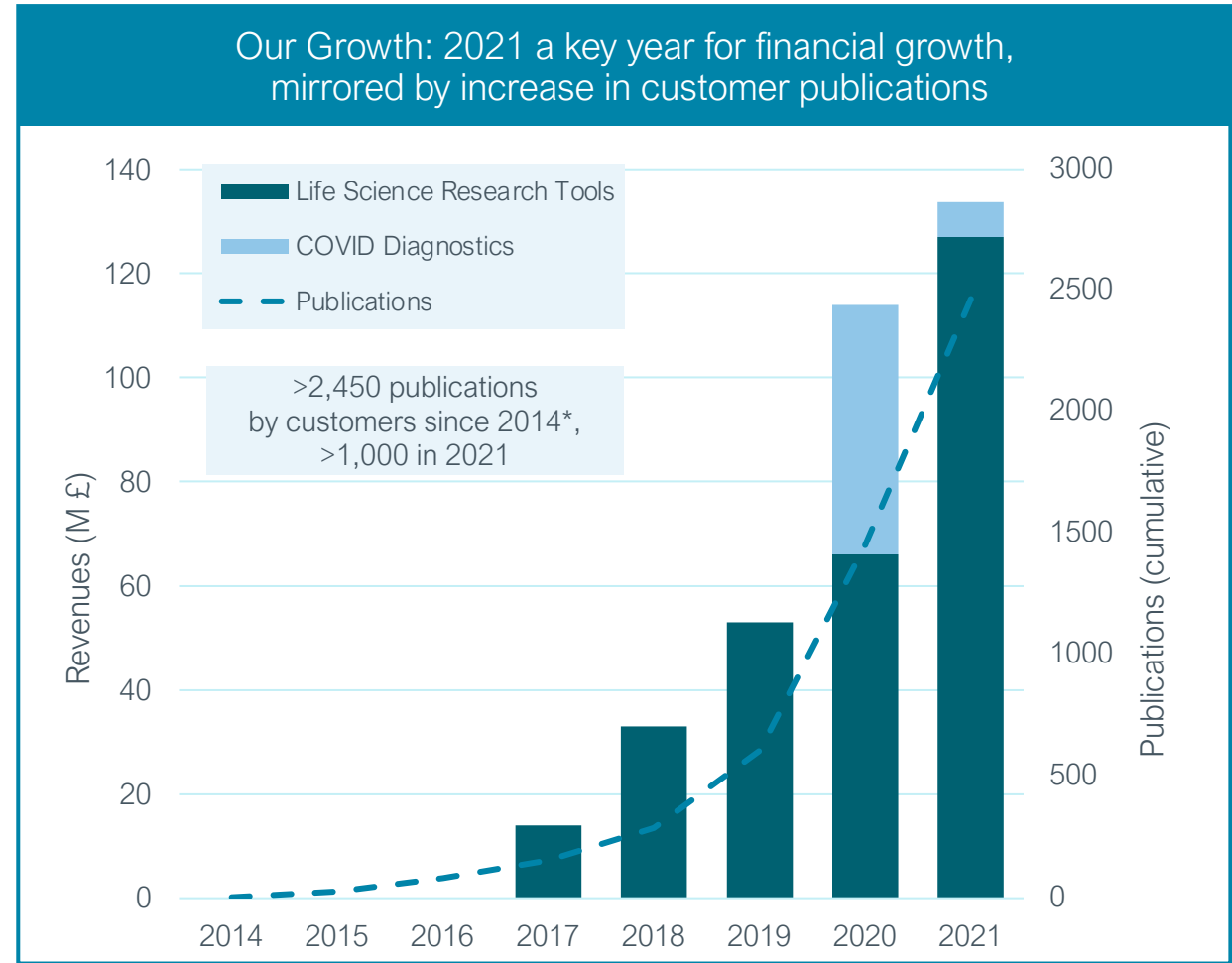
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Journey to today

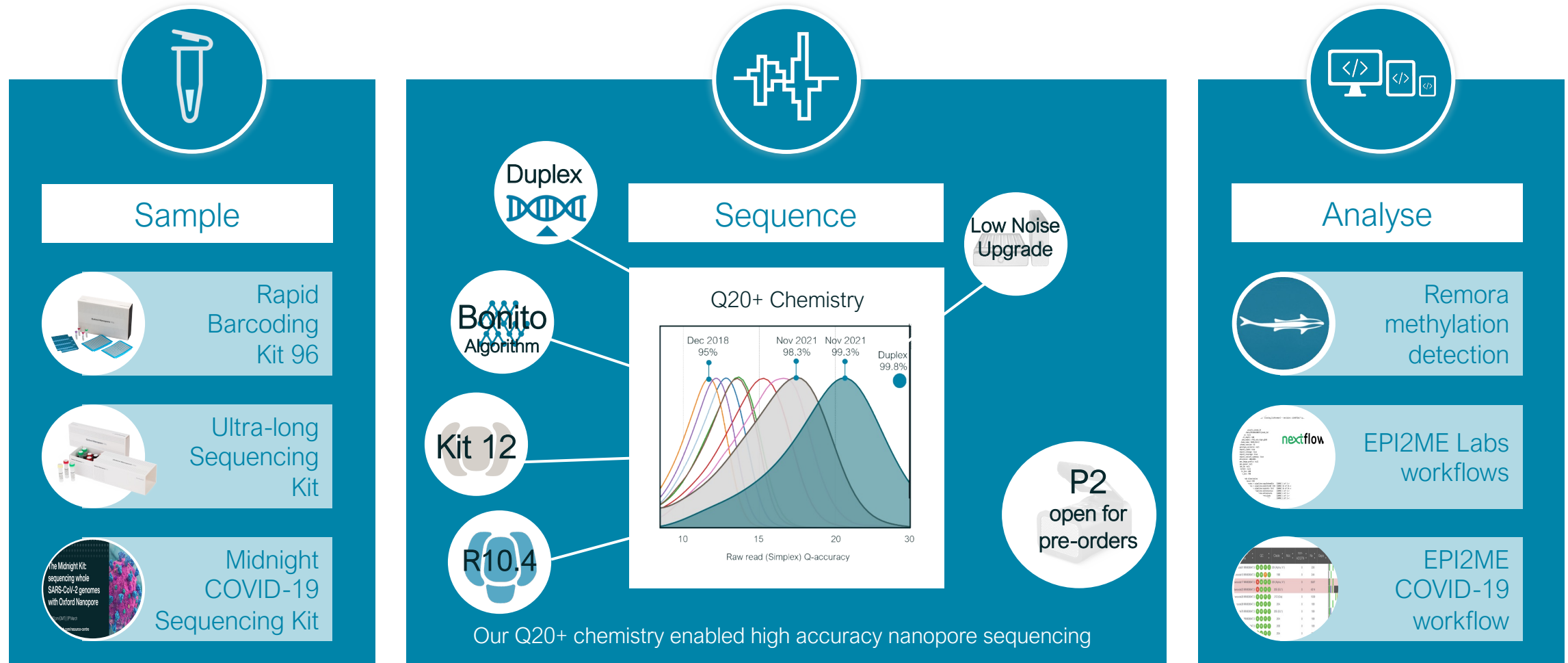
Investment in foundational IP, platform development and infrastructure



2021 Revenue: LSRT £127M
2021 Publications: > 1,000



Key product releases in 2021 driving performance, usability and range



High-accuracy nanopore sequence for comprehensive genomes: user data

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

nature biotechnology

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nature > nature biotechnology > articles > article

Article | Open Access | Published: 04 May 2020

Nanopore sequencing and the Shasta toolkit enable efficient de novo assembly of eleven human genomes

Kishwar Shafin, Trevor Pesout, ... Benedict Paten

Abstract

De novo assembly of a human genome using nanopore long-read sequences has been reported, but it used more than 150,000 CPU hours and weeks of wall-clock time. To enable rapid human genome assembly, we present Shasta, a de novo long-read assembler, and polishing algorithms na sequencer and our tool d. We achieved roughly >100 kb using three flow genome assembly in un HFI FN polished banlaic

To add to that: 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.

“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”

bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

bioRxiv posts many COVID-19 related papers. A reminder they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

New Results

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

Mantas Sereika, Rasmus Hansen Kirkegaard, Soren Michael Karst, Thomas Ysling Michaelsen, Emil Aarne Sorensen, Rasmus Dam Wollenberg, Mads Albertsen

doi: <https://doi.org/10.1101/2021.10.27.466057>

This article is a preprint and has not been certified by peer review [what does this mean?]

Abstract Full Text Info/History Metrics

ABSTRACT

Long-read Oxford Nanopore sequencing has democratized mic sequencing and enables the recovery of highly contiguous mic isolates or metagenomes. However, to obtain near-perfect gen necessary to include short-read polishing to correct insertions from homopolymer regions. Here, we show that Oxford Nanop to generate near-perfect microbial genomes from isolates or m shortread or reference polishing.

“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

Alexander Wittenberg @AW_NGS · Dec 2

Duplex only @nanopore assembly of the genome outperforms @PacBio HIFI-based assembly at the same coverage. Shown below five longest duplex reads. Learn more today: nanoporetech.com/resource-centr... #nanoporeconf #crops

ONT read	Length (bp)	Q-score Guppy	Alignment identity %
1	158.119	32.3	99.9
2	151.925	30.0	99.8
3	140.215	24.1	99.1
4	136.897	30.2	99.7
5	135.724	32.6	99.9

“...outperforms Pacbio Hifi at the same coverage”

Alexander Wittenberg, KeyGene, December 2021

Alexander Wittenberg @AW_NGS · Dec 1

Q30 consensus reads ~15-20Kb are great, however ~20-100Kb Q30 @nanopore duplex reads are truly disruptive. Shown is a 90Kb R10.4 duplex read with 99.94% identity against golden reference B73 NAM v5.0 #nanoporeconf #accuracy #crops

2021 highlights



INCREASED PACE OF INNOVATION

Chemistry and Kit upgrades

Launched Q20+ chemistry, the new “Kit 12” and R10.4 Flow Cells, delivering >Q20 (>99%) raw read accuracy and ~Q30 (>99.9%) accuracy using “Duplex”

Expanding device range

Announced development of the PromethION2 (P2), our most accessible high-throughput sequencer (expected to launch in H2 2022)

Enabling richer data

Initial release of Remora, a tool to enable high accuracy, real time methylation analysis



GROWING USER COMMUNITY DRIVING SCIENTIFIC IMPACT

Increasing user base and utilisation

- >6,300 total active accounts
- Strong starter pack and consumable growth
- Growth across all customer groups

1,000 papers published by the Nanopore community; a 23% increase from 2020; spans multiple scientific areas incl. human, cancer, plant, pathogen

Human genomics, at scale

- Emirati Genome Program
- Multiple pilot scale human genome projects, such as: Genomics England in cancer and NIH in neurodegenerative disease



STRONG OPERATIONAL & FINANCIAL PROGRESS

Record revenue and revenue growth in core LSRT business; 94% increase in 2021

Production and supply chain expanded and scaled to meet increased demand

Increased global headcount to > 800

- Expanded global commercial and marketing teams, including leadership positions
- Established Oxford Nanopore Diagnostics Team
- Wendy Becker and Adrian Hennah appointed to Board of Directors

Completed £602m IPO on LSE

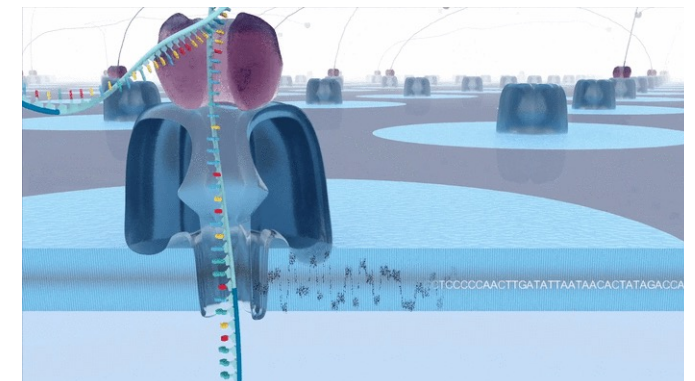
Direct single-molecule sensing

Read the actual DNA molecule, not a proxy

Nanopore sensing reads native DNA or RNA, not a copy or picture



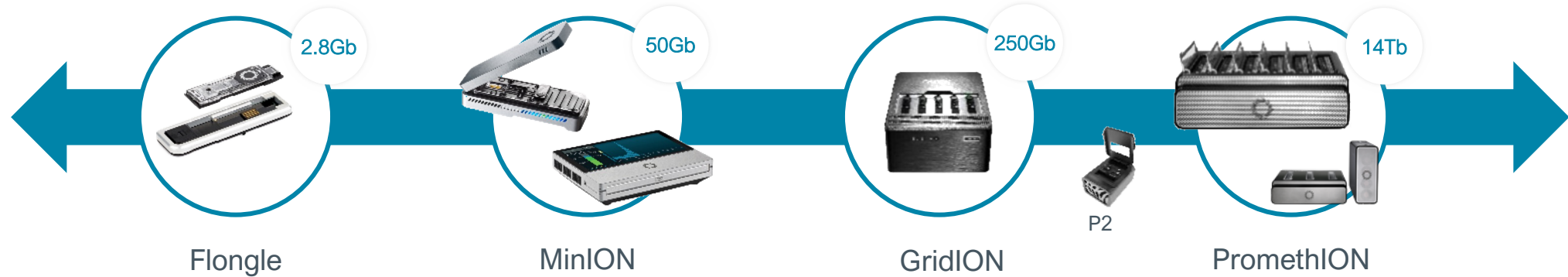
The power of native DNA



- ✓ Retain all the biological information, including methylation
- ✓ Simplify chemistry and hardware with no labels or optics required
- ✓ No GC bias, access the whole genome
- ✓ Read any fragment size

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

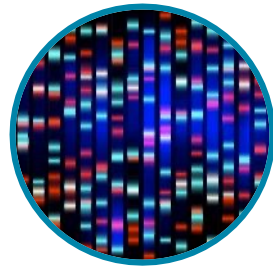
Targeted Sequencing

Animal WGS

Human WGS

Plant WGS

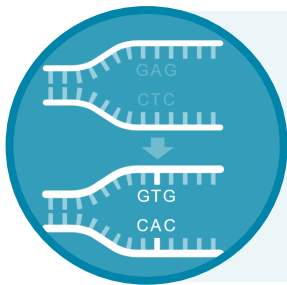
Transcriptomics



More comprehensive genomic insights

Today's SBS technologies vs Oxford Nanopore

Today, traditional SBS enables:



1. Single Nucleotide Variants

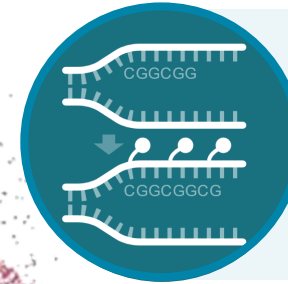
- e.g. Sickle cell disease



2. Insertion / deletions

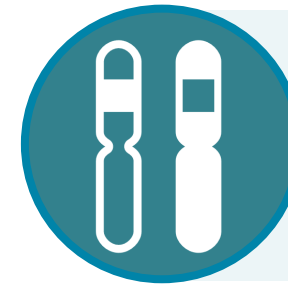
- e.g. Cystic Fibrosis

Nanopore sequencing *also* enables:



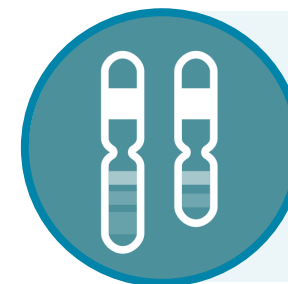
3. Methylation in real time

- e.g. fragile x syndrome
- DNA methylation patterns are globally disrupted in cancer



4. Structural Variation

- e.g. cancer, Alzheimer's, Parkinson's, Prader-Willi syndrome



5. Copy Number Variation

- e.g. cancer, autism, schizophrenia, ADHD



Unravelling the genome

Define mechanism of disease & variant associations which is missed by SBS technologies

“34% of all disease-causing variation is made up of variants that are larger than a single base-pair substitution”

“Structural variants contribute more base-pair differences between two human haplotypes than any other form of genetic variation & 30x more likely to impact gene expression”

Evan E. Eichler, July 2019, N Engl J Med 2019;381:64-74., DOI: 10.1056/NEJMra1809315

Class of human genetic variant	Size of variant (bp)	# per genome	Percent of genome:
SNV	1	4-5M	0.078
Indel	1-49	~700K	0.069
SV	>50	~25K	0.19
Inversions	>50	153	0.397
Copy-number variants	>1000	~500	0.232

Methylation: Impacts all variants above

ECONOMICS & SCALE OF GENOMICS



	1	2	3*
# of genomes / PromethION flow cell (20 - 30X)	1	2	3*
# of genomes per P48 device / year	~4,600	~9,200	13,800
Nanopore cost per genome	~ \$690	~ \$345	~ \$235

Rapid pathogen sequencing: Proud to provide tools in the fight against COVID-19

And building a strong potential pipeline beyond the pandemic



COVID-19 GENOMIC EPIDEMIOLOGY

More than **990,000*** SARS-CoV-2 genomes sequenced on nanopore in **>85 countries**

UCSF doctor detects 1st U.S. omicron case in 8 hours



- ✓ Sample to answer in as little as 8 hrs
- ✓ Simple to run, highly accessible
- ✓ Sample cost of under \$10.00

DRUG RESISTANT TUBERCULOSIS

A major global killer with rapidly increasing resistance to antibiotics. **> 400** samples run in clinical evaluation with **FIND**



- ✓ Sample to answer in as little as 7 hrs
- ✓ Cover ~200 drug resistance associated mutations in a single test: address drug resistance and multi-drug resistance
- ✓ Capability: detect presence / absence
- ✓ Potential to be highly competitive with POC diagnostics

RESPIRATORY METAGENOMICS PILOT STUDY

Identify **bacterial/fungal pathogens** & antimicrobial resistance associated with **hospital acquired pneumonia**



- ✓ Sample to answer in as little as 4 hrs
- ✓ 100+ ICU sample trial at St Thomas' Hospital, London showing high concordance with slower culture methods
- ✓ Clinicians adapting treatment in up to 33% of cases with much improved outcomes

Combining information depth with speed and scale

Identify novel markers for poorly diagnosed diseases

SOLVING DIAGNOSTIC ODYSSEYS FOR NEUROLOGICAL DISORDERS

‘Often difficult to diagnose due to **complex symptoms** & the challenging nature of these **repetitive sequences**, and limitations of existing genetic testing methods,’

1
Test

50
Diseases

Read Until
technology

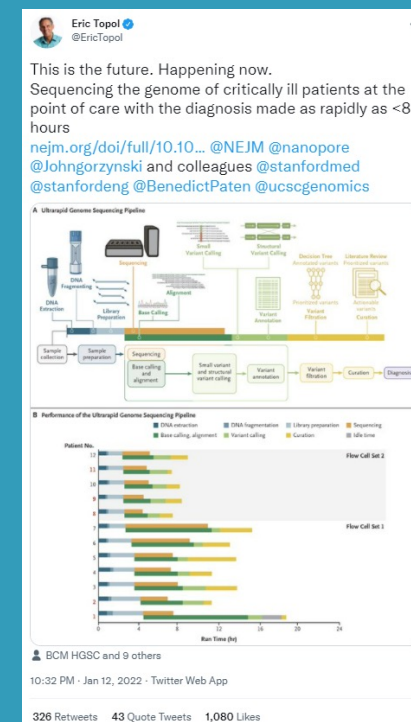
Rapid
answers

- ✓ Nanopore sequencing enables the interrogation of unusually long repetitive DNA sequences (STRs)
- ✓ Simple to run, highly accessible on MinION or GridION

STANFORD NEJM: SHOWCASING SCALABILITY/REAL TIME BENEFITS, AND CLINICAL UTILITY IN 12 CRITICAL CARE PATIENTS

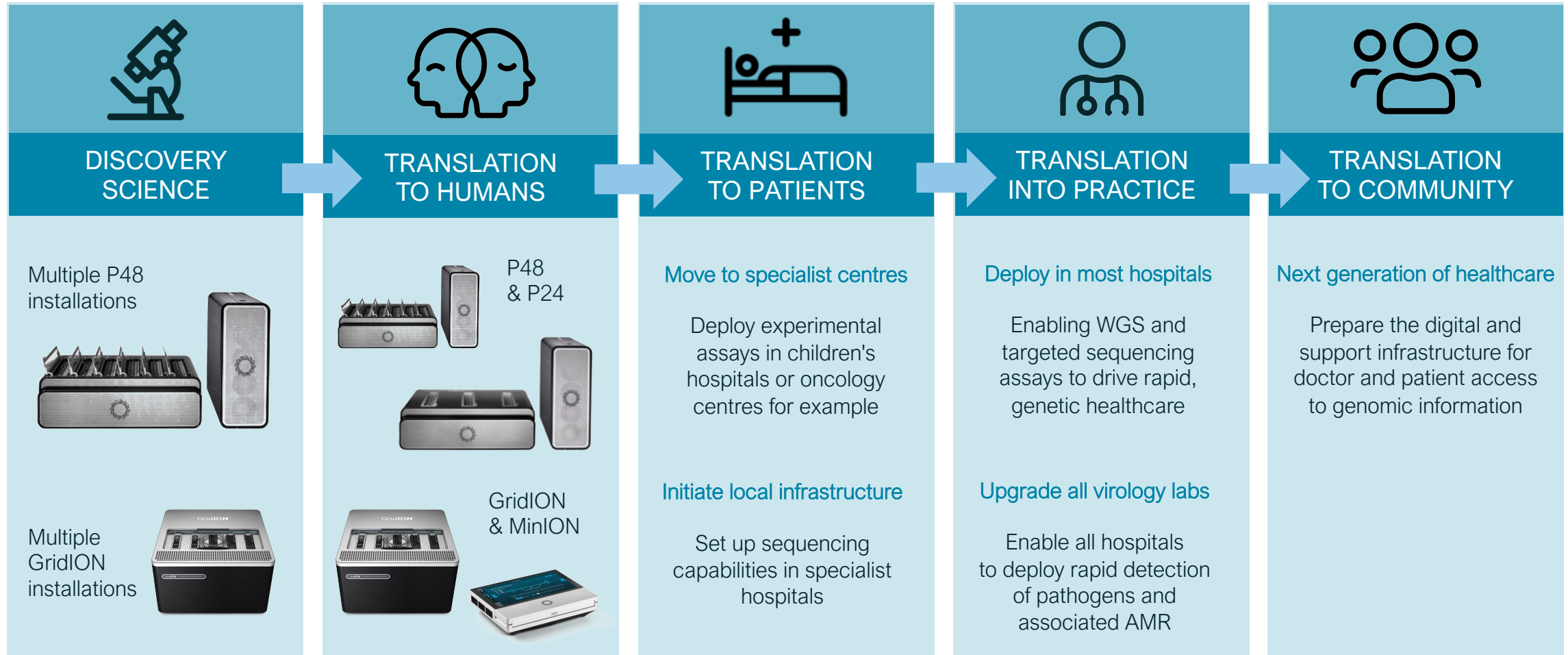


- ✓ Sample to answer in under 8 hrs (*Average seq. time <2.5 hours for 60x genome*)
- ✓ Multiple flow cells run; samples can be sequenced sequentially, reducing per-sample cost
- ✓ Findings confirmed by CLIA lab & informed clinical management
- ✓ Nanopore ultra-rapid pipeline found pathogenic variant that was NOT in (slower) “standard of care” panel



Moving from research into the community

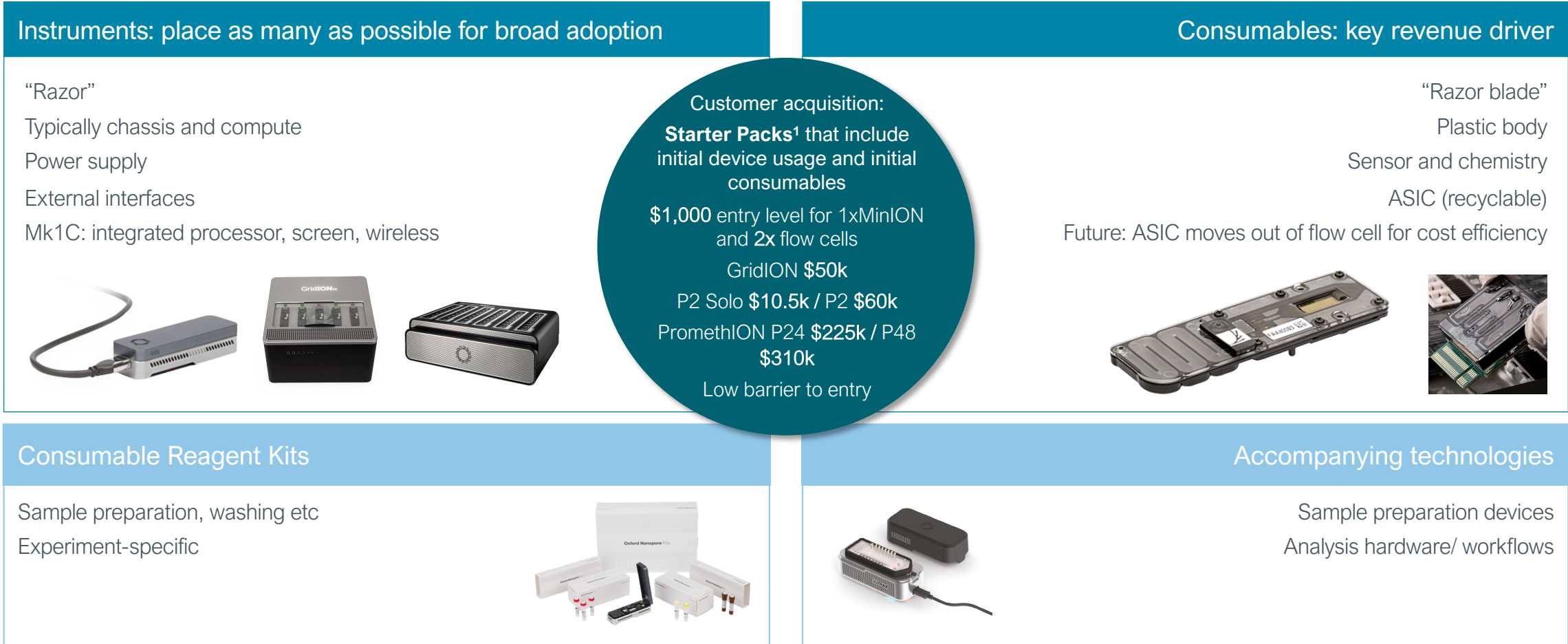
Roadmap for deployment of genomic healthcare



2021 Financial Review

Tim Cowper, CFO

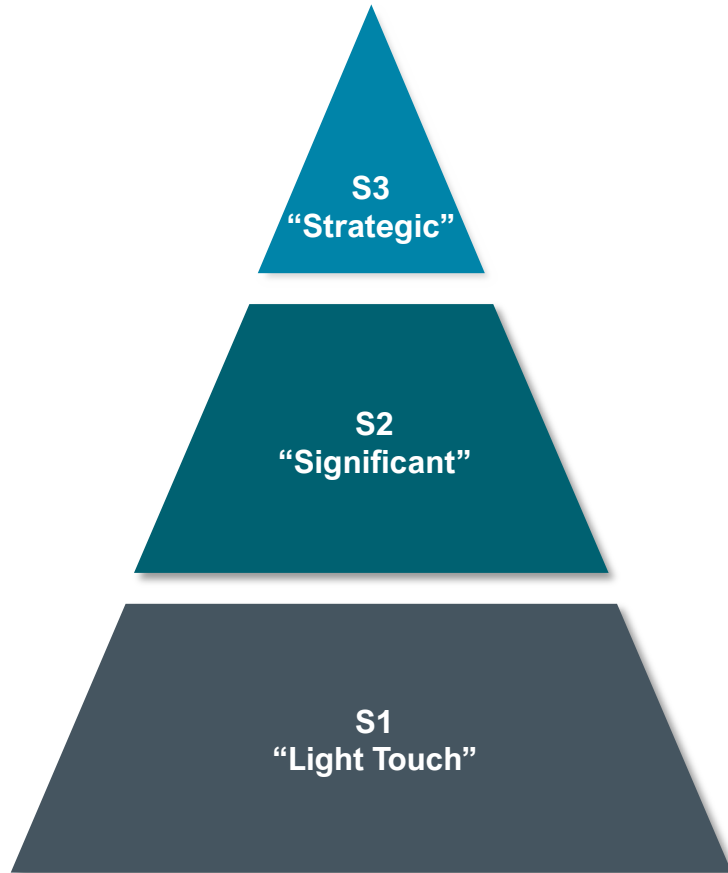
A differentiated business model...



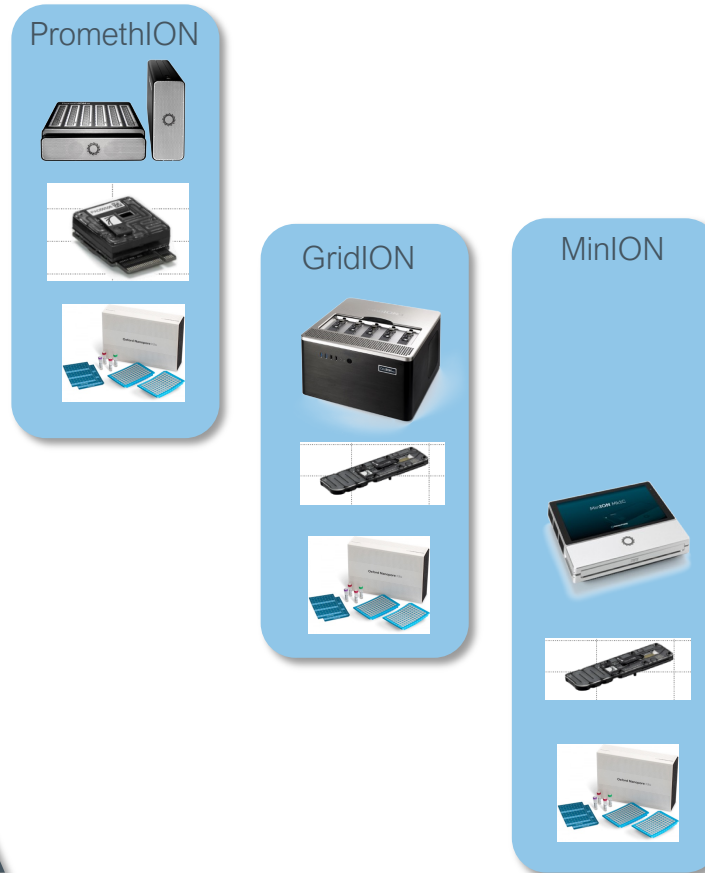
Note¹: Starter packs including a Cap Ex option

...with a device-agnostic, customer-centric approach...

Customer Groups



Selected Product Offerings



Business Dynamics

S3

- Typically large scale, multi-year customer projects
- Somewhat irregular revenue recognition in emergent phase
- Significant short-term growth opportunity

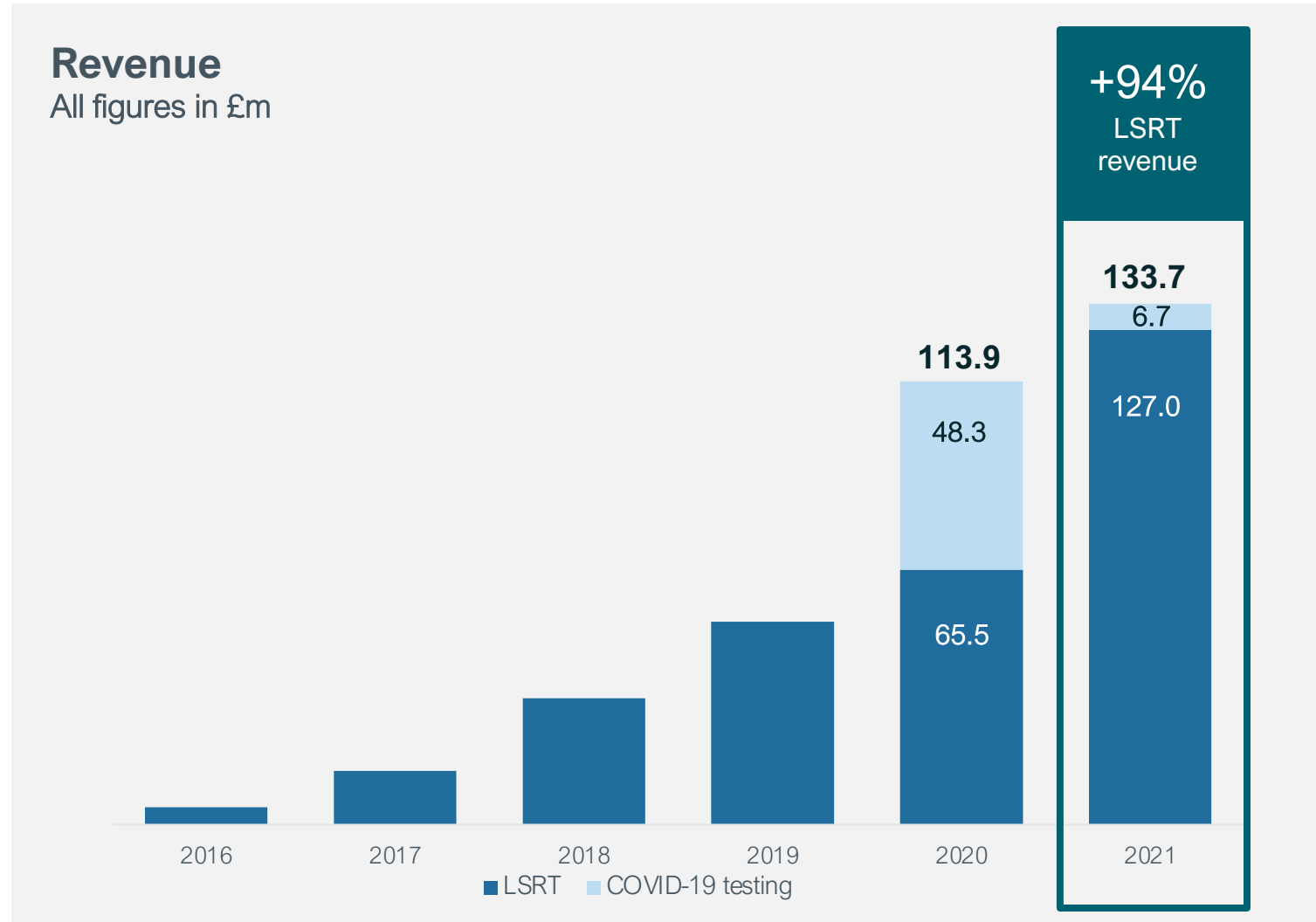
S2

- Medium scale, multi-month customer projects
- Tailwind from COVID sequencing in 2021
- Medium-term high growth opportunity

S1

- Smaller scale, varied frequency customer projects
- Entry point for nanopore projects
- Broad and diverse use cases, customers, revenues
- Stable growth opportunity

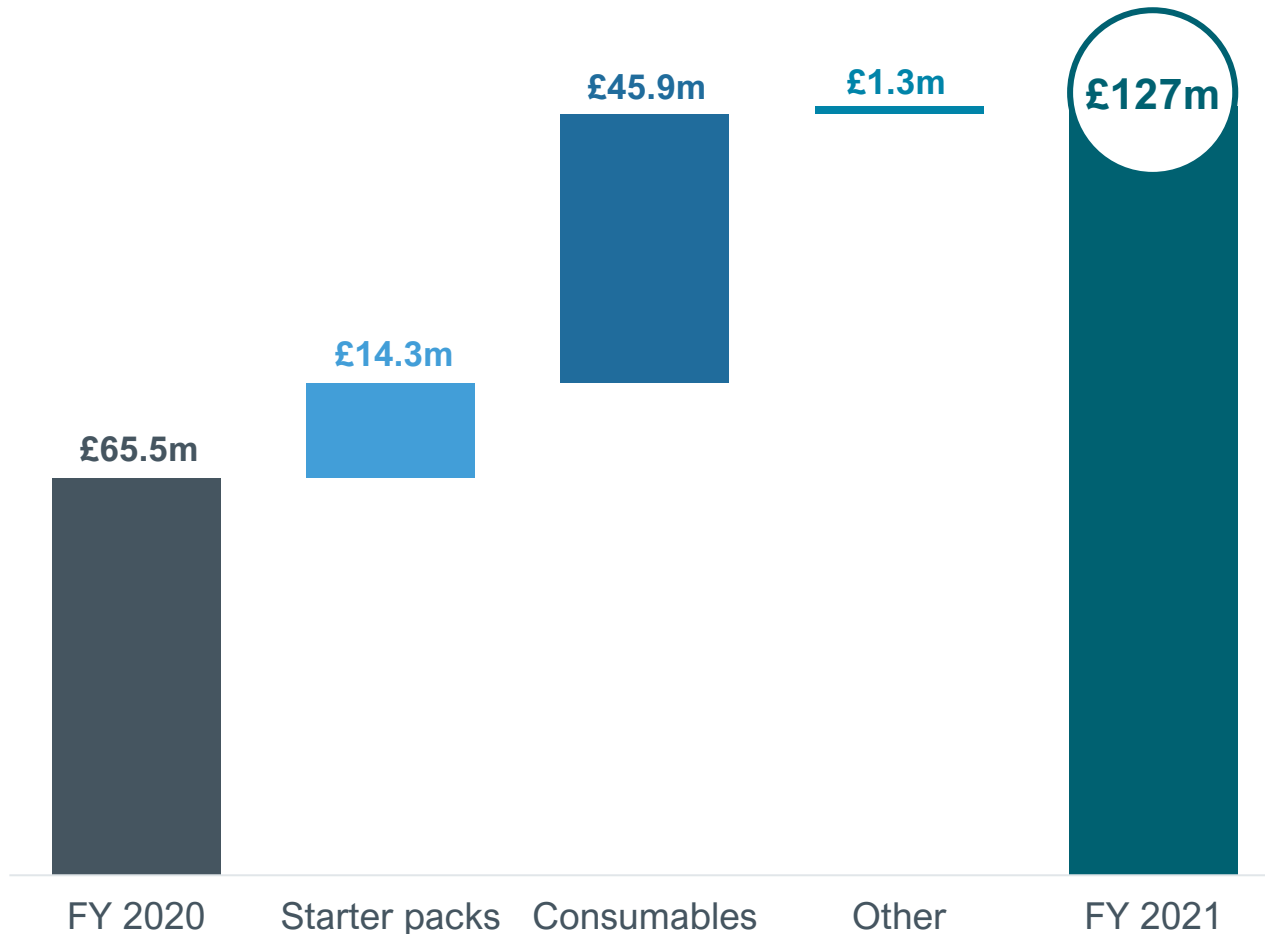
...delivering strong top-line growth



Strong LSRT growth; 94% year-on-year

- Second half expansion in Emirati Genome Program (EGP)
- Significant contribution from COVID-19 surveillance
- Continued robust underlying growth

Drivers of full year LSRT revenue growth

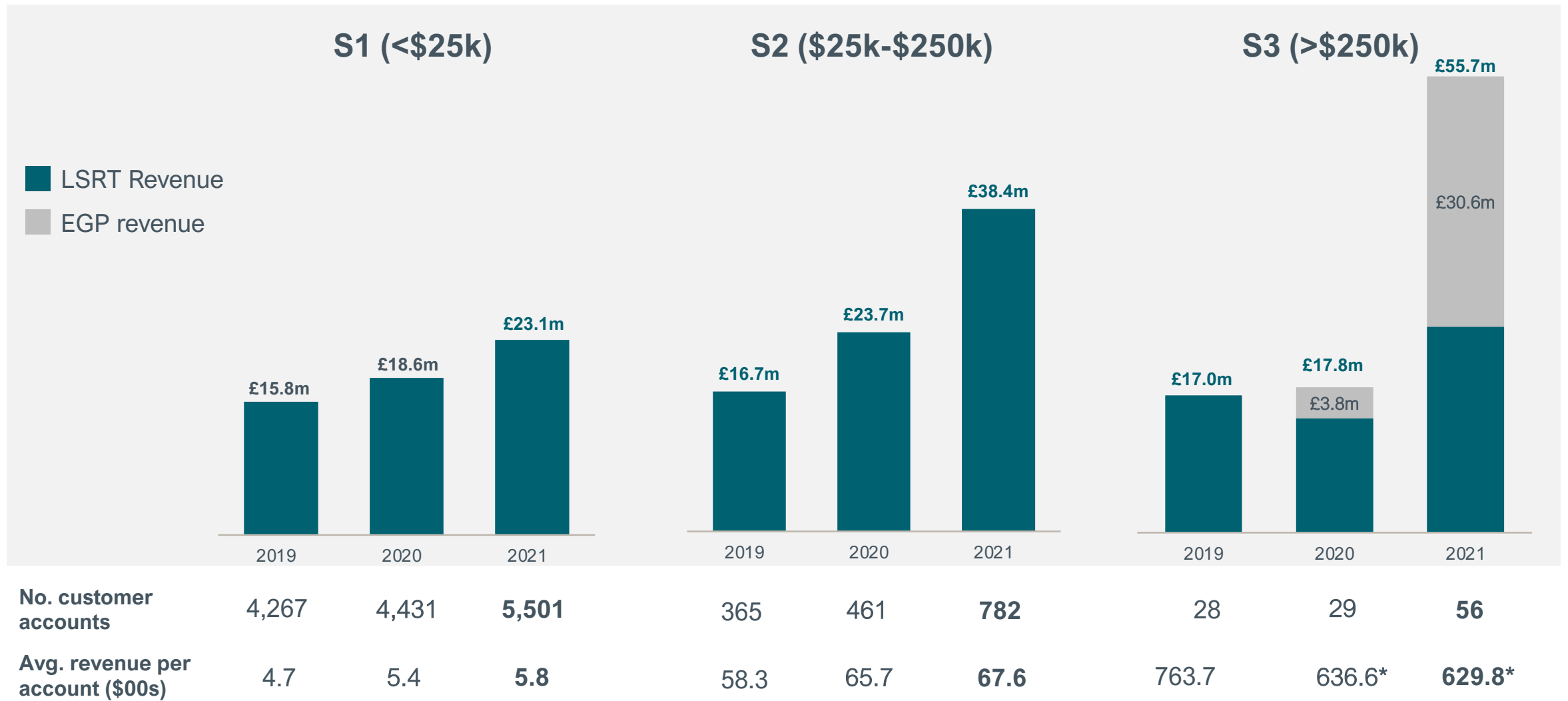


Starter pack revenue increased by 68% in 2021 to £35.1m (2020: £20.8m)

Consumables revenue increased by 116% in 2021 to £85.4m (2020: £39.5m)

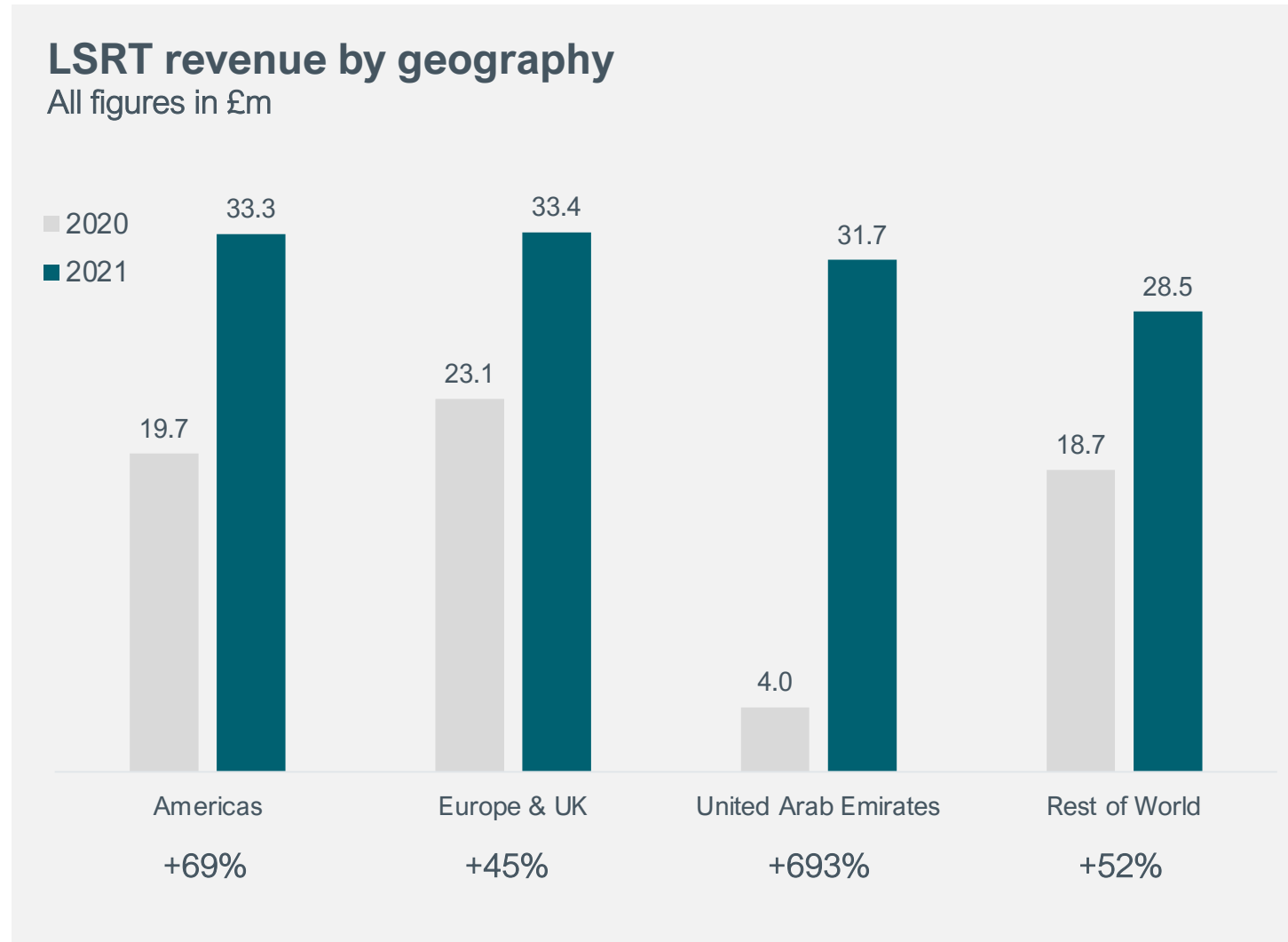
Other revenue increased by 25% in 2021 to £6.5m (2020: £5.2m)

Growth underpinned by customer diversification and increasing revenue per account



Note: Excludes COVID-19 testing revenue. Total LSRT revenue includes additional c.£10m p.a. from Indirect customers in 2021
 *Excludes revenue from EGP.

Revenue growth: diversified customer geography



Strong growth in Americas reflects increase in commercial resources

UAE growth driven by EGP

RoW growth offset by China headwind

Strategic approach to margin mix

Starter packs



Established consumables

Typical gross margin
~30%



Typical gross margin
>65%

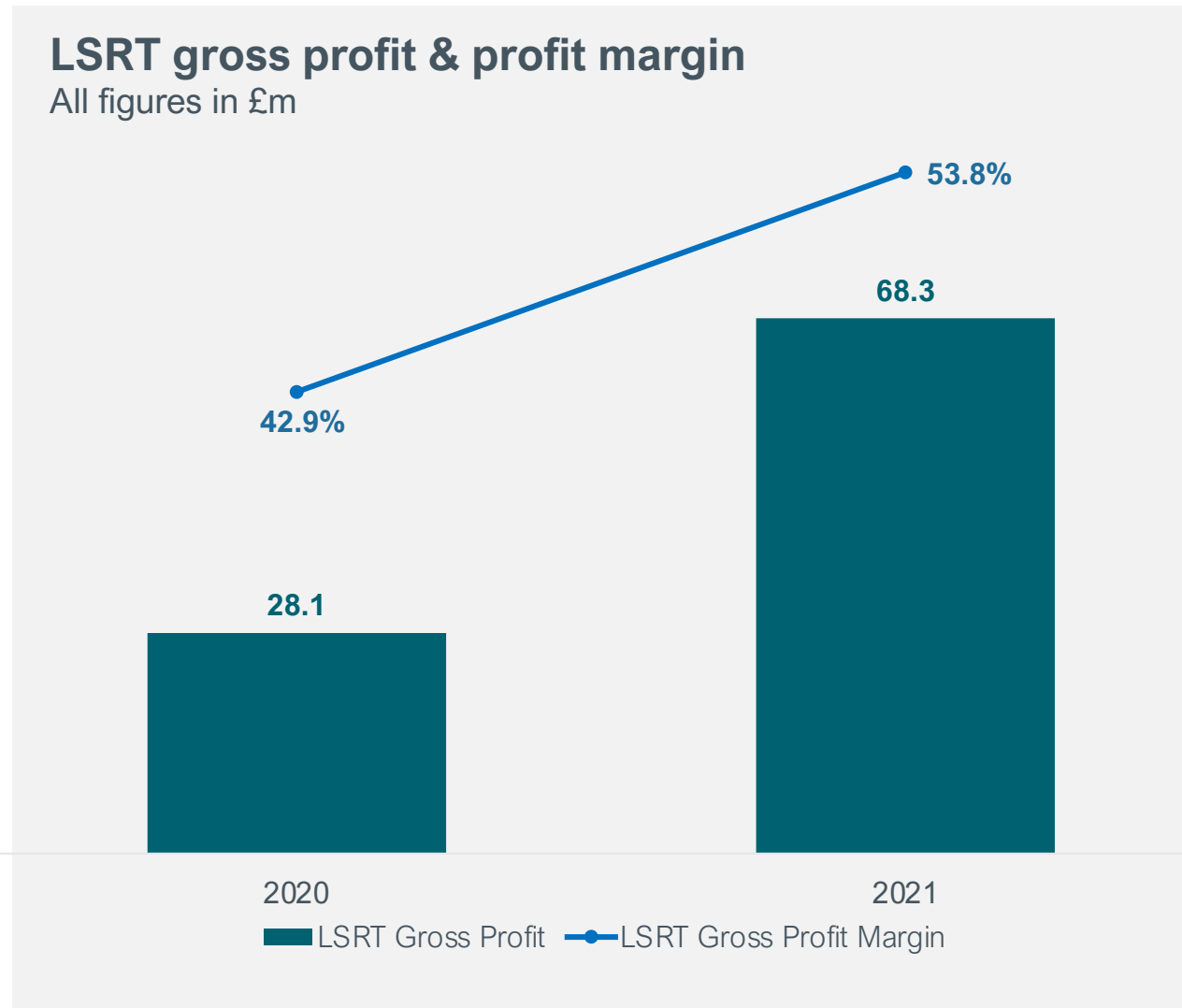


Starter packs typically have a lower margin but drive customer adoption

PromethION flow cell margins have increased substantially during the first year of full production

Group level gross margins increase with shift in consumable / starter pack product mix

Improving margins from our core LSRT business



143% growth in LSRT gross profit to £68.3m

LSRT gross profit margin increased in 2021 due primarily to:

- higher margins from PromethION flow cells
- greater proportion of consumables vs starter packs

Focus on manufacturing automation, greater use of capacity and improved design and production techniques

Summary income statement

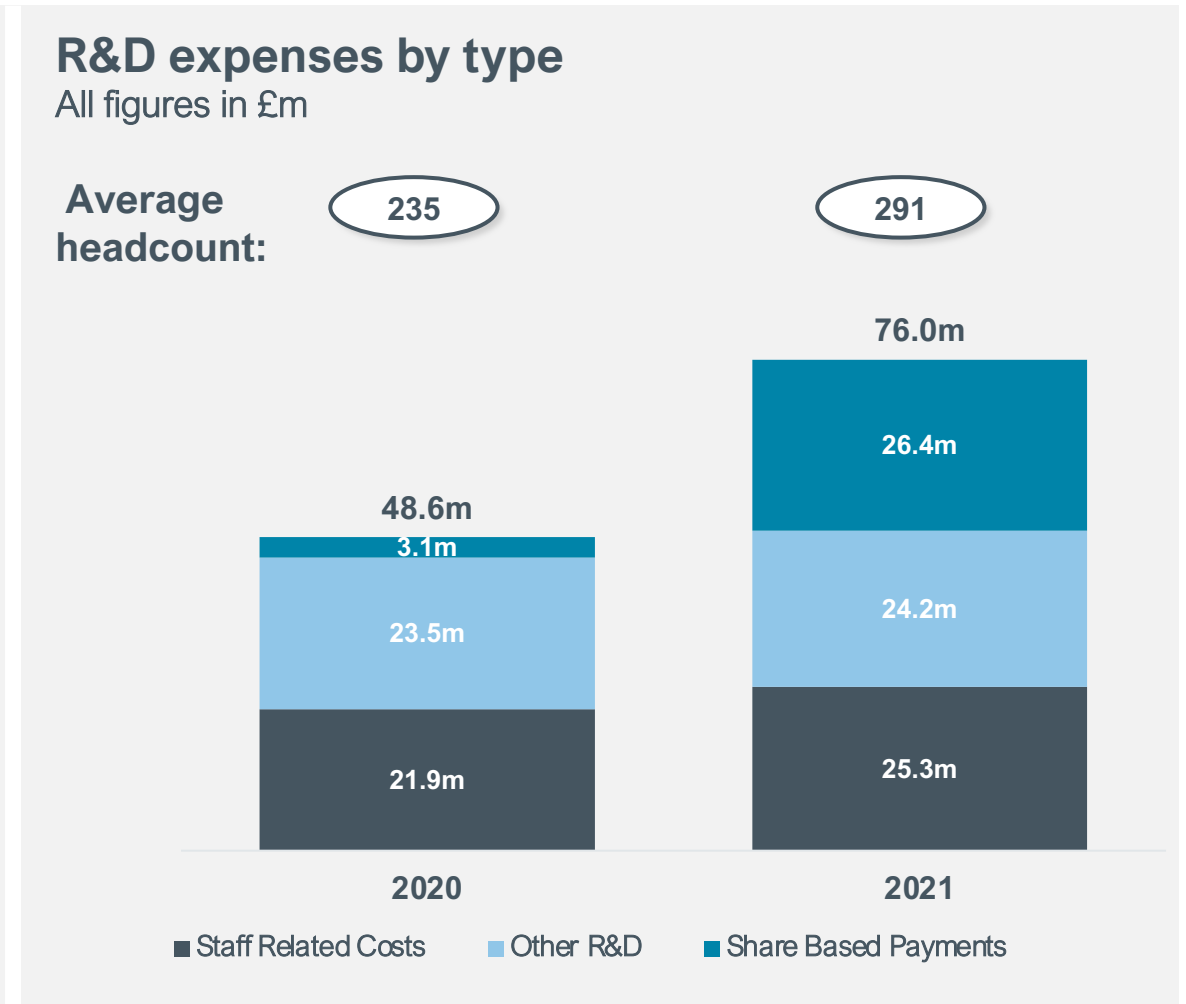
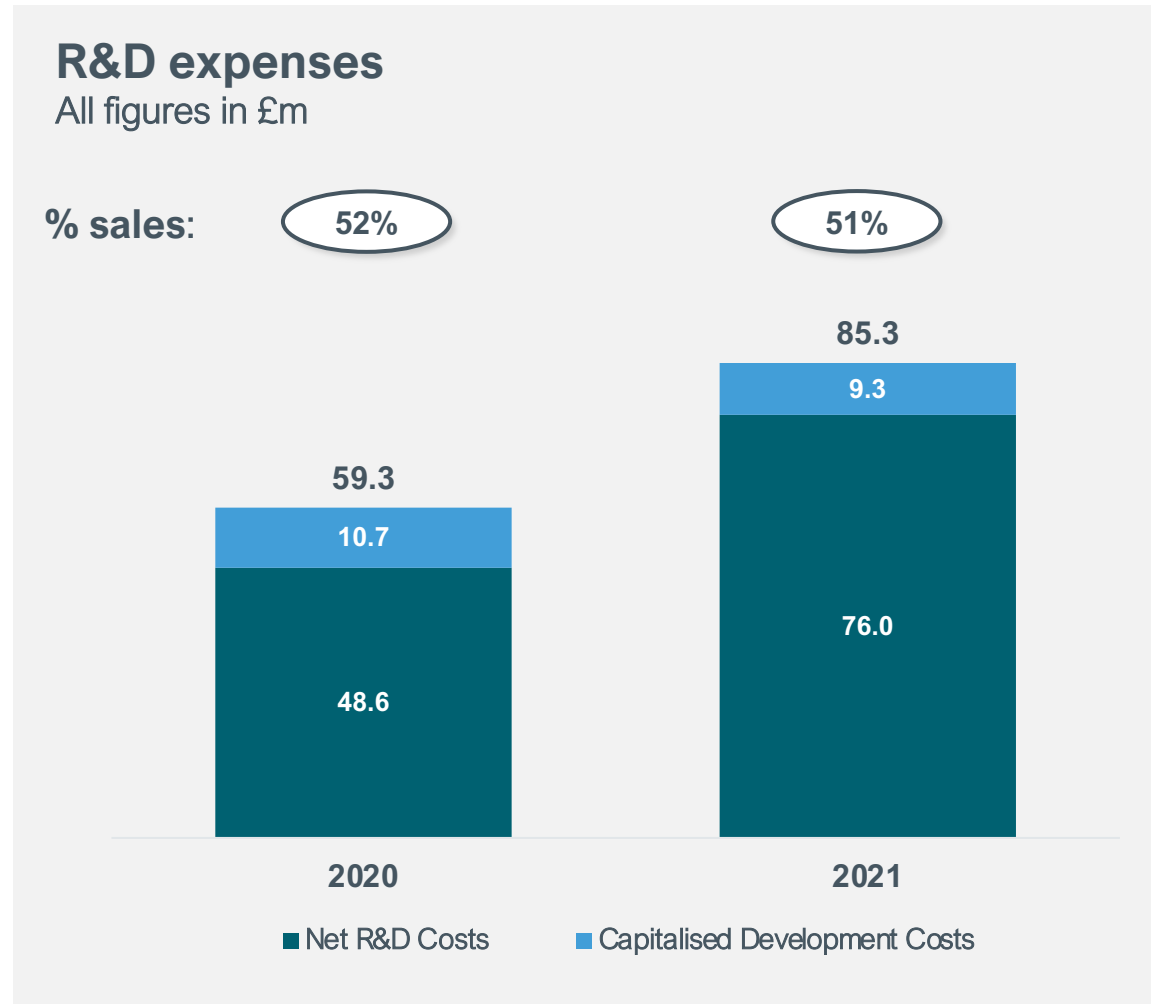
	2021 £m	2020 £m
Revenue	133.7	113.9
Cost of Sales	(60.5)	(67.0)
Gross Profit	73.2	46.9
<i>Gross margin %</i>	<i>54.8%</i>	<i>41.2%</i>
Operating expenses		
Research and development expenses	(76.0)	(48.6)
Selling, general & administrative expenses	(161.8)	(71.4)
Loss From Operations	(164.5)	(73.1)
Other	(1.5)	(0.1)
Loss before tax	(166.0)	(73.2)
Tax	(1.6)	11.9
Loss for the year after tax	(167.6)	(61.2)

Adjusted EBITDA

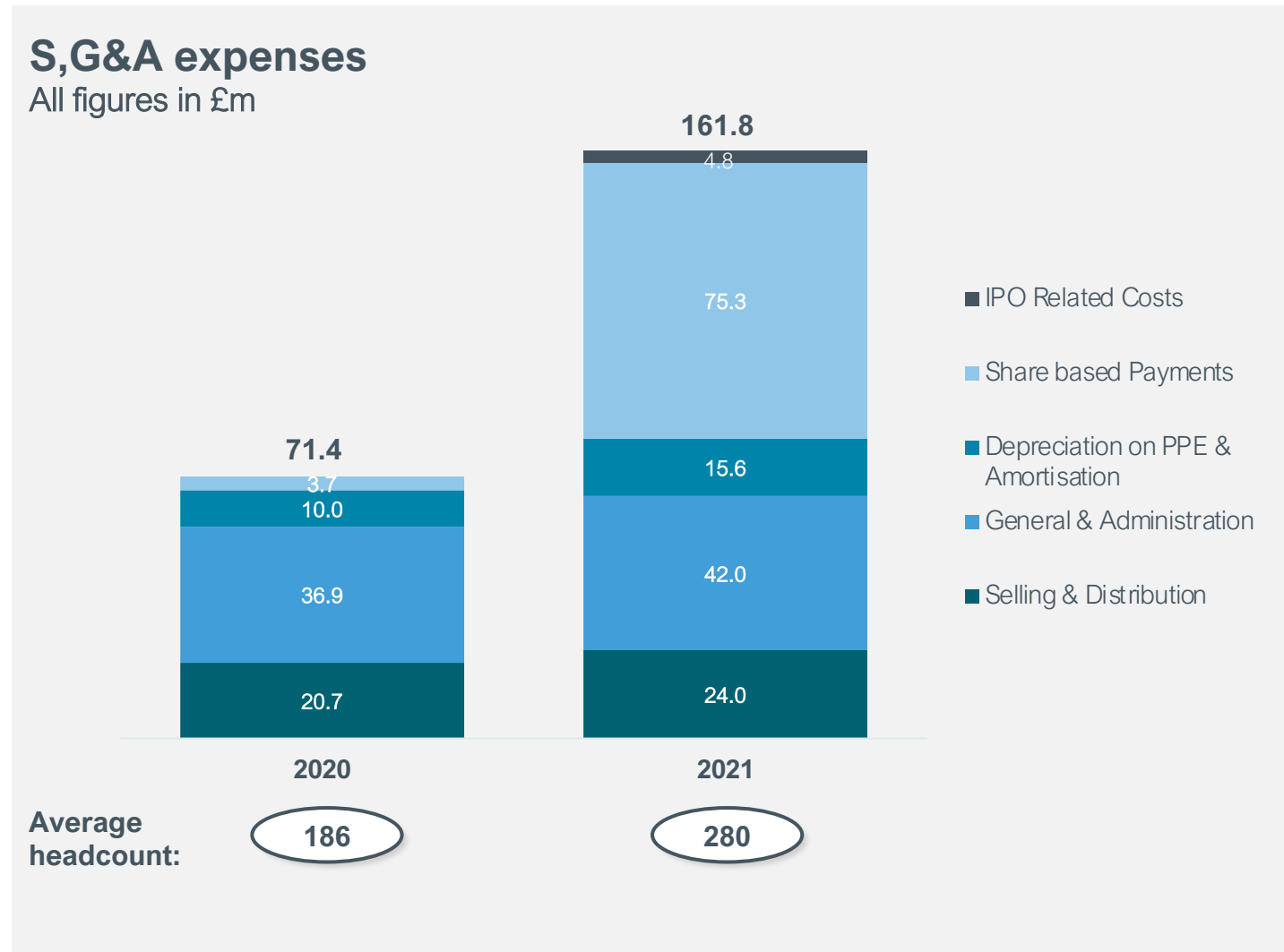
	2021 £m	2020 £m
Loss before tax	(166.0)	(73.2)
Depreciation	15.6	12.5
Amortisation	9.1	4.8
Other	0.7	0.7
EBITDA	(140.6)	(55.2)
Founder LTIP	39.3	0.0
Employers Social Security on pre IPO Share Awards	37.6	0.0
IPO Costs	4.8	0.0
Other	1.2	1.5
Adjusted EBITDA	(57.7)	(55.2)

Growing investment in R&D to underpin delivery of continuous innovation

2021 R&D spend focused on PromethION chip development and scale up



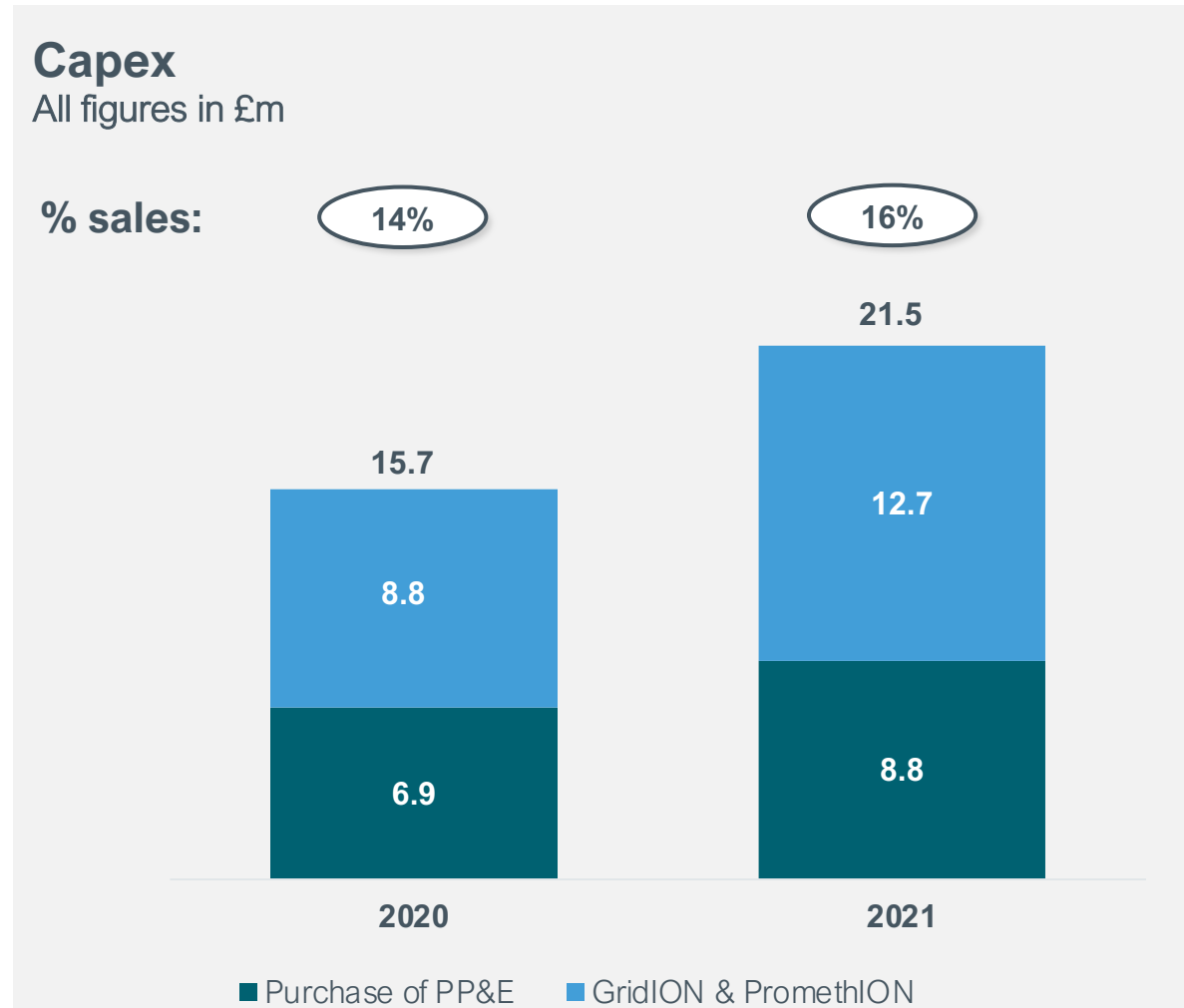
Selling, General & Administrative expenses



2021 includes share-based payments of £75.3m

S,G&A expenses, excluding founder LTIP share based payments, employers social security and IPO costs were 73% of sales in 2021 (2020: 63%)

Capex spend



Key areas of investment:

Purchase of PP&E

- 2021 focus on enhancing laboratories to assist R&D efficiency, and manufacturing automation.

Assets under Lease

(PromethIONs and GridIONs at customers)

- Driving future growth

Balance sheet

	2021 £m	2020 £m
Non-current assets	91.3	78.1
Current assets		
Inventory	63.1	35.6
Debtors	69.1	86.6
Other financial assets	130.6	
Cash and cash equivalents	487.8	80.9
Total assets	841.9	281.2
Non-current liabilities	(32.8)	(23.1)
Current liabilities	(105.0)	(72.2)
Net assets	704.0	185.9
Total Equity	704.0	185.9

Inventory has increased due to our long-term agreements with key suppliers focused on electric components

Cash, cash equivalents and short term treasury deposits of £618m

Updated financial guidance

FY 2021 Actual	<p>LSRT Revenue: £127m <i>vs. >£120m guidance</i></p> <p>Gross margin: 54.8% <i>vs. approx 55% guidance</i></p>
FY 2022 Guidance	<p>LSRT revenue: £145m to £160m <i>Previously £135m to £145m</i></p>
FY 2023 Guidance	<p>LSRT revenue: £190m to £220m <i>Previously £170m to £190m</i></p> <p>Gross margin: >60% <i>No change</i></p>
Medium Term (3-5 years) Guidance	<p>Compound annual revenue growth: >30% <i>No change</i></p> <p>Gross margin: >65% <i>No change</i></p> <p>Adjusted EBITDA: Breakeven by 2026 <i>No change</i></p>

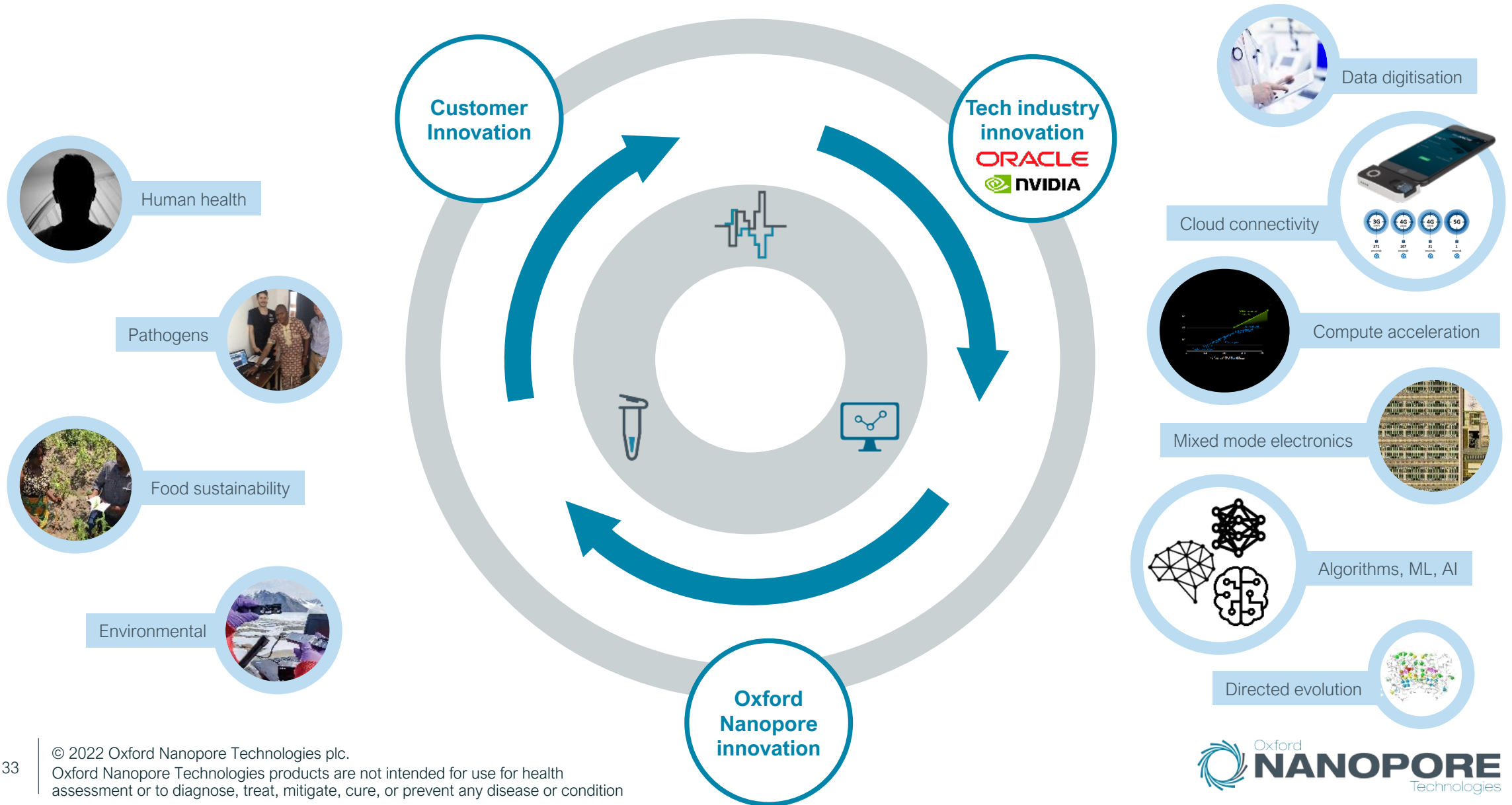
FY22 revenue guidance accounts for an expected significant decline in COVID testing revenue in 2022 and the recognition of revenue from the Group's largest customer in Q4 2021, previously expected Q1 2022

“Our goal is to enable the analysis of anything, by anyone, anywhere”

Summary & outlook

Gordon Sanghera, CEO

Innovation strategy for long term growth



Q&A

Gordon Sanghera, CEO

Tim Cowper, CFO

Thank you

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Full year cash flow

	2021 £m	2020 £m
Net cash outflow from operating activities	(53.8)	(63.8)
Net cash used in investing activities	(162.0)	(26.9)
Net cash from financing activities	622.9	158.6
Net (Reduction)/increase in cash and cash equivalents	407.1	67.8
Effect of foreign exchange rate changes (loss)/gain	(0.1)	(0.1)
Cash and cash equivalents at beginning of period	80.9	13.1
Cash and cash equivalents at end of period	487.8	80.9

Cash absorbed by operations reflects operating losses made in the year.

Net cash used in investing activities includes:

- £9.3m of capitalised development costs
- £8.8m of capex in property plant & equipment
- £12.7m of GridIOns and PromethIOns sent to customers

Net cash from financing activities includes:

- The Gross fund raising in April of £202m at £3.50 per share
- the Gross fundraising from the IPO of £428m at £4.25 per share