Origin

Preview

Investment Memorandum

A New Era in Gastro-Intestinal Diagnostics and Discovery

Origin

Origin Sciences is a privately funded research company with a general interest in diseases and conditions of the gastro-intestinal (GI) tract, and a current specific focus on the diagnosis of colorectal cancer (CRC).

The company has a research laboratory in Cambridge (UK) and a London-based office. Origin has lean but highly experienced management and research teams (see page 10), with a particular focus on innovation and product delivery.

Origin Sciences holds significant proprietary intellectual property relating to a unique medical device – Oricol™ – used for the collection of rectal mucosa in human subjects. It is a very novel and useful tool with a vast range of potential 'high performance' diagnostic applications – the primary diagnostic application being the early diagnosis of colorectal cancer.

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We're developing a **colorectal cancer screening test** that's simple, affordable and exceptionally accurate.

KEY INFORMATION

£11.6M

investment to date

from prior
funding rounds

£10.7M

current valuation

pre-money, fully diluted
as of June 2020

August 2020

next round

Full details
to be provided soon

It will save lives – and save health services money.

For every 17 people who read this sentence, 1 will be diagnosed with colorectal cancer in their lifetime

9%

global incidence rate
and growing

4th

most common cancer
worldwide

1.8M

new cases in 2018
worldwide

800K

deaths in 2018
worldwide

Colorectal cancer deaths are second only to lung cancer in Europe and the US.

Known as the 'Silent Killer', colorectal cancer is likely to overtake lung cancer as smoking rates decline.

16K

deaths in the UK
every year, and growing

42K

diagnoses in the UK
every year

51K

deaths in the US
every year, and growing

147K

diagnoses in the US
every year

Among cancers, colorectal cancer deaths are the most preventable – if detected early.

Diagnosis at	**% diagnoses** at this stage	**5-Year Survival Rate**		
		Persons	Male	Female
Stage I	15.7%	91.7%	90.7%	93.1%
Stage II	23.2%	84.1%	83.5%	84.9%
Stage III	26.6%	64.9%	64.2%	65.9%
Stage IV	23.3%	10.3%	10.3%	10.3%
Overall		58.4%	58.2%	58.6%

Net Survival % for adults aged 15–99 diagnosed with colorectal cancer between 2013–2017 in England
Office for National Statistics and Public Health England
(11.3% of cases are unstageable or of unknown stage)

But too often, it's detected too late.

Colorectal cancer (CRC) often presents itself very late in the progression of the disease. Typical symptoms are also very common indicators of other less serious ailments, and often those with early stage CRC have no symptoms at all.

This late presentation of the disease often leads to advanced stages at the time of diagnosis and a loss of the opportunity to deliver a curative procedure or operation. The disease becomes more difficult to manage, leading to complications and often premature death.

Current asymptomatic screening has poor health economics.

To catch cancer early, many health systems test everyone routinely.

Asymptomatic screening programmes test everyone considered to be at an elevated risk routinely, in the hope that disease can be diagnosed and treated early.

There are several problems with this strategy —

Screening is expensive.

General population asymptomatic screening is often extremely expensive, with little demonstrable health-economic benefit. Of course, every case of CRC detected early is a health benefit – but the economics are currently hard to justify. The incidence rate (at any one moment in time) for CRC in the general asymptomatic population is actually very small – it's a lifetime risk, and only regular and reliable screening will mitigate the overall risk in any single individual.

Tests are inaccurate and compliance is poor.

There are performance issues with most (if not all) affordable screening tests. In order to make such tests affordable and available to the masses, a stool-based test, such as FOBT (Faecal Occult Blood Test) or FIT (Faecal Immunochemical Test) will be employed. The great advantage of these tests is that the sample can be collected at home and sent to a laboratory for analysis. The first downside is that natural compliance is very poor (up to 50% of un-chased test recipients fail to return the sample), and those that do are often already marginally symptomatic.

Finally, there is an overriding performance issue in that such tests (although inexpensive) are also often inaccurate, particularly in the very early stages of disease. False positives lead to expensive, invasive and unnecessary further investigations, and false negatives defeat the purpose of the test, delivering false reassurances and wasting resources.

Different countries and territories employ dramatically variable healthcare systems and pathways that allow for differing methods of screening and triage – and at the heart of all pathways lies a health-economic equation.

It is fair to conclude that no single solution currently satisfies both the health *and* economic diagnostic conundrum when it comes to colorectal cancer.

Once a patient tests positive, **investigation is expensive – and it's often a false alarm.**

Currently, the only way to conclusively 'rule in' or 'rule out' disease is by means of a colonoscopy, sigmoidoscopy (limited reach) or a CT scan.

The former two tests generally allow for a diagnostic biopsy and visual inspection of the colon, and the latter allows for a visual inspection (only) for disease – usually used in emergency admissions and for patients that are too clinically vulnerable for the more invasive alternatives.

None of these confirmatory tests can be performed at a primary care level, and all are very expensive and not without related risk in their own right. **A colonoscopy in the UK/EU carries a gross cost of between £700 (GBP) and £2,500 (GBP)** depending on where and how it is administered. In the USA, the cost is generally double.

Confirmatory tests are usually administered under one of four individual circumstances:

1. Individuals that have tested positive for faecal occult blood (FOB) in an asymptomatic population screening campaign;
2. Individuals who have presented at a primary care level with sufficient symptoms to warrant further investigation;
3. Individuals who are considered 'at risk', for example those with a family history, and thus have a statistically higher probability of disease (requiring regular screening);
4. Individuals who have been subjected to an emergency admission due to overwhelming indications of disease, and who need immediate investigation.

In groups 1 and 2 (above), the true incidence rate for disease is approximately 5%–8% (depending on territory, test and policy).

This means that for every 100 patients investigated, up to 96% of subsequent tests were performed needlessly with considerable costs and a definable risk to the individual.

Group 3 typically sees an even lower incidence rate at approximately 2%, and the uptake rate (for those that qualify) is as low as 50% (colonoscopy is uncomfortable and not without risk). Thus the 'actual' diagnostic value in the group equates to approximately 1%.

Group 4 is fairly unusual, and the application of an alternative 'triage' test would usually be inappropriate and would not meet the needs of an urgent indicative prognosis.

Our simple screening test will allow health services to **triage patients reliably and economically.**

Globally, there is a desperate requirement for an easy and acceptable test that can be reliably used to 'triage' patients accurately and economically. Ideally, such a test could be ultimately 'pushed back' into the asymptomatic population – whilst justifying the balance of health and economics.

The initial Oricol™ CRC PreView test is set to meet the primary need (symptomatic, screening 'positive' and elevated risk population) and uniquely deliver accurate CRC triage – saving lives and money – the fundamentals of health and economics.

Longer term, it is anticipated that a highly reliable asymptomatic screening tool will find its health-economic position in the ever-changing and territorial marketplace.

We believe that once proven, economically justified and adopted, the principal Oricol™ CRC diagnostic test (Pre-View) will validate and demonstrate its position in an asymptomatic (general population) screening environment. Until such time, we intend to maximise the massive opportunity in the symptomatic, screening positive and at-risk (family history and genetically susceptible) groups.

History

Origin Sciences Limited was originally incorporated in 2003 with the intention of demonstrating a unique biological hypothesis proposed by Dr. Alexandre Loktionov. Dr. Loktionov proposed that cancerous tumours occurring in the gastro-intestinal tract exfoliate cellular material at massively increased rate when compared to healthy mucosa.

The diagnostic principle was simple. The cellular material is biologically carried through the Gastro Intestinal Tract (GIT) and gathers in the rectal mucosa. By collecting this material in a reliable and quantifiable manner, DNA could be extracted and quantified. A pre-determined DNA threshold would be an indicator of disease.

A simple and unique collection device was designed to deliver a robust mechanism for sample capture. Early clinical studies most certainly demonstrated that Dr. Loktionov's hypothesis was indeed correct but results did not quite reach the required levels of accuracy.

More studies were conducted with ever increasing subject numbers. As the numbers increased, diagnostic consistency appeared to deteriorate to a level that was inconsistent with the high demands set by the company. This inconsistency was attributed to several factors, not least the fact that the test relied upon absolute consistency in volumatic (surface area) material collection – something that proves to be difficult in constantly varying human anatomy.

However, parallel investigations at the time demonstrated that this unique mucosal sample, that the new device could retrieve, harboured a plethora of valuable genetic material not seen in any other easily accessible in-vitro human material, such as plasma or stool.

Such an exciting discovery led to the company diverting its attentions to qualitative test strategies in favour of the more restrictive quantitive hypothesis.

The company has now focussed on the qualitative assessment of the unique biospecimen and its contents and has developed reliable techniques for sample handling, sample preservation and transport, extraction, purification and amplification, in order to deliver unparalleled sensitivity and specificity for the presence of colonic tumours.

Recent developments enabled by emerging collaborative technologies has led to the implementation of a highly accurate diagnostic tool for the detection of colorectal cancer in human subjects. The principal test is due to be validated for commercial use in Q3 2021.

Management Team

The current management team has been carefully assembled to cover the diverse needs of the company as it rapidly and diligently focuses on the validation and commercial delivery of its principal product.

Chairman

Rupert Lywood

Rupert is a chartered accountant, with specialities in structured finance and venture capital. He has spent the last 25 years founding and building businesses in the energy, information, finance, medical and media sectors at a multi-billion pound level. Rupert is a co-founder of Origin Sciences.

Chief Medical Officer

Colin Ferrett

Colin is a consultant radiologist at Oxford University Hospital, having trained at Queen's University, Belfast, UC San Diego and UC Stanford in medicine and radiology. He is a co-inventor of the Oricol™ device and founder of Origin Sciences. Involved in diagnostics, staging and research of CRC for 20 years, he is the PI of the recent successful trial. He has collected samples from several hundred patients with suspected colorectal cancer.

Chief Financial Officer

Stuart Lawson

Stuart qualified as a Chartered Accountant at KPMG, and subsequently worked in the manufacturing sector – ultimately taking the role of CFO of a fully quoted company, leading 16 global acquisitions, and 4 green field start-ups – often in conjunction with Rupert Lywood (Chairman).

Non-Executive Board Member

Jay Luo

Mr. Jay Luo is the President & Partner of Dymon Asia Capital, a Singapore headquartered alternative asset management firm. Dymon Asia established a strategic partnership with Temasek, a Singapore-based investment company, in 2014. Previously, Jay was the Head of APAC for S.A.C. Capital Advisors.

Chief Executive Officer

Hugo Lywood

Hugo is passionate about discovery, innovation and commercial conversion. He has worked in a diverse range of fields including scientific education (retail), healthcare (delivery), property (enviro-friendly and affordable), hospitality and latterly primary care investigative and diagnostic solutions (ongoing). Hugo is also the original designer of the Oricol™ device.

QARA and Compliance Manager

Michael Chard

A long-standing (over 40 years) medical device expert, with experience gained through several roles including Quality, Regulatory, Operations, Project Management and Research and Development. Previous employers have included Unilever, Siemens and Alere as well as other SMEs. Notably, whilst with Alere, Michael oversaw production of 90M+ OTC products.

Chief Scientific Officer

Belinda Nedjai

Belinda is a Senior Lecturer in Molecular Epidemiology and epigenetics at The Queen Mary University in London. She has a PhD in functional genomics and genetics. In addition to being the CSO of Origin Sciences, she is also working on CRUK sponsored studies looking at early detection of cancer using methylation biomarkers for Cervical, Prostate and Breast cancer. Specialities include genetics, genomics, NGS, cellular and molecular biology, inflammation and cancer.

Scientific Advisory Board

A core component in the company's strategy is to continually explore the numerous clinical and scientific opportunities and innovations provided for by our proprietary IP, whilst also maintaining a full and thorough understanding of products under development (scientific and clinical).

The Origin Sciences Advisory Board is a collective of individuals each with specific and comprehensive expertise, whilst also being uniquely influential and well respected. All members of the Board are holders of share options in the company.

Chair

Dr. Belinda Nedjai

Belinda is a Senior Lecturer in Molecular Epidemiology and epigenetics at The Queen Mary University in London. She has a PhD in functional genomics and genetics. In addition to being the CSO of Origin Sciences, she is also working on CRUK sponsored studies looking at early detection of cancer using methylation biomarkers for Cervical, Prostate and Breast cancer. Specialities include genetics, genomics, NGS, cellular and molecular biology, inflammation and cancer.

GS Technology Specialist

Dr. Jo Mason

Genomics professional with a demonstrated history of implementing new technology to transform diagnostics in healthcare. Skilled in NGS technologies, population sequencing, Epigenetics, Bioinformatics, Diagnostics, Strategy, building high performance teams and leadership.

Biomedical Engineer

Prof. Molly Stevens

A Professor of Biomedical Materials and Regenerative Medicine, and the Research Director for Biomedical Sciences in the Institute of Biomedical Engineering at Imperial College. Recognised by The Times as one of the top ten scientists. She has also recently been recognised by the TR100, a compilation of top innovators in transforming technology.

Colorectal Surgeon

Mr. Jon Lacy-Colson

A Consultant Colorectal Surgeon at Shrewsbury and Telford Hospital Trust (SaTH) having completed higher surgical training in the West Midlands Deanery. He has a specialist interest in laparoscopic colorectal surgery, colorectal cancer and pelvic floor dysfunction.

GI Cancer Specialist

Prof. Rebecca Fitzgerald

Interim Director of MRC Cancer. Working on new screening methods for cancer of the oesophagus, with plans to roll out into routine clinical use using Cytosponge technology. Through public speaking and charity work, Rebecca raises awareness about heartburn, Barrett's Oesophagus and Oesophageal Cancer. Specialities include GI Cancer, Pre-invasive disease and Hereditary Diffuse Gastric Cancer.

University of Oxford

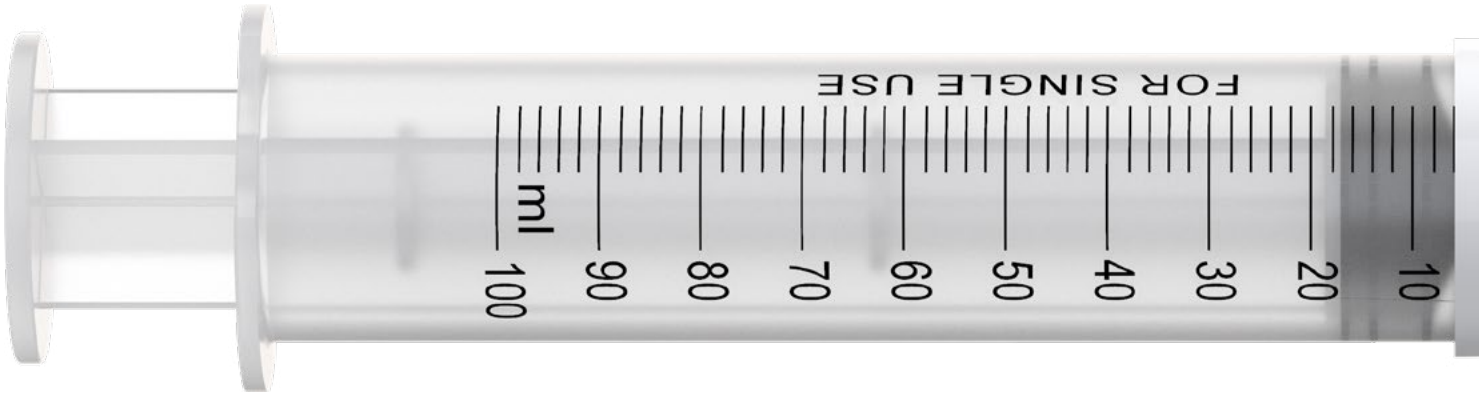
Prof. Daniel Anthony

Professor of Experimental Neuropathology, University of Oxford. He previously held a position as a retained lecturer at Trinity College Oxford before becoming an assistant professor in Neurobiology in Southampton. Daniel now runs a research facility in the Department of Pharmacology at the University of Oxford.

Oricol™

Our simple device for microbiome sampling

1 The subject lies on their side, and a standard clinical proctoscope (disposable and included with the kit) is inserted into the rectum (a very common procedure).



2 The device is then prepared and inserted into the proctoscope. A syringe is used to inject 80ml of air into the device.

The microbiome – the key to diagnosing GI disease

The principal physical product of the company is the Oricol™ sample collection device. This is a simple 'single use' in-vitro medical device that is used to collect a sample of the rectal mucosa in human subjects. This can then be analysed for extremely accurate diagnostics.

The device is the culmination of many years of refinement and improvement in terms of its clinical application, patient acceptability, manufacturability and collection performance.

The current leading method is stool sampling

By far the most common approach to understanding the gut is to analyse samples of a patient's stool. However, a true representation of the microbiome simply is not present in stool.

Furthermore, as patients find sampling their stool unpleasant, compliance if often low.

Oricol™ samples are **50–100,000 times richer** in biomarkers than stool

Watch an Explanatory Video at
www.originsciences.com

3 An elasticated membrane (balloon) is inflated against the rectal wall. The membrane is hydrophilic, attracting a thin layer of the rectal biofilm to its surface.

5 A stabilisation buffer is added to the sample (contained in a detachable component of the device), which is then sent to the laboratory for analysis.

4 After 10 seconds the membrane is retracted (back into the device), and the device removed from the proctoscope, which is then removed and disposed of.

6 The remainder of the device and syringe is then disposed of according to local legislation.

Better samples. Easier to collect. Preferred by patients.

The Oricol™ collection procedure can be performed on any adult (subject to safety criteria) without the need for any type of bowel preparation or anaesthesia. The procedure is safe, generally pain-free and has no side effects.

It can be conducted by any clinical professional trained in proctoscopy, and takes just a few minutes. The potential to contaminate the sample is extremely low.

The device has been successfully used on approaching 5,000 subjects worldwide with no adverse events reported – and very few reports of significant discomfort.

Further iterations of the device are under development, including a variation to be used in cervical disease investigations.

Intellectual Property

The device is protected by comprehensive patents in USA, Europe, China, India, Australia, Russia, Canada and Asia.

Further Intellectual Property rights are continually being evaluated and extended. This includes methodologies, registered designs, know-how and collaborative protection opportunities.

Granted Patents

- Australian Patent No. 2005258959
- Canadian Patent Application No. 2570714
- Chinese Patent No. ZL200580023091.X
- Chinese Patent No. ZL201010231002.3
- Eurasian Patent No. 011367
- European Patent No. 1776048
- Indonesian Patent No. ID P0026592
- Indian Patent No. 275466
- Israeli Patent No. 180153B
- Japanese Patent No. 4865709
- Mexican Patent No. 300385
- New Zealand Patent No. 552082
- Norwegian Patent No. 339684
- US Patent No. 8,992,438
- US Patent No. 9,339,259

Pending Patents

- Brazilian Patent Application No. PI 0512731-9

Compliance and Regulatory

The Oricol™ device is CE marked for distribution and use in the European Union as a sample collection device (IVD). The device is also currently used for 'research purposes' in other territories (with relevant permissions) including the USA.

The company's 'test' (PreView) is not yet validated for commercial use, and all investigations are currently performed under the strict permissions of the UK ethical authorities and the MHRA.

The company employs a full time QARA manager (Michael Chard – formerly responsible for ClearBlue pregnancy tests globally), and operates a strict Quality Assurance programme (ISO13485). All independent quality audits are up to date and have been concluded to a high standard.

QARA and Compliance Manager
Michael Chard

Manufacturing and Distribution

The device is currently manufactured in the UK under a sub-contracted supplier partnership arrangement. Such partnerships are designed to accommodate rapid volume expansion. Currently the device costs approximately £12 (GBP) to manufacture. It is believed that in time, this cost can be reduced to as little as £4 (GBP) once we increase production volumes and introduce some levels of enhanced production automation.

Currently, Origin Sciences are the exclusive distributor of the product. This enables us to fully control the application and use of the product to ensure that any subsequent (collaborative) intellectual property developments resulting from investigative use of the device are rigorously monitored and protected.

Other Diagnostics and Applications

Of course, the very unique mucosal sample and its very rich human organic content can be used for numerous other applications, including IBD/IBS detection and monitoring as well as for a broader range of alternate diagnostics. The device is currently in experimental use across a number of sites (UK and US) looking at a diverse range of applications including HIV monitoring and treatment and a number of other novel investigations.

The sample is also considered an extremely useful resource for microbiome research. Potential applications in this area have the potential to completely revolutionise healthcare through disease prediction, intolerance understanding and 'one stop' health monitoring.

The company will continue to seek collaborative opportunities that can benefit from the unique and novel mucosal sample delivered by the device. Several such arrangements are already in place, and we are in advanced talks with several parties with a special interest in microbiome research – a potentially enormous sector that could benefit hugely when combined with our IP.

Oricol™ CRC PreView

A simple colorectal cancer screening test with **incredible accuracy**

The Oricol™ CRC PreView test analyses Oricol™ samples to deliver a far more accurate diagnosis.

A Primary (or Secondary) Care Test used in any symptomatic or other 'Triage Setting' must demonstrate a beneficial health equivalence at least equal to that of (any) final determinative test (current pathway) in order to satisfy healthcare justification. Equally, such a test must meet the fundamental cost credentials (economic), before any such test will be adopted.

The Oricol™ CRC PreView test is targeting a sensitivity of no less than 97% with an associated specificity level of >99% (AUC= c.98%).

In comparison, a colonoscopy typically delivers a sensitivity level of around 96% (failure largely due to incomplete procedure) and a specificity of c.100% – you very rarely see a false positive in colonoscopy (mainly because of its biopic capability).

The mean (global) gross cost of a colonoscopy is c.$1,000 (USD), and the target price for an Oricol™ CRC PreView test is $500 (USD) (with geographical variations). Additionally, an Oricol™ CRC PreView test can be quickly performed in a primary care setting – further enhancing the gross QALY (Quality Altered Life Year) advantages.

(A CT scan cannot be compared in terms of performance or cost, simply because it is usually utilised either as an emergency diagnostic test, or as an alternative to colonoscopy/sigmoidoscopy in vulnerable patients considered unsuitable for the more invasive alternatives. A definitive tissue biopsy test is impossible to achieve with a CT scan.)

The Science

Origin Sciences currently employs two methodologies for colorectal cancer (CRC) detection using the unique mucosal sample delivered by the Oricol™ device.

The first (and currently most progressed) is DNA or genomic mutation detection. Where cellular material is exfoliated from the tumour site, it carries tumour derived DNA. The rectal mucus sample is an extremely rich source of such DNA.

There are a large number of recognised DNA mutations associated with colorectal cancer, that if accurately identified are a near absolute indicator of disease. Conversely, the absence of such mutations is a clear indication of the subject being CRC disease free.

The company has developed processes and systems for extracting, purifying and preserving human DNA from the rectal mucosal sample. This allows for subsequent amplification and sequencing of the sample for sophisticated DNA analysis and detection of the relevant mutations.

Currently the company is looking at a broad panel of mutations (50) but we hope in time to reduce the panel, with some economic savings, without compromising test performance.

In two recent cohorts (positive controls) of 16 and 24 samples respectively, the test has detected mutations accurately in 100% of cases (various stages and locations).

The other methodology currently being evaluated is DNA methylation detection. DNA methylation is the main method by which genomic activity is adjusted during life, especially during early development and as a result of environmental changes such as smoking and normal aging. It is a process by which methyl groups are added to DNA. This mechanism allows for the switching on or off of genes to adapt to environmental assaults, viral infection and also cancer.

Colorectal cancer arises as a consequence of the accumulation of both genetic and epigenetic alterations in colonic epithelial cells during neoplastic transformation. Epigenetic modifications, particularly DNA methylation in selected gene promoters, are recognized as common molecular alterations in human tumours, hence a strong rationale for our company to add methylation biomarkers to our final algorithm.

There is a wealth of scientific evidence supporting existing methylation biomarkers involved in CRC progression (at least 50 genes) that we will test in our samples to select the strongest to add to our algorithm made of genetic mutations. One advantage is that once DNA is extracted, we can interrogate both the genomic status (mutations) and the epigenetic status with DNA methylation.

One great advantage of methylation detection is the low cost when compared to mutation detection. We believe that with a sensible methylation panel, processing costs could be extremely low.

Market Potential

Healthcare Pathways

Symptomatic Triage

There is currently no reliable triage test available at a Primary Care level. Oricol™ CRC PreView is set to change that.

It will ensure that only those with a genuine likelihood of having colorectal cancer (CRC) are referred, and those with milder symptoms can be tested quickly.

Whilst different countries and territories employ widely differing healthcare policies and pathways, when it comes to symptomatic diagnostics, the pathway is fundamentally the same.

Any patient with symptoms typical of colorectal cancer will usually, in the first instance present to a GP at a primary care level. The GP will evaluate the 'risk level' of the subject being positive for CRC, often by employing a traffic light or qualification system. Patients considered low risk may be investigated (at a primary care level) for other ailments, those at a low/medium risk will typically be monitored and those at a medium/high risk will be referred to secondary care for conclusive rule-in/rule-out diagnosis, usually by means of a colonoscopy, sigmoidoscopy or CT scan.

In the UK, the referral system for patients with a suspicion of any cancer is known as the Two Week Wait (TWW), where patients must commence secondary diagnostics within two weeks of referral.

The incidence rate for colorectal cancer in this symptomatic group varies between 5% and 8% globally – the variation generally as a result of differing referral qualification procedures.

Of course, the system does miss cancers at initial presentation (primary care). Typically, these patients will remain symptomatic, and will eventually get to the referral stage once all other investigations have been exhausted or the CRC specific symptoms meet the qualification for referral.

Asymptomatic Screening

Ultimately, Origin Sciences would like to introduce a reliable screening test that can be used in the asymptomatic population.

It would deliver reliable results, rapid treatment for those with disease and absolute reassurance for those without. We anticipate that the additional cost (of the Oricol™ test) will balance against the cost of unnecessary investigations in the false positive group.

Asymptomatic screening tests again vary from territory to territory and from time to time depending on prevailing individual strategy.

Screening groups are usually selected by virtue of age and/or risk factor (CRC prevalence increases with age), and subjects are sent a home test kit (FOBT or FIT), where the subject is required to provide a small sample of stool, which is then sent to a laboratory for testing. Those that test positive are invited for further investigation, and those testing negative are given a clear indication.

There are two critical issues with such screening programmes. Firstly, compliance is poor. Up to 50% of subjects do not complete the test unless encouraged. And secondly, performance is inadequate to provide a reliable prognosis. Excessive false positives lead to an influx of unnecessary and expensive investigations, and false negatives provide false assurance and undetected disease. Performance levels vary from test to test.

Health Economics

At Risk – Monitoring

Oricol™ CRC PreView is ideally placed to offer a more cost-effective, equally accurate and far less unpleasant alternative to the current pathway and strategy.

Ultimately, the introduction of the Oricol™ test will save lives and money whilst providing reassurance to the millions of individuals globally living in daily fear of disease.

Where individuals are considered to be at a significantly elevated risk of disease (for example family history), they are often invited to attend regular screening tests (colonoscopy/CT scan, etc.). Such a group is large, and again, incidence rates are generally quite low – thus a large number of unnecessary investigative procedures are undertaken.

In addition, many individuals in the 'elevated risk' population opt out due to being purely asymptomatic, and not wishing to undertake an essentially invasive and uncomfortable procedure.

Origin Sciences has engaged the services of ScHARR (School for Health and Related Research – Sheffield UK) to conduct a full health economic evaluation and implementation strategy for the Oricol™ CRC PreView test.

ScHARR is recognised globally as a reliable provider of comprehensive and considered strategical reports – in particular relating to innovative diagnostics, pathway integration and product implementation, both at a primary and secondary care level, and in both the public and private sectors.

Key Opinion Leaders and industry influencers value ScHARR's impartial approach, and often engage in extended consultation to help understand the often cautious balance of health and economics.

Whilst the ScHARR report is an ongoing exercise, a few essential statistics stand out, and demonstrate the huge potential of the Oricol™ device and subsequent pipeline tests:

- Over 8 million diagnostic colonoscopies are administered in the EU and USA each year (private and state) at a cost of more than £8B.
- Implementation of the Oricol™ CRC PreView test and planned derivatives could reduce the need for diagnostic colonoscopies by approximately 80% – replacing a cost burden of over £6.4B, whilst maintaining (and likely improving) the pathways and healthcare of over 6.4M symptomatic individuals.
- 100s of millions of asymptomatic screening tests (for CRC) are conducted globally each year – producing vast numbers of false negatives and false positives.

Right now, a reliable, non-invasive and affordable triage test **simply does not exist.**

Despite a desperate and demonstrable need for such a test, Oricol™ CRC PreView is not destined to enter a competitive marketplace.

It is intended to solve a huge pre-existing problem and allow for a streamlined patient pathway whilst saving both money and lives.

The product is not designed to compete with colonoscopy or CT scans. Instead it is a tool used to reliably and economically qualify the need for such tests, without the risk of missing disease.

Asymptomatic screening is a different matter altogether. The huge numbers in potential screening groups makes this an extremely attractive market. Such tests need to be inexpensive, and most are. However, the low test cost comes at a huge price with numerous false positives and false negatives. The false negatives cost lives, and the false positives must be investigated. This is an excellent application for the Oricol™ CRC PreView test.

DIRECT COMPETITION

Exact Sciences

Exact Sciences (NASDAQ: EXAC) launched their primary product (ColoGuard) in 2014. The company has a fluctuating market cap between $13B and $16B. Cologuard is a stool-based screening test sold mainly in the US.

The ColoGuard test has a sensitivity of 92.3% and a specificity of 86.6% (all stages of CRC), but at a retail price of $649 USD.

The test is performed at home (stool collection) and sent to a laboratory for analysis. There is some clinical fraternity 'dissatisfaction' in that the test does not require clinical intervention, and as such does not provide for reimbursement.

Origin Sciences have prepared a full analysis on Exact Sciences and continue to monitor activities with a view to exploration of potential partnership or acquisition discussions in the future.

Others

Numerous companies are looking at a variety of methodologies in a drive to deliver reliable and cost-efficient tests that meet the demanding balance of health benefits and economic viabilities. Origin Sciences constantly reviews all such developments.

Competing tests are either expensive or inaccurate.

Oricol™ CRC PreView

Sensitivity	>97%
Specificity	>99%
Price	~$500 USD

* Targets

GENERIC TESTS

FOBT

FOBT (Faecal Occult Blood Tests) are very low cost, generic stool-based tests that can be performed at home, and then sent to a laboratory for analysis. Essentially, as the name suggests, the test is looking for the presence of haemoglobin (blood) in the sample. Blood in stool is a primitive indicator of disease, but can be caused by many other factors, and as such the test delivers huge numbers of false positives. In addition, CRC does not always lead to traces of blood in stool – hence, the test often misses disease.

FOB tests have a sensitivity of c.75% and specificity of c.70%.

FIT

FIT (Faecal Immunochemical Test) is a more sophisticated (but also more expensive) stool-based test that similarly seeks and evaluates traces of blood in the stool.

Blood Tests (Liquid Biopsies)

Simple diagnostic blood tests are widely recognised as the 'holy grail' in healthcare. Indeed, they are simple and quick to administer, and only impede minimal inconvenience on the patient.

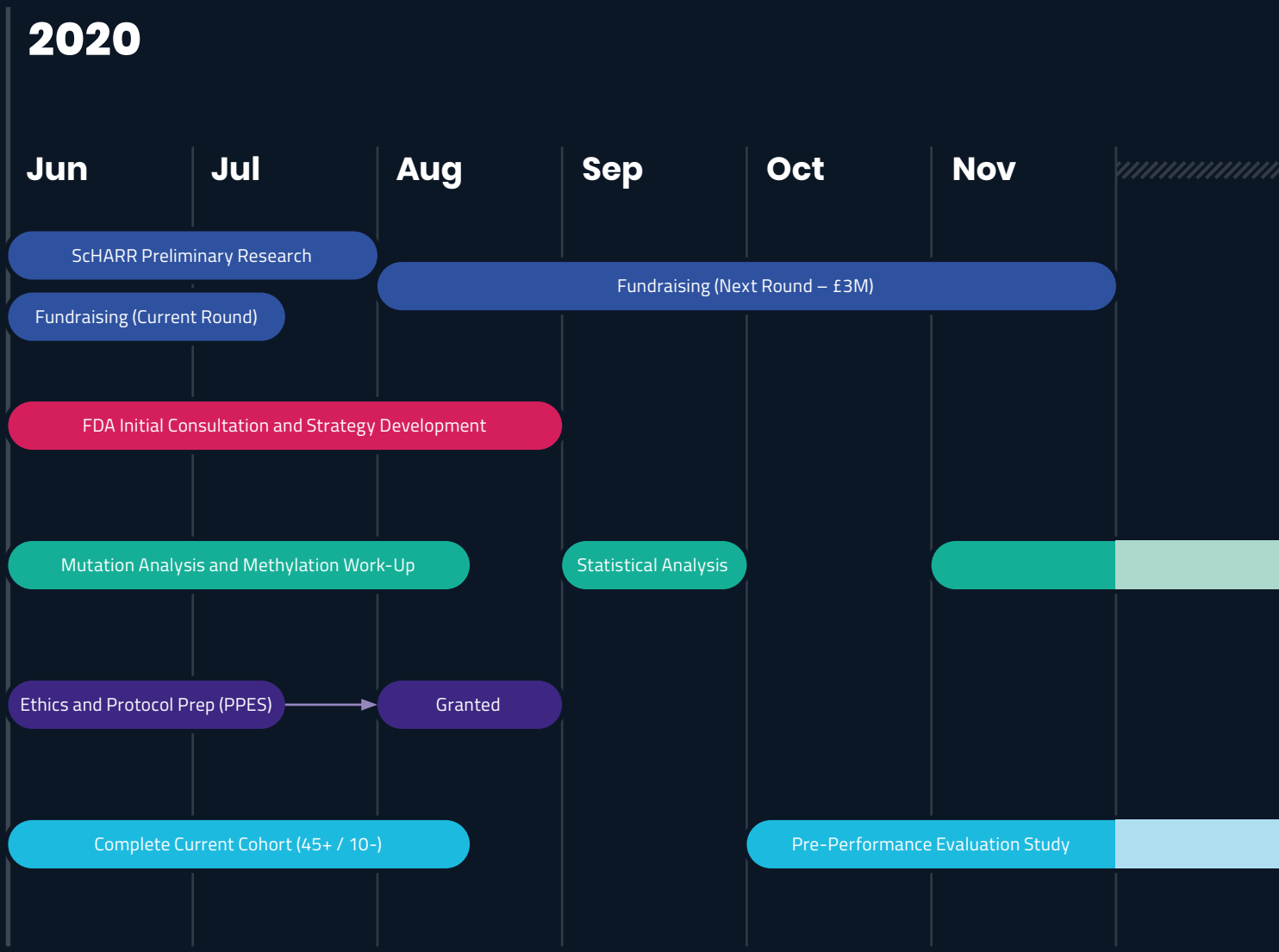
Huge progress has been made in so many areas (including a broad range of cancer diagnostics) over the last decade or so – indeed many individual tests have been proven, validated and routinely introduced, and have subsequently demonstrated great health economic success and undoubtedly saved numerous lives. This sadly, is not commonly the case with gastro-intestinal (GI) disease/illness detection and diagnosis.

Blood tests do not perform well for the detection and diagnosis of GI disease.

We believe that the main reason is that the gastro-intestinal tract is largely insulated and somewhat isolated from the remainder of the human organs including blood. This would largely indicate why blood tests tend not to deliver accurate indicators in early stage GI disease.

Preliminary comparisons (plasma vs. rectal mucosa) have demonstrated that in CRC confirmed cases (stages 1-3), **rectal mucosa has outperformed plasma in at least 80% of cases**. Successes (c.20%) in blood are solely attributed to vascular intrusion (typically seen in very late stage and often secondary untreatable disease).

Roadmap



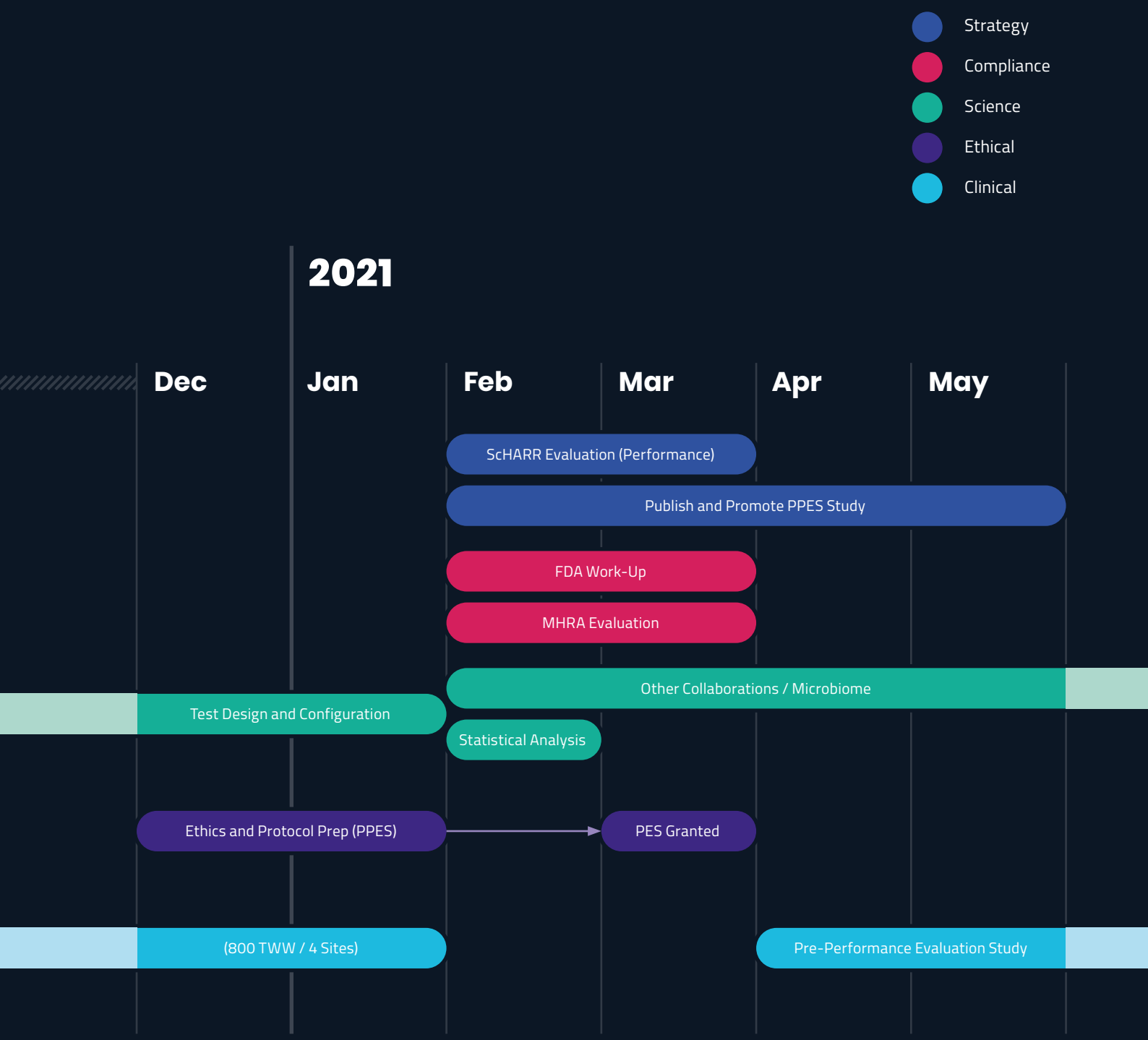
Covid-19

No current Investment Memorandum would be incomplete without including global pandemic implications – in particular when relating to any form of healthcare product.

As with almost every business around the globe, Origin Sciences had no immunity from the impacts of Covid-19. Very early in the pandemic we saw all non-Covid clinical studies suspended, and this has impacted our ability to procure new samples.

Thankfully, at the time of writing, most of our clinical sites are starting to resume non-Covid research, albeit occasionally adopting alternative diagnostic pathways. We believe that we have suffered a three to five-month delay in delivering our primary commercial diagnostic product.

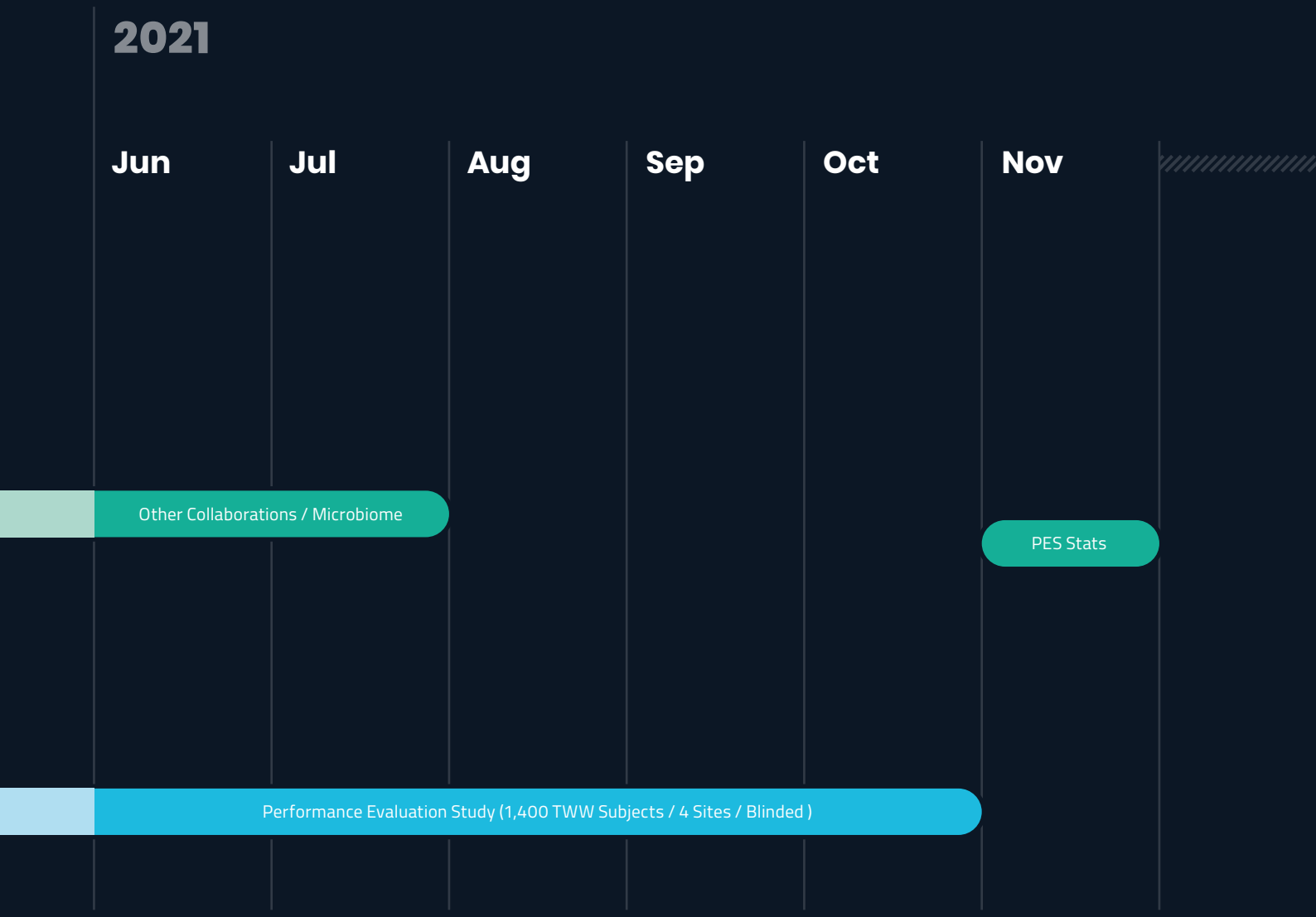
In terms of related cost, we can apportion around £200K (GBP) in lost costs (mostly fixed overheads). Thankfully we have been able to take advantage of several government schemes in order to mitigate many day-to-day costs.



The 'Covid Cloud', however, may carry a silver lining. The immense and rapid impact of Covid-19 has led to equally rapid changes in healthcare pathways across the globe. Many of these changes are likely to become continuing policy as we eventually start to return to a 'new normal'. One very relevant and notable change is that more tests and triage are being pushed back towards Primary Care in an effort to relieve pressures on the secondary care sector. This may prove to be good news for Origin, as this is precisely the position in which we wish to place our launch product, Oricol™ CRC PreView – and that product really is truly unique.

ASSUMPTIONS

- Timelines assume that current cohort can commence immediately.
- Timelines assume that Ethics opens to new applications by mid July.
- FDA and ScHARR consultations are underway
- Timelines assume dropping the NIHR – instead managing internally.
- The Pre-Performance Evaluation Study will be both Primary and Secondary Care.

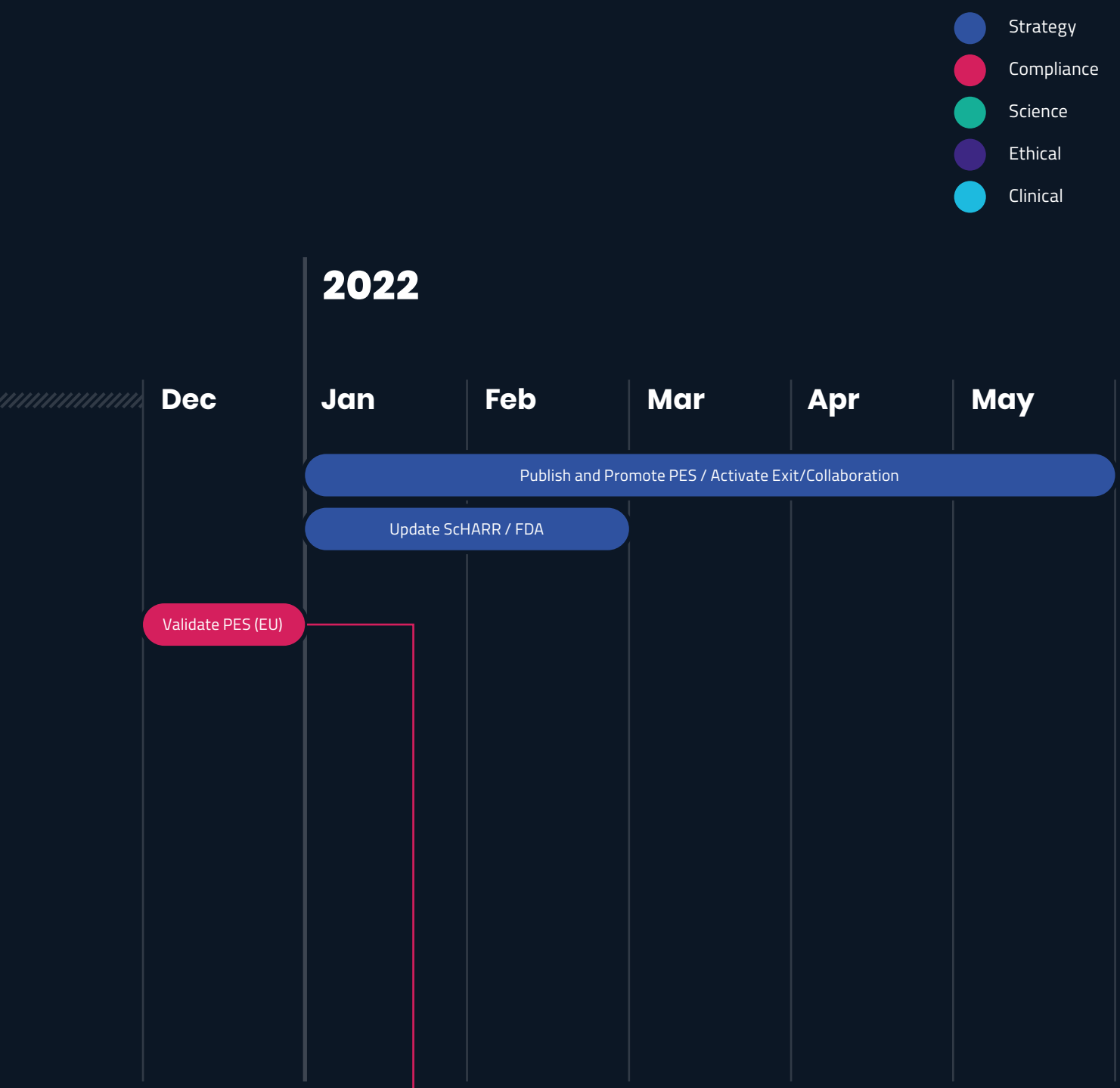


Oricol™ CRC PreView Test Development

The Management Team have a structured 18-month roadmap leading to the validation of the Oricol™ CRC PreView test for commercial diagnostic use in the EU. Final validation is expected to be granted in December 2021.

We estimate that in order to get to final validation we will need to recruit a further 2,000 subjects across two separate studies (PPES and PES).

In tangent to core verification and validation work, we also have plans to consult on, and integrate provisional FDA requirements (as a part of our studies) in order to fast-track US approvals once the product is CE marked in the EU. As a part of this process we shall also evaluate the merits and requirements of screening test validation in the US under FDA legislation.



Point of Commercialisation

Origin Sciences will likely seek exit or collaborative operational opportunities once the product is unequivocally qualified.

Next Steps

Our next funding round will open for subscription in **August 2020.**

Funds raised will take the business through to product validation.

Validation will lead to an exit or operational funding collaboration.

Details are still being finalised — for the latest information, just get in touch.

Contact

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Origin

Any request for more information and specific feedback regarding any part of this investment opportunity should in the first instance be directed to the Chief Executive Officer (Hugo Lywood), who will either directly address or refer enquiries to the relevant and most appropriate individuals within the business.

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