Vision and Mission

Our mission is to build on Argonaute patented technology to solve some of the challenges confronting the siRNA field
Our aim is to develop a pipeline of new Argonaute siRNA drugs by a sequence of collaboration deals with pharma partners
Our vision is to make Argonaute a UK leader in the gene silencing field

"After twenty years in development, with many stumbles along the way, gene silencing drugs are now on the cusp of becoming a common prescription. Starting in the next few months, anyone you know with heart disease may be offered by their GP a twice yearly injection of the first of these siRNA drugs. Inclisiran, owned by Novartis, is the first major drug in a new field. Over the next three years the NHS has committed to treating 300,000 heart disease patients where a high level of bad cholesterol has a genetic cause. The NHS estimates Inclisiran will prevent 55,000 heart attacks over the next decade. Argonaute has its own Inclisiran-like drug candidate. However, the beauty of siRNA drugs is they offer a way to treat a broad range of conditions originating from a faulty gene. SiRNA drugs to treat aspects of diabetes, hepatitis and fatty liver are all in development. This is a narrow field in terms of competition, and getting narrower as the leading biotechs are picked off by the global pharma giants. If Argonaute can deliver on its scientific promise, the potential commercial opportunities are endless."
Anthony Parker, Executive Chairman, Argonaute RNA

What is Gene Silencing? – A Nobel Prize winning discovery. Normally via a subcutaneous injection in the upper arm, the drug introduces to target cells, which might be in the liver, a short RNA sequence that matches part of a particular gene sequence. This loads a defence mechanism in the cell to ensure production of the target gene is short-circuited. So small interfering RNAs (siRNA) harness the natural cellular RNA interference (RNAi) pathway to selectively silence disease-causing genes, without altering patient DNA. This is in contrast to gene-editing. We do not confront the ethical issues of introducing permanent or heritable genetic change. Our proprietary Crook-siRNA platform technology targets genes to safely and temporarily switch off production of proteins proven to cause disease. We can treat multiple diseases for which there are currently no drug options or very poor options.

Problem – Companies in our field typically use extensive chemical modification to protect siRNA drugs from being degraded by the body's natural defence mechanisms. We do it differently. We use a unique DNA sequence to confer special properties on our RNA silencing drug. Any new player in our space confronts a patent landscape in which chemical modification strategies have been comprehensively staked out. The land has been grabbed. However, our unusual use of DNA bases rather than chemical modifications allows us to steer around competitor patents, giving us freedom to engage with pharma companies in partnering/licensing conversations.

Our Unique Approach – We use natural nucleotides. Others use unnatural nucleotides. With our innovative method of stabilising siRNA we have achieved the world's first safe and substantive cardiovascular disease gene knockdown with a chemically unmodified siRNA sequence, generating excellent data in a large *in vivo* (mouse) trial. **This is the primary inflection point achieved since our funding round in May 2021.**
Our propriety Crook platform prevents rapid degradation and unwanted immune activation. We do this without the extensive chemical modification typical of rival technologies. By taking an alternative route to chemical modification we see a 25% reduction in the cost of our pre-clinical and clinical development programs versus our competitors. A similar benefit with respect to speed of development is also achievable.

World Class Team – CEO, Dr Mike Khan (former CMO of Silence Therapeutics) led Phase 1 and Phase 2 clinical trials for siRNA therapies. Mike is director of the one of the foremost cardiovascular disease prevention clinics in the UK, an expert advisor to NICE and a former NHS commissioner. Mike is supported by a highly experienced Science Team including siRNA project leaders from AZ and GSK. Our Board has specialists in patent law, finance, chemistry and biology. Argonaute has its own biology laboratory facility, managed by Dr Pamela Panetta, at the Science Creates biotech hub in Bristol. Our drug manufacturing plans are evolving in partnership with CatSci Ltd, one of our major shareholders.

Market Opportunity – The first RNAi drug was approved in 2018 for the treatment of a rare disease (ATTR Amyloidosis, 1350 patients, $306mn sales FY 2020). Since then, a further three rare disease siRNA therapies have been approved. The inflection point for the field has now come, from rare disease treatment to blockbuster. Novartis is currently launching FDA-approved Inclisiran, branded Leqvio. It aims to cut bad cholesterol in half for patients unresponsive to statins and could save 30,000 lives over the next decade. Novartis expects ***$2bn a year in sales by 2026, and $6bn of sales by 2030***. Argonaute has its ***own version in the pipeline***, plus seven other gene candidates in its patent estate.
Our recent trial data indicates that, as far as we can judge from information in the public domain, we are uniquely positioned to address acute disease targets, where the duration of knock-down has to be for a short time period only (e.g. Acute Respiratory Distress Syndrome, COVID, Sepsis).

Intellectual Property – Our platform technology was originally developed by Professor Jo Milner at the University of York. The platform patent was assigned to Argonaute RNA in January 2016. As of December 2021, we have two broad patent families each with broad claims; one protecting targets for acute diseases; the other protecting targets for the treatment of chronic diseases. In November 2021, we received an 'Intention to Grant' from the GB Patent

Office, with respect to one of our chronic disease drug assets, ARGO101. This asset is now under National Examination in five countries: China, Japan, USA, Europe, Canada. **This is our second inflection point.**

Business Model – We have a platform technology and a pipeline of potential drugs to treat acute and chronic diseases. Most license deals and research collaboration agreements between biotech and pharma seek to own rights to a particular drug, with options on more. A typical deal includes an upfront payment followed by milestone payments. We aim to fund drug development via deals with pharma partners. A first deal will leverage probability of further deals. The core platform nature of our technology is that progress with developing any one of our drugs will prove up the value of our platform and expand our deal options. In terms of targets, we aim to have, within 18 months of this funding, one full IND data suite and patent positions that will allow the signing of multiple industry collaboration agreements. We are engaging with large pharma to explore R&D collaborations.

Competition – Relatively small pool of competitors mainly in the US with multi-billion dollar valuations (Alnylam, Arrowhead, Ionis). Silence Therapeutics in the UK.

Exit Strategy – We believe our exit will come via acquisition. Five competitors have seen over $24 bn in M&A and licence activity since 2016, as big pharma scrambles to take positions in the RNAi space and gain a competitive advantage. One competitor, Dicerna, was bought last November by Novo Nordisk for $3.3bn. The deal closed in December, so swiftly because the way to the acquisition had been paved by an existing research collaboration agreement.

Funding Requirements – To fund the development of our leading acute disease drug candidate, where our platform has major advantages over the competition. We aim to complete a full IND enabling study and enter licensing discussions within 18 months from this raise, signing multiple research collaboration agreements over the same period.

Round Type: Pre-Series A

Mechanism: Advanced Subscription Agreement

Final Round Size: £1m to £5m

Valuation: ASA at 20% discount to valuation agreed in Priced Round

Current Cash Runway: To December 2022 with no acceleration of spending

Expected Date for Round Close: April 4th (ASA), Priced Round in Q3 2022.

SEIS or EIS Status: Knowledge Intensive EIS eligible, previous advance assurance May 2021.