SILENCE THERAPEUTICS

37th Annual Canaccord Genuity Growth Conference

Silencing the gene, Curing the patient

AUGUST 2017

Forward looking statements

The information contained in this presentation is being supplied and communicated to you on a confidential basis solely for your information and may not be reproduced, further distributed to any other person or published, in whole or in part, for any purpose. In accordance with the prohibition on market abuse contained in Part VIII of the Financial Services and Markets Act 2000 (as amended) (the "Act"): (i) you must not pass this information to any person; and (ii) you must not base any behaviour in relation to any securities or other Qualifying Investments (as that term is defined in the Act) which would amount to market abuse on such information until after it is made generally available.

This presentation is being communicated in the United Kingdom only to (a) persons who have professional experience in matters relating to investments falling within Article 19(1) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (b) high net worth companies and other bodies falling within Article 49(2) of the Order; or (c) persons to whom this presentation may otherwise lawfully be distributed (all such persons being referred to as "relevant persons"). This presentation is only directed at relevant persons, and any investment or investment activity to which this presentation relates is only available to relevant persons or will be engaged in only with relevant persons. Solicitations resulting from this presentation will only be responded to if the person concerned is a relevant person. Other persons should not act upon this presentation or any of its contents.

The distribution of this presentation in certain jurisdictions may be restricted by law, and persons into whose possession this presentation comes should inform themselves about, and observe, any such restrictions. Although reasonable care has been taken to ensure that the facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, the contents of this presentation have not been verified by Silence Therapeutics plc (the "Company") or any other person. Accordingly no representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information and opinions contained in this presentation and no reliance should be placed on such information or opinions. None of the Company, or any of its respective members, directors, officers or employees nor any other person accepts any liability whatsoever for any loss howsoever arising from any use of such information or opinions or otherwise arising in connection with this presentation. No part of this presentation, or the fact of its distribution, should form the basis of or be relied upon in connection with any contract or commitment or investment decision whatsoever. This presentation does not form part of any offer of securities, or constitute a solicitation of any offer to purchase or subscribe for securities or an inducement to enter into any investment activity. Recipients of this presentation are not to construe its contents, or any prior or subsequent communications from or with the Company or its representatives as investment, legal or tax advice. In addition, this presentation does not purport to be all-inclusive or to contain all of the information that may be required to make a full analysis of any transaction. Further, the information in this presentation is not complete and may be changed. Recipients of this presentation should each make their own independent evaluation of the information and of the relevance and adequacy of the information in this document and should make such other investigations as they deem necessary.

Securities in the Company have not been, and will not be, registered under the United States Securities Act of 1933, as amended (the "Securities Act"), or qualified for sale under the law of any state or other jurisdiction of the United States of America and may not be offered or sold in the United States of America except pursuant to an exemption from, or in a transaction not subject to, the registration requirements of the Securities Act. Neither the United States Securities and Exchange Commission nor any securities regulatory body of any state or other jurisdiction of the United States of America, nor any securities regulatory body of any other country or political subdivision thereof, has approved or disapproved of this presentation or the securities discussed herein or passed on the accuracy or adequacy of the contents of this presentation. Any representation to the contrary is unlawful.

Safe Harbour statement: this presentation may contain forward-looking statements that reflect the Company's current views and expectations regarding future events. In particular certain statements with regard to management's strategic vision, aims and objectives, the conduct of clinical trials, the filing dates for product licence applications and the anticipated launch of specified products in various markets, the Company's ability to find partners for the development and commercialisation of its products as well as the terms for such partnerships, anticipated levels of demand for the Company's products (including in development), the effect of competition, anticipated efficiencies, trends in results of operations, margins, the market and exchange rates, are all forward looking in nature.

Forward-looking statements involve risks and uncertainties that could cause actual results to differ materially from those expressed or implied by the forward looking statements. Although not exhaustive, the following factors could cause actual results to differ materially from those the Company expects: difficulties inherent in the discovery and development of new products and the design and implementation of pre-clinical and clinical studies, trials and investigations, delays in and results from such studies, trials and investigations that are inconsistent with previous results and the Company's expectations, the failure to obtain and maintain required regulatory approvals, product and pricing initiatives by the Company's competitors, inability of the Company to market existing products effectively and the failure of the Company to agree beneficial terms with potential partners for any of its products or the failure of the Company's existing partners to perform their obligations, the ability of the Company to obtain additional financing for its operations and the market conditions affecting the availability and terms of such financing, the successful integration of completed mergers and acquisitions and achievement of expected synergies from such transactions, and the ability of the Company to identify and consummate suitable strategic and business combination transactions and the risks described in our most recent Admission Document.

By participating in this presentation and/or accepting any copies hereof you agree to be bound by the foregoing restrictions and the other terms of this disclaimer.

© Silence Therapeutics 2017

About Silence Therapeutics

Only quoted European RNA interference player

Key Performance Indicators:

- Net cash position of £34M as of 6th of January 2017
- Operating cash burn of £10M in 2016
- Market cap: £96M
- EV: £67M (including £11M Arrowhead)

Headcount:

~42 FTE

Listing:

AIM, London Stock Exchange

Our facilities

HQ in London



R&D in Berlin



© Silence Therapeutics 2017

Our business model



Drug development

- Develop enabling technology
- Identify suitable target genes
- Progress programmes through the clinic internally or through partnering deals
- Explore collaborations, in-licensing opportunities and transactions to accelerate our timelines

Monetising our intellectual property

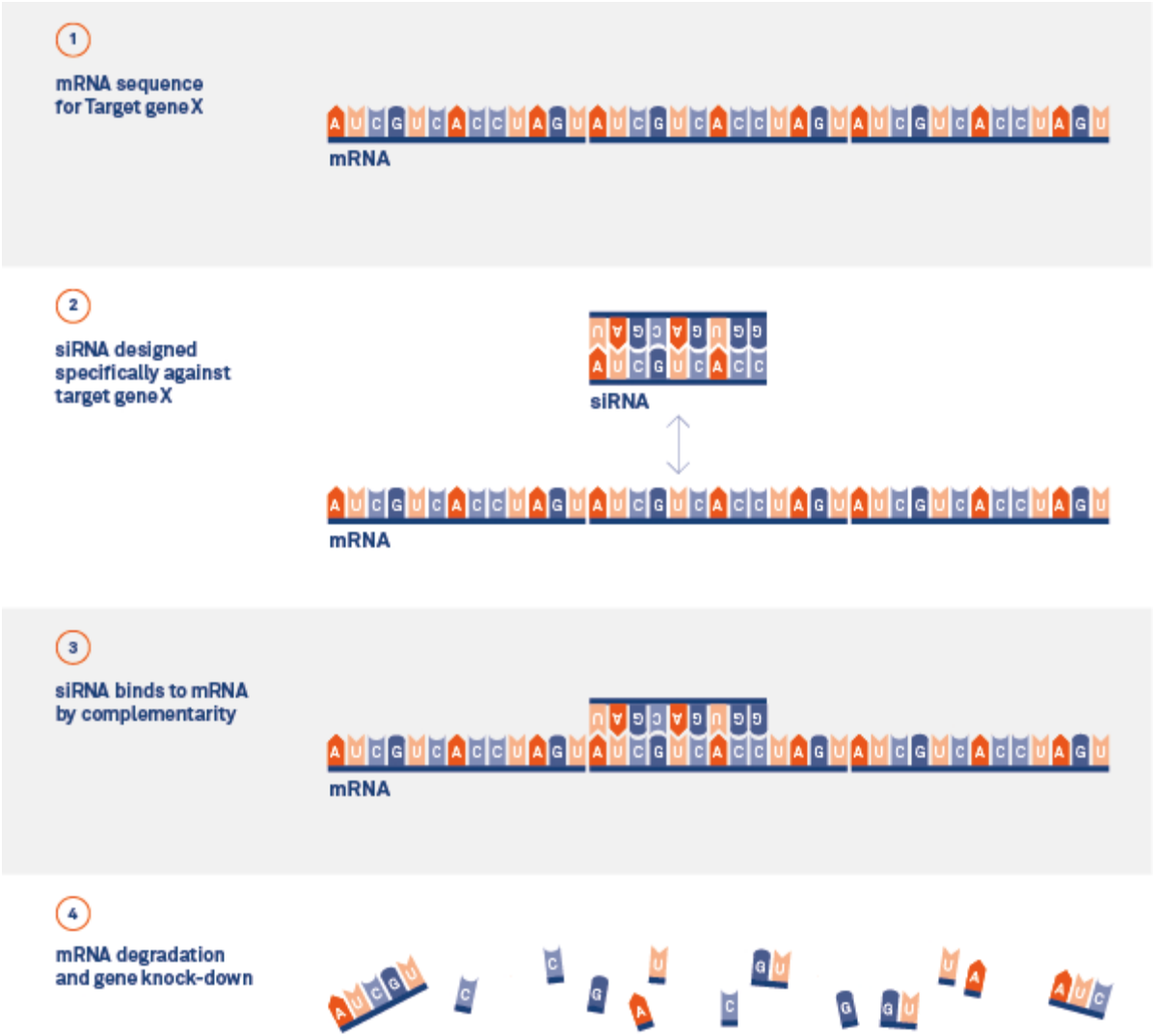
- Generate and maintain patent protection for our inventions and technology
- Defend our IP if third parties infringe
- Monetise unexploited uses of our IP through out-licensing deals

Innovation

- Develop new technology to improve the performance of current pipeline candidates
- Explore targeting of new cell types and novel siRNA structures
- Generate new IP to add to our portfolio

© Silence Therapeutics 2017

How do our drugs work?



RNA interference is...

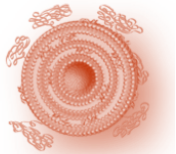
> A Nobel prize-winning discovery

> A natural pathway that can be harnessed to inhibit the expression of disease-causing genes without altering DNA

We can specifically target any gene in the genome with our short interfering RNA (siRNA) molecules

© Silence Therapeutics 2017

siRNA delivery: a look back



Our previous delivery platform: Lipid nanoparticles (LNP)

- Suitable for **larger cargos** (mRNA, CRISPR)
- Our LNP systems are able to mediate RNAi **outside the liver**, in endothelial cells
- **Intravenous** administration (infusion) required
- **Dose and clinical applications limited** by the toxicity of a lipid based delivery
- **Complex and expensive** manufacturing
- Lipid nanoparticles were widely used for **siRNA** delivery but the **field** has generally **moved on to conjugate structures**

We have overcome the limitations of lipid nanoparticles for siRNA delivery in the liver. LNP still of interest for other applications

© Silence Therapeutics 2017

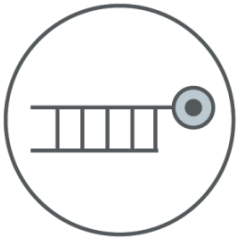
Our new platform technology: the delivery issue is now solved in the liver



+



=



siRNA:
Inhibition of a specific target gene

Targeting ligand:
Specific delivery of siRNA to a target cell type

Our medicines:
GalNAc-siRNA conjugates

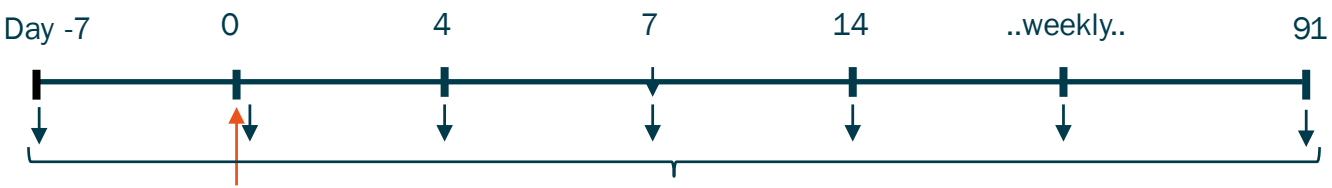
- GalNAc can deliver therapeutic siRNA **specifically to hepatocytes**
- GalNAc-siRNA is an **established technology** and has been **de-risked**
- GalNAc-siRNA conjugates can be **administered subcutaneously** and are **well tolerated**
- **Suitable for chronic and less severe** clinical applications

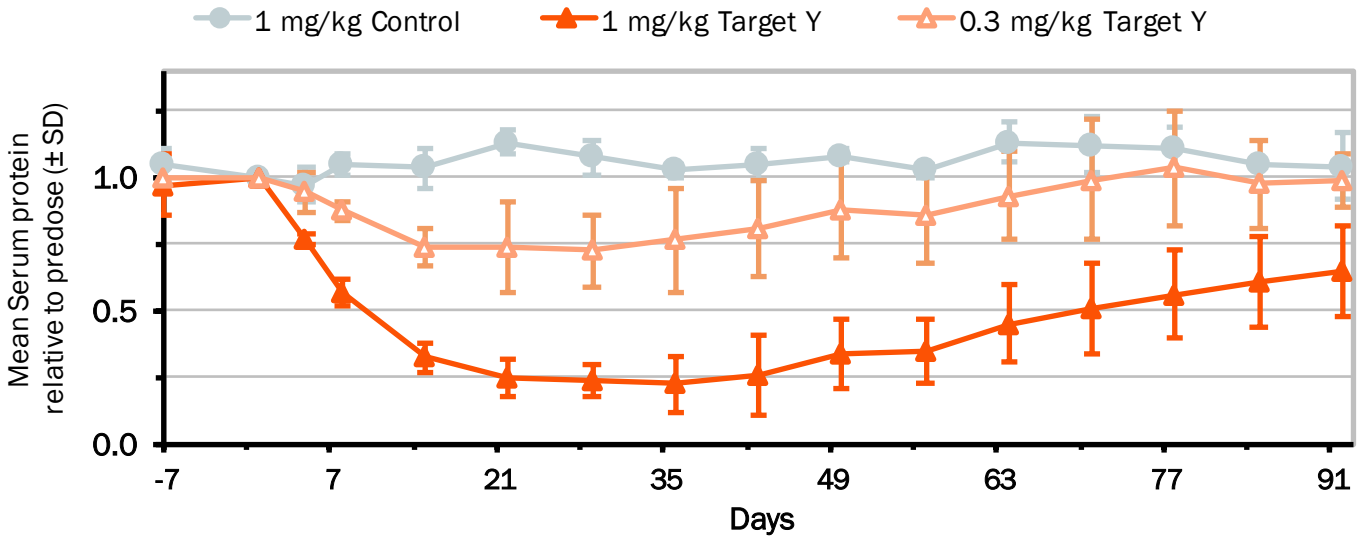
Our GalNAc-siRNA platform has **FTO and competitive performance**

© Silence Therapeutics 2017

Competitive GalNAc-siRNA performance observed in higher species







- No altered pro-inflammatory cytokines
- No skin reactions
- No behavioral changes

Well tolerated in higher species

Durable target inhibition achieved safely. **Infrequent dosing supported**

© Silence Therapeutics 2017

What are the key properties of our RNAi medicines?



Rapid drug discovery process:

Known target mRNA sequence. Algorithmic bioinformatic design and fast screen for lead identification

Speed and no druggability issues

Highly specific:

Single target gene, single cell type affected

Specificity

Tailored for patients:

siRNA drugs can be designed to target a specific mutation

Precision

Potency: High % target KD with low dose

Duration: Long-lasting effects support infrequent dosing

Well tolerated: Wide therapeutic window

Patient friendly: Subcutaneous administration

Freedom to operate: IP generated to protect our drugs

Defined Target Product Profile

Stringent process: Only high conviction drug candidates are progressed

© Silence Therapeutics 2017

How do we select target genes and indications for our pipeline?

Key criteria

- Hepatocyte expression
- Validated role in disease
- Attractive clinical path
- Commercially viable

Target nomination

> In-depth analysis and KOL survey

> Defined TPP criteria

Not limited to hepatic applications

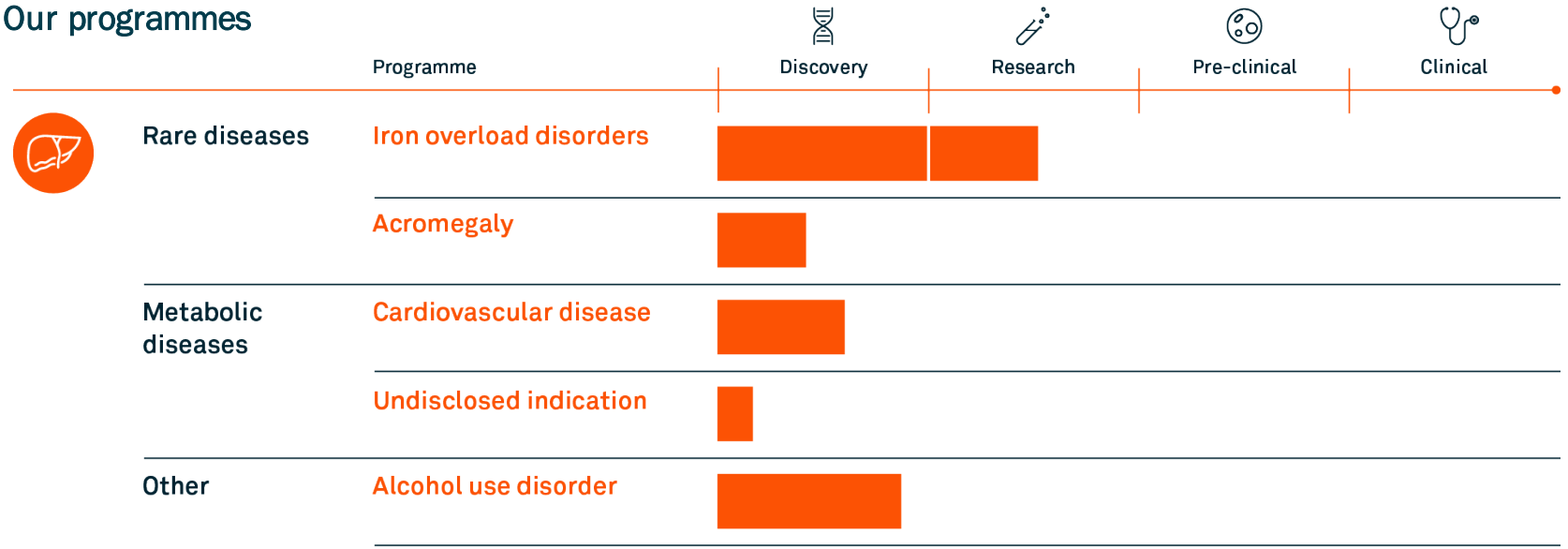


We are also able to treat conditions affecting organs other than the liver with the same highly specific approach

© Silence Therapeutics 2017

Our pipeline

Our programmes



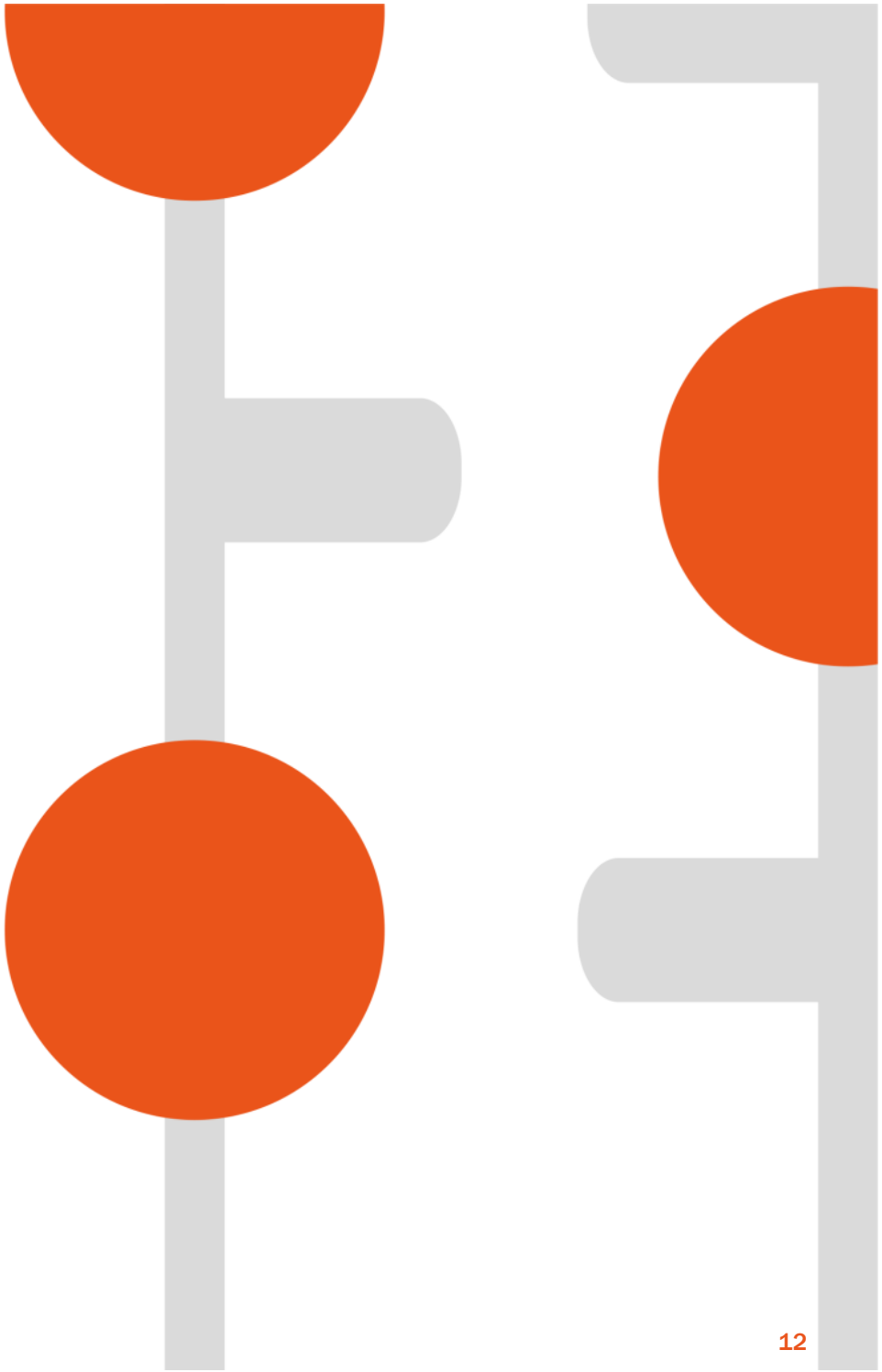
Out-licensed programmes (AtuRNAi™)



Quark NOVARTIS

© Silence Therapeutics 2017

Our Intellectual Property on chemically modified siRNA structures



© Silence Therapeutics 2017

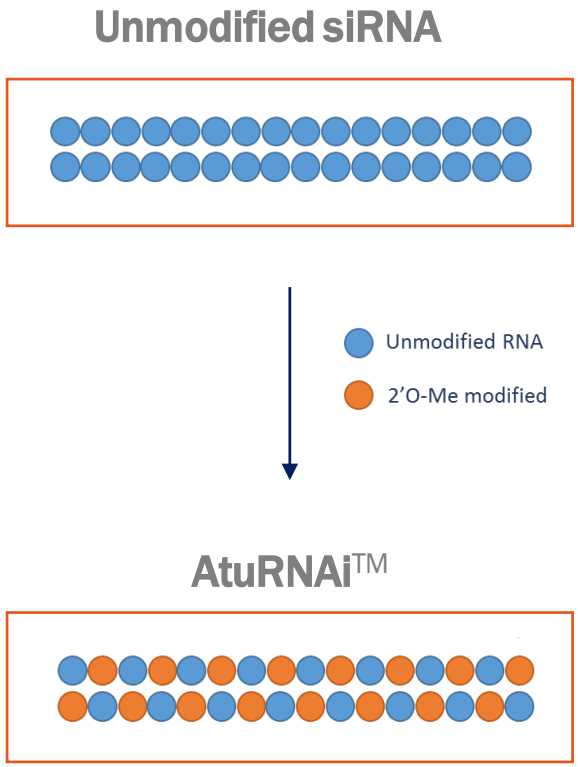
What are chemical modifications?

- **Chemical modifications are required** to increase stability and potency, and to reduce immune stimulation of RNAi drugs

- **AtuRNAi™: our proprietary siRNA modification patterns.** Key IP: issued patents in EU, US, Japan, Australia, Korea, etc

  - **Out-licensed to Quark Pharmaceuticals** (partnered with Novartis and Pfizer). Historic licensees include AstraZeneca

  - **Excellent safety profile** consistently observed in the clinic



Original siRNA modification patent (filed in 2003)

© Silence Therapeutics 2017

Field leading IP position in modified siRNA

Chemical modifications are vital to prevent the degradation of therapeutic siRNA molecules and to enable potent RNA interference. **Silence was a pioneer in developing a robust chemical modification technology.**

> Our patent portfolio protecting our modification technology includes:



3 granted patents

4 patent applications



6 granted patents

4 patent applications

> Similar claims granted and pending in a variety of other countries, including: AU, BR, CA, CN, IL, IN, JP, KR, MX, ZA

© Silence Therapeutics 2017

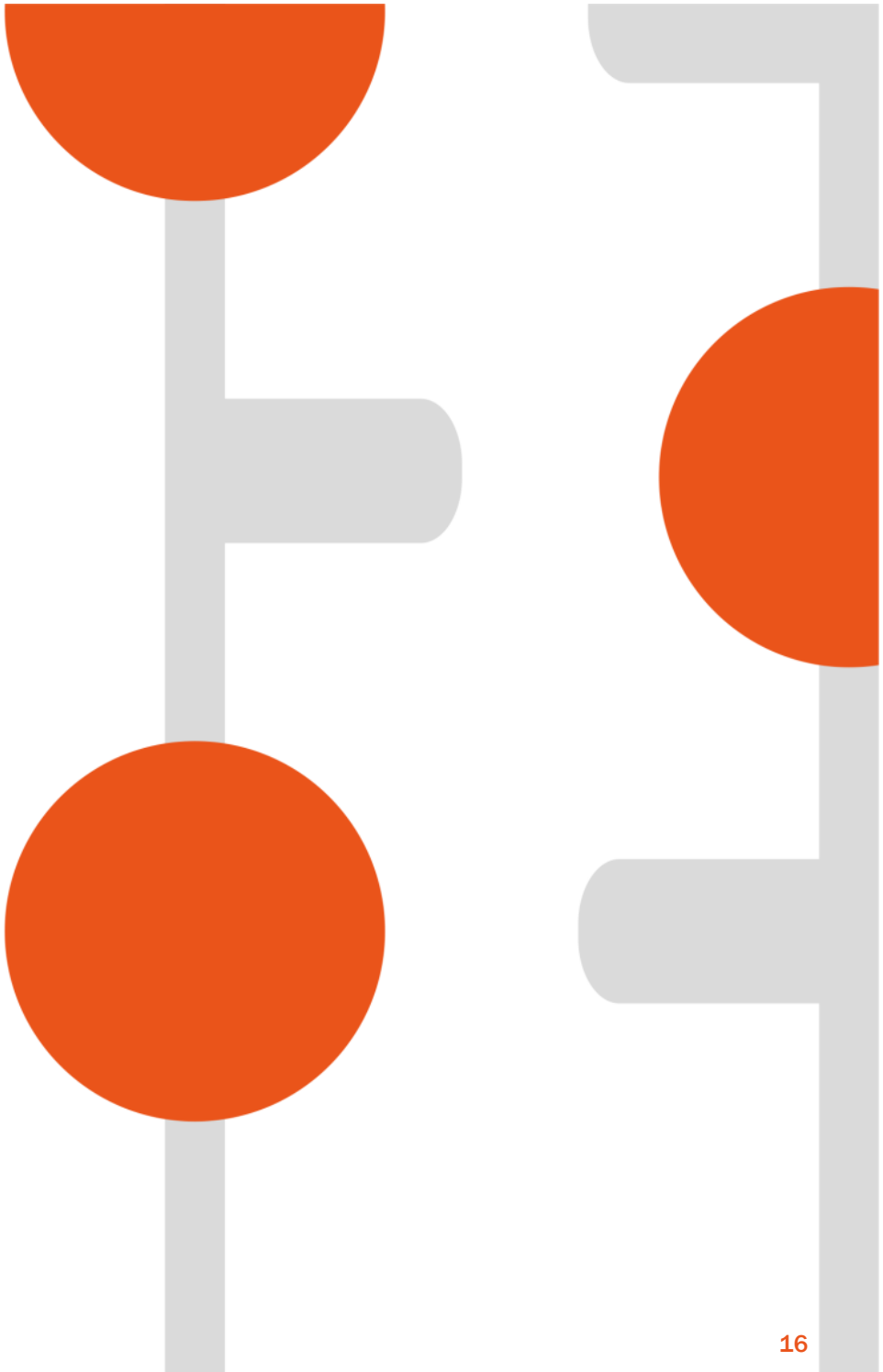
Recent patent filings

In addition to our patent estate protecting our chemical modification technology, we are strengthening our GalNAc-siRNA IP portfolio in 2017 by filing:

- Several lead sequence patent applications
- 2 linker chemistry patent applications
- 4 RNAi construct patent applications
- 2 modification rules patent applications

© Silence Therapeutics 2017

Why Silence?



© Silence Therapeutics 2017

Value inflexion points and upside risk



- ✓ **R&D progress:** Internal GalNAc-siRNA pipeline progressed rapidly, aiming to reach clinical development in late 2018. **R&D day planned in Q4 2017**
- ✓ **Licensee clinical progress:** Quark Pharmaceuticals has reported a positive AKI Phase 2 readout and Phase 3 DGF results are expected in 2018. Potential for revenue stream
- ✓ **Field validating event:** Patisiran Phase 3 readout in September 2017
- ✓ **IP potential for more licenses:** We believe that at least 4 of Alnylam's late-stage siRNA products (including Patisiran) need a license under our patent estate. Granting licences for these products would have a material financial impact on Silence
- ✓ **Arrowhead stake:** Financial upside and scope for potential collaborations

© Silence Therapeutics 2017