Halozyme
www.halozyme.com

Enhanced hyaluronidase-based drug delivery

Halozyme has developed ENHANZE, a recombinant human hyaluronidase-based drug delivery technology that enables and optimizes subcutaneous drug delivery for appropriate coadministered therapeutics.

Biotechnology pioneer Halozyme has developed ENHANZE, a drug delivery technology that can enable and optimize the subcutaneous (SC) drug delivery of coadministered therapeutics. ENHANZE is based on Halozyme's proprietary recombinant human hyaluronidase rHuPH20, which works locally and transiently to depolymerize hyaluronan (HA) in the extracellular matrix of the SC space, which enables bulk fluid flow and increases the dispersion and absorption of many coadministered therapeutics. With the use of this technology, multiple biologics and other compounds that are typically administered intravenously may instead be delivered subcutaneously, potentially resulting in both a better experience for patients and increased efficiency of drug delivery that may result in decreased overall healthcare costs.

The company believes ENHANZE is the technology of choice for pharmaceutical companies looking to enable SC delivery of intravenously administered therapeutic agents or to optimize existing SC delivery formulations. Halozyme has ongoing collaborations with eight top global biopharmaceutical companies and is looking to expand its network of partnerships.

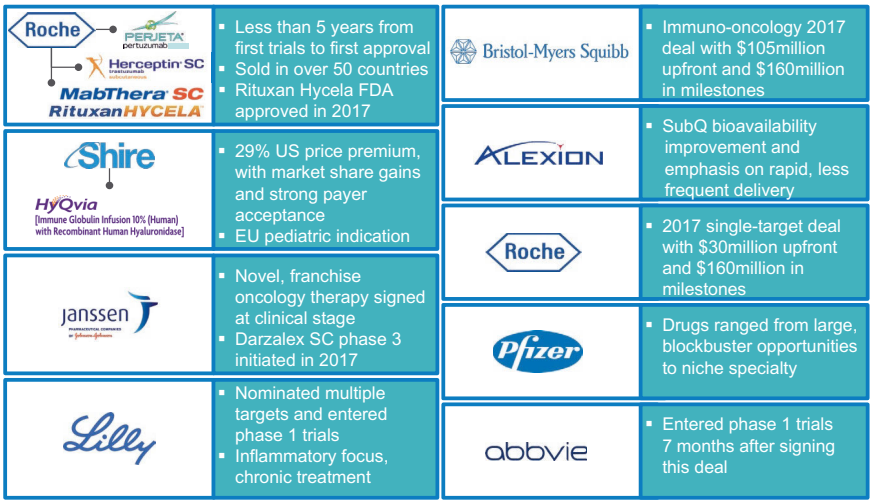

Fig. 1 | Halozyme's ENHANZE partnership network. ENHANZE is the platform of choice for companies looking to enable subcutaneous (SC) delivery of intravenously administered therapeutic agents or to optimize existing SC delivery formulations. Halozyme is looking to expand its existing network of partnerships. FDA, US Food and Drug Administration. Source: clinicaltrials.gov; press search; Halozyme financial filings.

Enhanced delivery

Hyaluronan is a naturally occurring glycosaminoglycan with repeating disaccharide subunits of *N*-acetylglucosamine and glucuronic acid that forms a gel-like matrix with water in the SC space. Hyaluronan provides resistance to bulk fluid flow within the extracellular matrix and limits large volume SC dispersion and absorption.

Hyaluronan is broken down and replenished as part of normal body function, with a daily turnover rate of ~33%. Halozyme's rHuPH20 depolymerizes HA locally and transiently in the extracellular matrix, which enables the rapid delivery of higher-volume SC injections (2–20 mL) and even larger SC infusions (up to 600 mL)[1–3].

ENHANZE can shorten the dose administration time of intravenous drugs when administered subcutaneously, from hours to minutes.

- Herceptin SC administration reduces delivery time from ~30 minutes (with intravenous Herceptin) to ~5 minutes[1].
- Rituxan Hycela (US)/MabThera SC (Europe) administration time was reduced from ~3–4 hours to ~5–7 minutes[2].

ENHANZE may also reduce the administration frequency for drugs already being delivered subcutaneously.

- Shire's (formerly Baxter Healthcare Corporation) HyQvia is administered as a single monthly SC injection for the majority of patients, compared with weekly multisite injections required for SC immunoglobulin formulated without ENHANZE[3].

ENHANZE may improve the pharmacokinetic profiles of coadministered therapeutics owing to enhanced absorption, which results in an increase in C_{max} (maximum serum concentration) and acceleration of T_{max} (time taken to reach C_{max}), and may lead to increased bioavailability of the coadministered therapeutic. In addition, reduced therapy administration time can translate into an improved experience for patients and into health system efficiencies, such as reductions in nursing time, increased patient turnaround, and reduced product waste, all of which can result in a decrease in overall healthcare costs[4,5].

"ENHANZE has become the industry go-to technology for converting intravenous therapies to subcutaneous administration," said Helen Torley, Halozyme's president and CEO. "Our goal is to help our partners and healthcare providers make the injection of life-saving medicines less burdensome for patients."

Enhanced partnerships

Halozyme has standing partnerships for ENHANZE with eight global top biopharmaceutical companies—Roche, Pfizer, Janssen, Shire, AbbVie, Eli Lilly, Bristol-Myers Squibb and Alexion (**Fig. 1**)—and is looking to expand its network of partnerships.

Halozyme is ideally positioned to partner with companies seeking to enable and optimize SC drug delivery for therapeutics. A dedicated and experienced alliance management team will support partners in designing their drug development process with ENHANZE. The team provides support throughout the complete life-cycle from preclinical development to commercialization, including formulation, preclinical testing and predictive modeling, clinical trial design, review of datasets and reports, and regulatory advice.

According to Renee Tannenbaum, vice president of global alliance management at Halozyme, "In our ENHANZE partnerships, we are successful if our partners are successful. Our technology can provide a competitive edge for our partners and our goal is to act with speed to improve the probability of success of our partnered programs."

1. Genentech, Inc. Herceptin [full prescribing information]. (Genentech, South San Francisco, CA, 2017).
2. Genentech, Inc. Rituxan Hycela [full prescribing information]. (Genentech, South San Francisco, CA, 2017).
3. Baxter Healthcare Corporation. HyQvia [prescribing information]. (Shire US Inc., Lexington, MA, 2016).
4. De Cock, E., Pan, I., Sandoval, M., Millar, D. & Knoop, A. Healthcare professionals' perceptions of the impact on clinical management of switching from the intravenous to the subcutaneous formulation of trastuzumab. Poster presented at the 9th European Breast Cancer Conference, Glasgow, UK, 19–21 March 2014.
5. Scottish Medicines Consortium. *Trastuzumab, 600mg/5mL Solution for Injection (Herceptin®)*. SMC No. (928/13). (SMC, 2014).

contact
Cindy Atwell, Senior Director, Strategy, and Business Development
Halozyme
San Diego, CA, USA
Tel: +1-848-794-8889
Email: info@halozyme.com