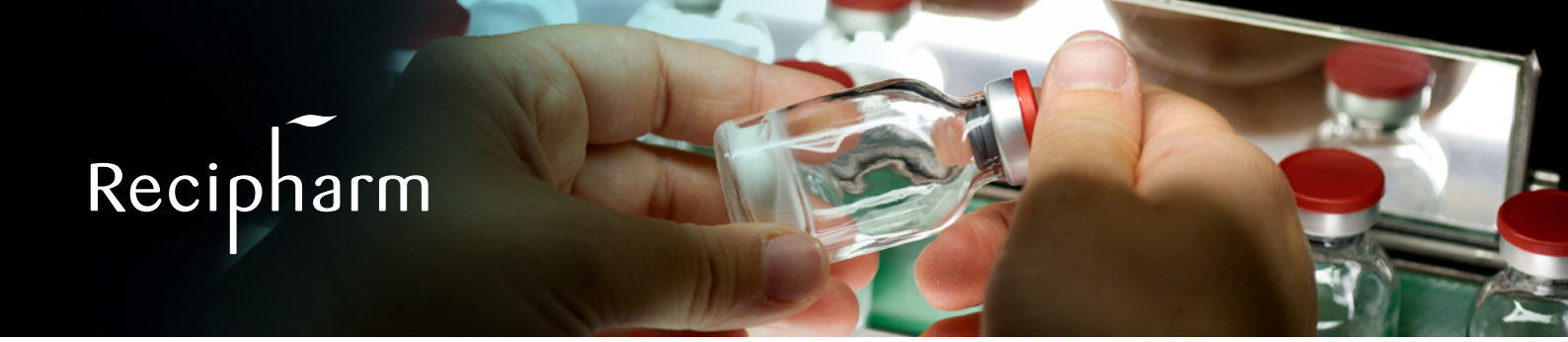


Supporting first lyophilised mRNA vaccine to pivotal trial

Recipharm's technology transfer and manufacturing services helped Arcturus meet its supply needs for its Phase III trial by lyophilising ARCT-154, a promising next-generation self-amplifying mRNA COVID-19 vaccine candidate.

Arcturus Therapeutics Holdings Inc. is a global late-stage clinical mRNA medicines and vaccines company with enabling technologies: (i) LUNAR® lipid-mediated delivery, (ii) STARR™ mRNA Technology (samRNA) and (iii) mRNA drug substance along with drug product manufacturing expertise. Arcturus' diverse pipeline of RNA therapeutic and vaccine candidates includes mRNA vaccine programs for SARS-CoV-2 (COVID-19) and Influenza, and other programs to potentially treat ornithine transcarbamylase (OTC) deficiency, and cystic fibrosis, along with partnered programs including glycogen storage disease type III, and hepatitis B virus.

Founded in 2013, Arcturus Therapeutics is an innovator of several advanced enabling pharmaceutical technologies: LUNAR® lipid-mediated delivery and STARR™ self-replicating mRNA technology (self-replicating or self-amplifying mRNA also commonly referred to as SAM, saRNA, or replicon RNA), which are utilized for vaccine programmes for SARS-CoV-2 (COVID-19), among other targeted diseases and indications. Arcturus's versatile RNA therapeutics platforms can be applied to multiple types of nucleic acid medicines, including messenger RNA, small interfering RNA, replicon RNA, antisense RNA, microRNA, DNA, and gene editing therapeutics.

In Q4 2020, Arcturus engaged Recipharm to support the manufacture of clinical trial supplies of Arcturus's COVID-19 vaccine candidate in an ongoing Phase I/II clinical trial. Further, the company needed to manufacture and release more than 100,000-units of ARCT-154 mRNA vaccine finished drug product in support of clinical Phase III trial study.

Arcturus challenge – find a better supply solution

When Arcturus presented its mRNA vaccine candidate to Recipharm, it was at the stage of a frozen product, a ready-to-administer sterile injectable for Phase I & II clinical trials. The inherent cryogenic logistics and storage costs associated with mRNA vaccines, as well as their intended markets (under-served populations with less access to developed healthcare infrastructures) created an additional burden for Phase III clinical trial and commercialisation.

To mitigate these challenges, Recipharm collaborated with Arcturus in the technology transfer, qualification and cGMP manufacturing of the lyophilised product to ease the complexities of distribution and extension of vaccine shelf-life.

Tight timelines, even tighter collaboration

This innovation, developed in collaboration with Arcturus, was a first for self-amplifying mRNA vaccines developed during the COVID-19 pandemic. Being a vaccine intended to fight a current coronavirus strain, timelines were extremely tight and there was little room for error, let alone a major change to the vaccine's Target Product Profile, during technology transfer.

Requiring both technical capabilities and operational excellence, Arcturus relied on Recipharm's current Good Manufacturing Practice (cGMP) expertise to deliver the innovation successfully. Lyophilised formulation complexities also added to the technology transfer challenges.

Regardless of the batch size, a manufacturer has to unload the freeze-dried sterile product to crimp each unit, perform 100% visual inspection and conduct secondary packaging at room temperature, all within the qualified bulk hold time. This meant strict storage temperature requirements of -20° (C) must be achieved soon after production.

The solution

From the very start, the collaboration between Recipharm's technical and development experts and Arcturus's process scientists and manufacturing technology engineers was success-orientated, motivated by critical delivery timelines. Engaging Recipharm's technical transfer experts as well as the resources of the company's biochemistry department, it was possible to identify the potential bottlenecks and quickly create a viable solution.

Working with Recipharm means engaging the full force of its science, drug development and manufacturing capabilities. The Arcturus programme fully incorporated the broad range of technologies Recipharm offers, including advanced digital manufacturing management platforms, a selection of product and data analytics, and advanced aseptic high-speed fill & finish and packing systems. Recipharm is developing new Lipid Nanoparticle (LNP) mixing capabilities, which could be essential to future commercialisation and global supply for Arcturus production. Arcturus further leveraged Recipharm's cGMP facilities and its class-leading lyophilisation capabilities to successfully deliver the innovative solution.

The customer outcome

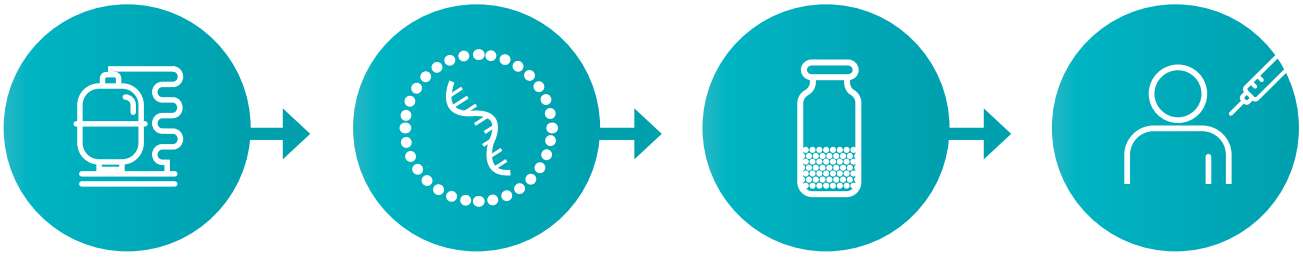
Recipharm de-risked the lyophilisation process for the cGMP final drug product. Chemistry, manufacturing and control fillings quickly followed to validate the change during technology transfer of the original formulation.

To accelerate the programme, Recipharm and Arcturus initiated tight collaboration between logistics and manufacturing to create a repeatable, stable and qualified process that can be accomplished from start to finish, plus packaging within the desired product hold time. Recipharm's quality assurance and controls also helped keep the intensive project pace both parties were striving to accomplish.

Ultimately, tight collaboration and experienced capabilities combined to deliver the finished drug product on time and in full. Recipharm's experience in managing the complexity of biologic projects meant the company could support the successful delivery of a pivotal trial.

Timelines were accelerated to meet the demands of the global COVID-19 pandemic response and, despite a number of unique requirements, the Arcturus project succeeded thanks to the consultative, professionally and personally orientated relationship Recipharm fosters with its clients.

mRNA drug product manufacturing process



About Recipharm

Recipharm is a leading contract development and manufacturing organisation (CDMO) headquartered in Stockholm, Sweden. We operate development and manufacturing facilities in France, Germany, India, Israel, Italy, Portugal, Spain, Sweden, the UK and the US and are continuing to grow and expand our offering for our customers. Employing around 9,000 people, we are focused on supporting pharmaceutical companies with our full service offering, taking products from early development through to commercial production. For over 25 years we have been there for our clients throughout the entire product lifecycle, providing pharmaceutical expertise and managing complexity, time and time again. Despite our growing global footprint, we conduct our business as we always have and continue to deliver value for money with each customer's needs firmly at the heart of all that we do. That's the Recipharm way.