SEQENS

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SEQENS MOBILIZES ITS INNOVATION TO SUPPORT THE UNPRECEDENTED RESEARCH ON THE COVID-19 AND PREPARES ITS UNIQUE INDUSTRIAL NETWORK FOR ANTI-VIRUS PRODUCTION, FOR EXAMPLE HYDROXYCHLOROQUINE.

Pending the availability of a vaccine, which will necessarily take time, the race against the clock is underway for the identification and rapid development of an anti-viral, a molecule effective against COVID-19. Research is taking place at an unprecedented speed with more than 1,900 clinical trials listed worldwide since the start of the pandemic, 912 in the process of patient testing. The challenge is immense, the stakes are high and speed is of the essence. Facing this challenge, the Seqens teams has mobilized their world-renowned know-how and skills in the synthesis of active ingredients, intermediates and precursors, as well as high-specialty polymers.

Systematic screening of databases

How should we proceed? Methodically. All the potential candidate molecules for a treatment against COVID-19 are identified through systematic compilation of bibliographic analyses using screening of clinical databases and chemical abstracts. These molecules may be either new chemical entities or molecules already marketed for another therapeutic indication (so called repositioning). The latter path allows the drug to be made available more quickly, the toxicity having already been evaluated in humans.

From the mass of potential candidates thus identified, the researchers at Seqens proceed to a new selection in order to target molecules with the potential to improve and accelerate industrialization, by simplifying and reducing the synthesis stages but also by using innovative proprietary solutions. The central idea is to offer pharmaceutical companies, biotech and public research the most effective solutions but also finding the fastest routes to the market in the context of this severe crisis. “As fast as possible” but “robust”.

Seqens ready with a hundred candidate molecules and participates on the INOVA COVID-19 platform

Seqens is already able to provide service and solutions to its customers on more than a hundred molecules.

In the first phases of R&D and to make its solutions robust, Seqens’s researchers with expertise crossing a wide range of sectors: organic synthesis, analytical sciences, process engineering, process safety as well as thermodynamic and kinetic modeling are collaborating at all levels. All this combined with original and highly efficient optimization methods.

For a rapid and broad as possible provision of its offer, Seqens participates on the INOVA COVID-19 platform, a platform for coordinating all the achievements of the global players fighting against the coronavirus.

Hydroxychloroquine and its precursors: an example of unique know-how

Besides China, France and the United States are the two most active countries in terms of COVID-19 clinical trials. Two countries that are also the most active in testing hydroxychloroquine, which is the subject of 174 clinical trials. Two countries in which Seqens has a very strong R&D and industrial presence. It is therefore logical that we have positioned Seqens – within a few weeks – with an offer of the main precursors of the active ingredient to our customers and prospects and now Seqens teams are ready for mass production.

This case study is the subject of the rest of this article.

A unique context

The prescription of hydroxychloroquine is authorized by decree in several countries worldwide for trials on COVID-19 patients. This has been the case for example in France since March 25, 2020 by the Ministry of Health with association with Lopinavir/Ritonavir. Hydroxychloroquine is traditionally prescribed for rheumatoid arthritis, lupus erythematosus (discoid and subacute) and lucitis.

According to the results of numerous clinical trials, the world requirements for hydroxychloroquine could rise between 4 to 10 times the usual demand for this product.

The objective for the Seqens teams was to provide, in record time, to its customers and prospects, the active ingredient and its precursors. We are ready, the challenge was taken up.

Seeking internal expertise at Seqens

The history began at our Lahr site in Germany. In the 1990s, our teams participated in the development of one of the synthons of the hydroxychloroquine molecule (HC) which is the reaction assembly of hydroxynovaldiamine (HND) and the heterocyclic molecule, the 4,7-dichloroquinoline. The precursor is acetyl-butyrolactone allowing the synthesis of a first intermediate, 5-chloro-2-pentanone, which is then reacted with N- (2-hydroxyethyl) - ethylamine. The reaction product is purified by distillation before being hydrogenated under an ammonia atmosphere to obtain HND. The high-pressure hydrogenation capacity of our specialized unit allows the synthesis of the HND side chain under good conditions of safety, quality and yield.

From expertise mastered to practice

From the expertise developed in Lahr, three of our European sites (Aramon and Limay in France, Lahr in Germany) have been mobilized to enable the production of more than 150,000 kgs of NHD annually. It is the combination of our crossed skills and our recognized entrepreneurial spirit that allowed such a rapid set-up: less than 30 days were necessary to establish the prerequisites in R&D (Seqens Lab) then to set up a complete industrial infrastructure, enabling the start of the first industrial production for the end of the second quarter of 2020.

A complex production chain but within the reach of Seqens teams

In addition, Seqens had to cope with the scarcity of precursors to HND due to the availability of material, the closing of borders in the main producing countries (India, China) and unprecedented price inflation. In early April, Seqens made the decision to internalize these precursors and in particular chloropentanone and AB-lactone.

It is the group's innovation center, the Seqens'Lab, which successfully optimized our existing process of chloropentanone in Germany in less than a week and adapt it to the production capabilities at the production site of Bourgoin-Jallieu. At the same time, the development team at our English site in Middlesbrough studied the internalization of AB-lactone.

Seqens teams' ability to respond to a major challenge within a few weeks

With the example of hydrochloroquine and its precursors, Seqens demonstrates its ability to respond in a few weeks to a major challenge. Our teams are proud to have cross-linked many technologies and multi-functional expertise, to have been able to mobilize in record time our R&D capacities and our industrial capabilities - unique in the world - of specialized factories.

Seqens will play its part in helping to guarantee the security of supply of medicines essential to the health of our citizens while ensuring the highest level of quality, safety and respect for the environment.

With its 24 industrial sites and 3 R&D centers, the 3,200 employees of Seqens are proud to design, develop and produce pharmaceutical active ingredients and intermediates as well as specialty ingredients essential to guarantee the availability of essential goods or to fight the spread of the pandemic

press@seqens.com / www.seqens.com / Linkedin : SEQENS / Twitter : seqens_group