ICOpre® Briefing Document (April 2021 update)

Introduction:

In 2019, Iconovo announced a strategic initiative to develop ICOpre as a generic inhaler platform to the Ellipta® inhaler from GSK. Iconovo has made significant progress in the development of ICOpre since this announcement. ICOpre is developed for a global registration including the USA as an AB-rated substitution for Ellipta®.

Iconovo is a well-established, leading Swedish company that offers innovative and effective inhalation platforms for a global market. Iconovo possess a unique combination of engineering and pharma expertise where Iconovo can provide the optimal combination of customized inhalers and tailored formulations. Iconovo offers clever and reliable products for people suffering from respiratory and other diseases to help them manage their disease and restore health.

Iconovo offers four proprietary inhaler platforms that can be licensed to pharmaceutical companies seeking an inhaled product solution. ICOpre is the fourth inhaler platform developed by Iconovo inspired by the successful partnering of the previous three inhaler platforms. ICOpre has been developed in Iconovo's laboratory by its own specialists in inhaler engineering, powder formulation and analytical characterization.

The opportunity:

Ellipta® is an inhaler developed by GSK that is used as the inhaler of choice for their new products launched to treat asthma and COPD. Ellipta is currently approved with five different products: Relvar® / Breo® (vilanterol-fluticasone furoate), Anoro® (vilanterol), Incruse® (umeclidinium), Trelegy® (vilanterol-fluticasone furoate-umeclidinium) and Arnuity® (fluticasone furoate). These products combined represent the largest future market opportunity for generic inhalers as other best-selling inhaled respiratory products have already lost its market exclusivity.

The combined sales for the Ellipta® products mentioned above and forecasted for 2025 is the following:

Class:	**Brand:**	**2020 Global Sales (USD bn)[1]**	**2020 US Sales (USD bn)[1]**	**2025 Global Sales (USD bil.)[2]**
ICS / LABA	Breo® / Relvar®	1.4	0.6	1.4
LAMA / LABA	Anoro®	0.7	0.4	0.8
LAMA	Incruse®	0.3	0.1	0.4
ICS / LABA / LAMA	Trelegy®	1.0	0.7	2.2
ICS	Arnuity®	0.1	< 0.1	< 0.1
	TOTAL	3.5	1.9	4.9

To the best of Iconovo's knowledge, there are four inhaler developments aiming for a substitutable inhaler to Ellipta®, including ICOpre from Iconovo. Iconovo aims to be ready to launch ICOpre at the time of the patent expiry for each of the Ellipta® portfolio products, the first being a generic Breo® product in the US. Although uncertainties exist about order of entry into the various territories in the global market and its implications for market share, Iconovo notes that a market share of 10-15 % volume market share at a 25 % discounted price would give a sales potential of 100-150 USD million

[1] Source: GSK Annual report 2020
[2] Source: Global Data analyst consensus forecast

for Breo® / Relvar® alone. Later to be followed by additional ICOpre product launches, the major launch being a generic ICOpre to Trelegy® in 2030.

Patent situation:

Patents protect many aspects of innovation and the patent expiry time below is currently the best knowledge available regarding when a generic copy of the current Ellipta® products can be launched in the US. Drug-device products are usually protected by patents for both the drug and the device. A generic version of the brands of Ellipta® can only be launched once the basic molecule patents have expired including any SPC prolongations and market exclusivity provided by regulatory authorities.

The patent expiry for the various products in the Ellipta® portfolio is the following in the US[3]:

Brand:	**Drug (year):**	**Device (Year):**
Arnuity®	2021	2030
Breo® / Relvar®	2025	2030
Incruse®	2027	2030
Anoro®	2030	2030
Trelegy®	2030	2030

As can be seen from the table above, there are several Ellipta® products where the drug patent will expire earlier than the device patent, opening an opportunity for companies that can launch a generic product without infringing on Ellipta® intellectual property. The patent landscape is different in different geographies.

Regulatory requirements:

The regulatory requirements are different between the European regulations (EMA) and the US regulations (FDA). Regulators in both territories demand that only products with the same formulation type can be approved as a generic alternative, meaning that only dry powder inhalers can be approved as generic alternatives to originator dry powder inhalers. In Europe, the operation of the device can be different from the originator operation, while FDA has a demand for the generic inhaler to operate in a similar way. A term like “similar operation” will always leave room for interpretation by regulatory authorities adding risk to the development. In Europe, you can usually get approval by showing equivalence on several in vitro device parameters and a pharmacokinetic equivalence trial, while in the US, you also need a pharmacodynamic clinical trial showing equivalence. It means that the regulatory pathway in the US has higher demands to claim bioequivalence than the European pathway, thereby also being more risky and costly. However, the value of the US market is significant, and the higher regulatory hurdles should also mean less intense competition in the marketplace.

[3] Orange Book (USA)

ICONOVO

ICOpre

ICOpre – pre-metered dual cavity multi-dose dry powder inhaler

ICOpre is a pre-metered dual cavity dry powder inhaler with 30 individually sealed doses protected by aluminum foil. It features the same easy, three-step user operation as the well-known Ellipta®, Open-Inhale-Close. Each dose comes from two compartments that are inhaled simultaneously, which makes ICOpre suitable for mono, duo or triple products. A dose counter makes it easy to see the number of remaining doses. ICOpre is color-coded according to the substance and strength.

Picture: ICOpre® inhaler

ICOpre Design Principle:

ICOpre is designed to be operated in the same way as Ellipta® but based on new technological principles that will give it freedom to operate outside of the current Ellipta® patents. Iconovo has developed a proprietary internal design with a unique injection molded disk and cavity opening to go free from these patents. Not only will any company launching ICOpre avoid the infringement risk but also earn a patent protection for almost 20 years. In addition, following its heritage in Sweden, ICOpre has been given a clean attractive Scandinavian exterior design.

Timing:

The development of ICOpre started in Q1-2020 based on conceptual and design ideas in Iconovo. Iconovo used an integrated process based on a small team in a shared laboratory with internal experts in inhaler engineering, powder formulation and analytical characterization to accelerate the product development. Iconovo also applies a parallel development process for all generic Ellipta products and plans to out-license the whole portfolio of generic Ellipta products in ICOpre. The successful application of the development approach has resulted in excellent in-vitro equivalence for ICOpre already after less than 12 months of development.

Iconovo plans to out-license ICOpre once the inhaler design is optimized with the powder formulations for Breo® / Relvar® (fluticasone furoate / vilanterol), in-vitro equivalence is achieved, and the product is ready for a first pilot pharmacokinetic trial. This is expected to happen in H1-2022. Iconovo is actively talking to various parties to ensure that the licensing process is fast and effective and captures the value created by Iconovo.

Few companies in the world have an unpartnered project and the capabilities to develop both the inhaler device and the powder formulations for a generic Ellipta product.

Ideal partner set-up

The financial terms offered to Iconovo for the license to the generic Ellipta portfolio in ICOpre will be of high importance in the partnering decision. Another important criterion will be the global footprint offered by potential partners as Iconovo regards ICOpre as a global opportunity that should capture market in the major regions in the world, including the US with its high regulatory demands. Iconovo would also favor a portfolio agreement where the same partner would launch the whole range of products and reap benefits in shared use of manufacturing facilities.