ICOpre™ Briefing Document

Introduction:

On October 25, 2019, Iconovo announced a strategic initiative to develop ICOpre™ as an alternative generic inhaler platform to the Ellipta® inhaler from GSK. ICOpre™ will be developed for a global registration including the USA as an AB-rated substitution for Ellipta®.

Iconovo possess a unique combination of engineering and pharmaceutical expertise, where Iconovo can provide the optimal combination of uniquely designed inhalers and tailored formulations that deliver the right dose to the lungs.

Iconovo offers reliable, competitively priced dry powder inhaler solutions based on four differentiated technical platforms. It means that pharmaceutical companies seeking a fast and safe way to reach the market with their products can feel assured that Iconovo will reduce project risk, development cost and shorten time to commercialization.

Iconovo offers three inhaler platforms immediately available for customization with inhalation powder, and soon also ICOpre™ as a fourth inhaler platform. A comprehensive service package is offered by Iconovo including device design, formulation development, analytical testing and documentation.

The highly skilled employees of Iconovo have significant experience in developing both inhaler devices and dry powder formulation in our own laboratory for formulation development, inhaler customization and characterization of inhaler product. In addition, there is an extensive network of inhalation expertise that can support with additional analysis when relevant.

The opportunity:

Ellipta is an inhaler developed by GSK that is used as the inhaler of choice for the new products launched to treat asthma and COPD. Ellipta is currently approved with five different products, 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 launches of 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 2023 is the following:

Class:	Brand:	2019 Net sales (USD bil.)[1]	2023 Net sales (USD bil.)[2]
ICS / LABA	Breo® / Relvar®	1.2	1.2
LAMA / LABA	Anoro®	0.6	0.8
LAMA	Incruse®	0.3	0.4
ICS / LABA / LAMA	Trelegy®	0.6	2.0
ICS	Arnuity®	0.1	0.1
	TOTAL	2.8	4.5

All Ellipta® products are currently protected by various patents, the most important being the basic molecule patent and patents on the Ellipta® device. A generic version of the brands of

[1] Source: GSK Annual report 2019

[2] Source: Factset consensus estimates (Danske bank: Iconovo report 2020-04-14)

Ellipta® can only be launched once the basic molecule patents have expired including any SPC prolongations and market exclusivity provided by regulatory authorities.

Patent situation:

Patents can 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. It makes a difference between patents protecting the pharmaceutical products and patents protecting the Ellipta® inhaler. The launch timing of various generic copies of Ellipta® would be restricted by the following patent expiry times[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 device patent, opening an opportunity for companies that can launch a generic product without infringing on Ellipta® intellectual property.

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 from 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.

ICOpre™ Design Principle:

ICOpre™ will be 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. As it will be operated in the same way as Ellipta® and documented with both in vitro and in vivo data, it can be approved by FDA as a substitutable product to the relevant Ellipta® product developed (one of the five products described above).

All relevant new technological principles developed for ICOpre™ will be protected by new patents to be filed by Iconovo.

[3] Orange Book (USA)

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ICOpre™ Features:

ICOpre™ is a pre-metered dry powder inhaler for carrier-based or spray-dried formulations. It features the same easy, three-step user operation as the well-known Ellipta®: Open-Inhale-Close. With 30 individually sealed doses protected by aluminum foil it is perfect for one month's supply. 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.

Feature:	Benefit:
Pre-metered device, pre-filled with 30 individually sealed doses	Consistent dosing, ideal for once-daily products
Two-compartment system	Suitable for mono, duo or triple products. Each formulation can be developed separately
Exact dose counter	Easy to see the remaining number of doses
Three-step operation: Open-Inhale-Close	Easy to use
Same operation as Ellipta®	Developed for global registration including USA as an AB-rated substitution for Ellipta®
Aluminum foil seal	Good humidity protection
Suitable for both carrier-based and spray-dried formulations	Versatile inhaler for many types of molecules

Timing:

The development of ICOpre™ started in Q1-2020 based on conceptual and design ideas in Iconovo. The development plan aims at a timely launch of the generic ICOpre™ to Relvar® / Breo® Ellipta®. At the point in time of partnering there will be a prototype of ICOpre™ combined with feasibility data for the first powder formulation in ICOpre™. Iconovo offers a unique investment opportunity as it has the integrating capabilities to develop both the inhaler and the inhalation powder. Few companies in the world have an unpartnered project and the capabilities to develop both parts of an inhalation product.

Partner interest will be explored during 2020 with an agreement most likely happening in H2-2021 or H1-2022, unless strong early interest triggers an earlier agreement.

Ideal partner set-up

Iconovo aims for a global partner that can launch both in Europe and in the US with its high regulatory demands. Ideally, the same partner would agree to launch generic ICOpre™ products to all the current Ellipta® products on the market. It would give increased focus and coordination on the path of development, would leverage synergies in the development, bring economies of scale in manufacturing and align decision-making. However, final partner selection will also be dependent on interest and financial terms offered.