What are Amarin's plans and timing for VAZKEPA initial commercial launch in Europe?

For Europe, the brand name of icosapent ethyl is VAZKEPA. This is the same drug approved in the United States and select other countries under the brand name VASCEPA®.

Regulatory Approval

As announced on March 30, 2021, the European Commission granted marketing authorization for icosapent ethyl in the European Union for cardiovascular risk reduction under the brand name VAZKEPA "to reduce the risk of cardiovascular events in adult statin-treated patients at high cardiovascular risk with elevated triglycerides (≥150 mg/dL) and

- established cardiovascular disease, or
- diabetes, and at least one other cardiovascular risk factor."

This approval was based on the results of more than a decade of VAZKEPA (icosapent ethyl) development and testing, including successful completion of the landmark REDUCE-IT® cardiovascular outcomes global study. In the REDUCE-IT study, patient enrollment from Europe was second in aggregate number only to the patient enrollment in the United States.

For countries of Europe that are not part of the European Union (e.g. Switzerland), separate application is required. Regarding the United Kingdom (UK), based on their public guidance, it is expected that regulatory authorities there will rely on the CHMP opinion for review and approval of VAZKEPA reflecting that the European Medicines Agency (EMA) centralized review was nearly complete at the time that BREXIT became effective. Based on such public guidance, regulatory approval in the UK is expected soon after the approval by the European Commission.

In Europe, Amarin did not pursue labeling for the original niche indication approved in the United States (lowering of triglyceride levels in patients with very high triglycerides ≥500 mg/dL) for various reasons. Those reasons include that the market need is larger for the cardiovascular risk reduction indication and the supporting data for the effectiveness of VAZKEPA for this larger opportunity is more extensive, including cardiovascular outcomes study data which was not available when the drug was originally approved in the United States.

Market Need

The need for preventive cardiovascular care beyond currently available therapy is large in Europe, as it is throughout the world. In the European Union, there are approximately 49 million people reportedly living with cardiovascular disease, including approximately 38 million diagnosed with ischemic heart disease, stroke or peripheral heart disease.[1] The proportion of patients dying from cardiovascular disease is reportedly higher in Europe than in the United States and there are more patients on statin therapy in Europe in aggregate than compared to the United States.[2]

Caring for cardiovascular disease in Europe is expensive, with current spending estimated to exceed €200 billion annually.[1] This significant public health burden, combined with the availability of cardiovascular outcomes study results with VAZKEPA, likely contributed to the clinical practice guidelines updated in 2019 by the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) recommending use of icosapent ethyl.[3,4] Numerous key opinion leaders in Europe have expressed to

Amarin that they are looking forward to the commercial availability of VAZKEPA in Europe to help them improve care for their patients.

Market Access and Commercial Launch

Amarin is preparing to launch VAZKEPA in Europe with a team of experienced professionals. In larger countries of Europe, Amarin plans to self-launch VAZKEPA as these countries represent larger market opportunities and the cost of creating such infrastructure is more readily offset by potential revenue growth. In smaller European countries, economic analyses suggest that relying on existing third-party infrastructure of in-country commercial partners is likely more cost-effective than creating such infrastructure, and in these smaller market opportunity countries Amarin will likely consider commercial partnerships with proven companies.

Physician targets to be educated about VAZKEPA in Europe tend to be more concentrated than in the United States. In addition, the efficiency of launching a product and educating physicians in Europe should be aided by digital communication and other efficient forms of education and promotion. Having said that, education usually takes time and a premature new product commercial launch, without appropriate education, will likely lead to slower uptake. Amarin is planning to pursue pre-market education regarding VAZKEPA prior to making the product available commercially in select countries. Amarin's commercial launch of VAZKEPA in Europe is being led by industry veteran Karim Mikhail, senior vice president, Commercial Head Europe. Mr. Mikhail has extensive cardiovascular and international experience and a track-record of success to rely on in building multi-billion-dollar brands.

Key to the success of any product in Europe is securing market access. As described in a separate FAQ on this website, Amarin intends to pursue market access for VAZKEPA on a country-by-country basis. Unlike the centralized EMA approval process in the European Union, process and timing of being granted market access varies by country. With demonstrated clinical results in reducing high-cost events such as heart attacks and strokes, and with no other product approved for VAZKEPA's label indication, Amarin believes that it is well positioned to achieve reimbursement for VAZKEPA in Europe.

Amarin intends its initial commercial focus to be in those countries where market access can be promptly and reasonably obtained. Amarin plans to use available clinical data to educate payors, cardiologists and other healthcare providers of the favorable benefit-risk profile of VAZKEPA. Amarin commenced 2021 with approximately 50 experienced professionals in Europe preparing for approval and commercial launch. Based on 2021 plans, Amarin seeks: 1) net pricing in European countries that reflects the clinical value of VAZKEPA based on demonstrated cardiovascular risk reduction and the high costs associated with heart attacks, strokes and other adverse cardiovascular events which VAZKEPA helps prevent in at-risk patients, whereas pricing in the United States was based on the original triglyceride-lowering indication without outcomes study data; 2) at a minimum to launch in Germany during 2021 after an initial product awareness campaign with a priority on specialists (e.g., cardiologists); and 3) to build its European staffing for VAZKEPA to approximately 300 people by the end of 2021.

Exclusivity

With the recent EMA approval, VAZKEPA is granted 10 years of regulatory exclusivity in Europe (11 years if a second indication for the product is approved). The regulatory exclusivity period commenced upon product approval. In addition, patents for VAZKEPA in Europe are anticipated to extend until mid-2033 with additional pending patent protection that could extend into 2039. As Amarin did not seek approval for VAZKEPA in Europe based on the niche triglyceride-lowering indication initially sought and obtained in

the United States, patent litigation and related generic competition regarding that niche indication are not expected in Europe until at least 2029, eight years into the ten year regulatory exclusivity period.

Dated: April 6, 2021

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[1] http://www.ehnheart.org/cvd-statistics.html

[2] European Society of Cardiology: Cardiovascular Disease Statistics 2017, European Heart Journal, Volume 39, Issue 7, 14 February 2018, Pages 508–579; European Heart Network Report, 2017

[3] European Society of Cardiology https://www.escardio.org/The-ESC/Who-we-are

[4] European Atherosclerosis Society https://www.eas-society.org/page/about_eas