What is Amarin's perspective on the focus of Matinas Biopharma on the importance of bioavailability and triglyceride lowering?

At Amarin, we encourage research and development from others. There is knowledge to be gained both when such R&D works and when it fails.

The product candidate that Matinas Biopharma is studying, MAT9001, reportedly completed its first study in 2013. To our knowledge it is not yet approved for marketing or sale in any country. We understand that Matinas Biopharma intends to complete a study of its product candidate for the treatment of patients with severe hypertriglyceridemia (TG $\geq$500 mg/dL, also known as very high triglycerides). We are not aware of any cardiovascular outcomes study commenced for this product candidate.

With limited clinical data available for MAT9001, including no cardiovascular outcomes data, it is premature to assess whether the product works effectively or not. But we can share our views regarding its suggested differentiation regarding triglyceride lowering and bioavailability.

Triglyceride (TG) Lowering

Pancreatitis: For treatment of pancreatitis in patients with very high triglycerides, the degree to which TG levels are lowered may be important, but this has not been demonstrated in any outcomes study. Moreover, lowering very high TG is an indication for which many products compete, most of which products are generic and some of which are relatively inexpensive. Matinas has had many years to develop its product for this indication. If they are successful in doing so, they will then need to convince managed care to cover their product. Securing broad managed care coverage can be challenging without outcomes data in a market with multiple generic products unless the new product is priced very inexpensively (such a low price may be difficult to accomplish for MAT9001 given the likely high cost of producing such a product to high quality standards).

> N.B.: Amarin's revenue from VASCEPA® (icosapent ethyl) for patients with very high TG levels seeking TG lowering is less than 7% of VASCEPA revenues (approximately $40 million per year in the U.S. based on 2020 results). When Amarin launched VASCEPA for treatment of very high triglycerides Amarin did so expecting the label to be expanded shortly thereafter, however, that pathway closed. Moreover, when Amarin launched VASCEPA for its original indication (i.e., for TG-lowering in adult patients with very high TG levels) we witnessed unpromoted off-label use of VASCEPA for cardiovascular risk reduction because at that time there was not another product approved for this approach to cardiovascular risk reduction. This also is different today as VASCEPA has proven cardiovascular risk reduction results with established managed care coverage making it less likely that heath care professionals will seek to prescribe an unproven alternative in lieu of VASCEPA. That is especially the case in light of the failure of the STRENGTH cardiovascular outcomes study of an omega-3 drug class product, EPANOVA®, that, like MAT9001, is not pure EPA.

Cardiovascular risk reduction: For treatment of at-risk patients for cardiovascular risk reduction, the U.S. Food and Drug Administration (FDA) made it very clear in 2015 that they will not rely on TG lowering as a surrogate biomarker. Since that time there have been multiple products which lower TG but failed cardiovascular outcomes studies, including other omega-3 mixtures. Such history makes it unlikely that the FDA has reversed its position. Moreover, analysis of results of Amarin's successful REDUCE-IT® cardiovascular outcomes study show that relatively little of the cardiovascular benefit was derived from TG lowering alone. Rather, the benefit was derived from the multifactorial effects of icosapent ethyl. These multifactorial effects are unique to icosapent ethyl. Such effects have not been shown for any other

drug. Leading medical societies caution that the clinical results demonstrated with icosapent ethyl should not be generalized to any other product.

We encourage Matinas Biopharma to conduct its own cardiovascular outcomes study.

Bioavailability

The indications for which VASCEPA is approved are for chronic (long-term) treatment. It is unclear whether rapid uptake of a drug due to enhanced bioavailability is important for chronic treatment and clinical effect in the indications publicly considered. Most recently, EPANOVA® had data showing enhanced bioavailability and significant TG lowering, however, that drug failed to demonstrate cardiovascular benefit in the STRENGTH cardiovascular outcomes study.

Again, we encourage Matinas Biopharma to conduct its own cardiovascular outcomes study.

Historically, Matinas has made comparisons of MAT9001 to VASCEPA based on two relatively short-term, pharmacokinetic and pharmacodynamic studies. As described above, data from short-term studies does not predict clinical outcomes. The current study being conducted by Matinas of MAT9001, while longer than its earlier studies, is still relatively short term. Furthermore, it is unclear if the product used in the prior studies was actual VASCEPA and it appears that the dosing of VASCEPA in such studies was not consistent with VASCEPA's approved label. We recognize that conducting a cardiovascular outcomes study requires conviction about the science together with several hundred million dollars of capital resources and time. We hope that Matinas decides to pursue this path to seek to add to the body of reliable scientific evidence in the field. Until they have success in doing so, their hypotheses are unproven. Until proven, a healthy dose of skepticism is warranted in this case in particular as many other product candidates, even with similar composition, have tried similar paths and failed.

Dated: January 29, 2021