12 November 2013

There is an important matter for which I respectfully request your personal and immediate attention.

I am hopeful that upon review of this letter you will agree with me that a potential exists for both a massive reduction in health care cost and a marked improvement in the health of an unmet population representing millions of Americans To that end, I'm requesting you to personally explore and validate the assertions and circumstance detailed below.

There currently exists a critical decision pending in the FDA. This decision regards expanding the use of an approved drug called Vascepa for dyslipidemia. This expanded use is called the Anchor indication. By expanding the Vascepa label to include dyslipidemia, this approved pharmaceutical grade EPA agent (marketed by Amarin Corp) with a safety profile similar to placebo, will provide physicians with an effective, well-tolerated and safe drug with which to fight the insidious effects of Diabetes that's sweeping America. My estimates are that expanding use of Vascepa for this additional indication could achieve a 20% reduction in health costs from fewer cardiovascular events in those with Diabetes and improved the health of among 26 million Americans with Diabetes.

The Cost of Diabetes is $245 Billion Annually:

The current estimated cost to the US economy from Diabetes is $245 billion each year; $176 billion in direct medical costs and $69 billion in reduced productivity. Much of this cost due to Cardiovascular Disease since Diabetics are among those at a highest risk developing Cardiovascular Disease.

The Affordable Care Act, Diabetics and Dyslipidemia:

While few Americans understand the full extent of the Affordable Care Act, most intuitively know the success of this program will be determined by its ability to reduce health care cost over time. There are few larger opportunities to achieve this goal than successfully reducing the risk of Cardiovascular Disease (CVD) for the 26 million Americans suffering with Diabetes. The opportunity for cost savings from reducing CVD events in this population is staggering. The American Association of Diabetes states that 68% of Diabetics deaths are noted as caused by heart disease on the death certificate. Since so many Diabetics die from CVD, clinicians are focused on managing key lipid markers known to be associated with higher risk of CVD events. Most Americans are familiar with the family of Statin drugs used to control bad cholesterol but unfortunately there is not an analogous solution available to clinicians to treat other lipid abnormalities such as High Triglycerides. The AACE (American Association of Clinical Endocrinologists) published guidelines state that Triglycerides levels over 150 m/dL put a Diabetic at high risk for developing CVD. The currently approved drugs for treating High Triglycerides unfortunately raise bad cholesterol and so clinicians have lacked an optimal therapy that helps Diabetics reduce Triglycerides levels safely. Consequently what is desperately needed is an extremely safe, well tolerated drug that can be effective at lowering Triglycerides for this segment of the population at highest risk for developing CVD. In addition to lowering Triglycerides, another lipid abnormality that increases risk is called Dyslipidemia. Dyslipidemia is simply the condition when two or more Lipids are considered abnormally high for the patient, in this case Diabetics. Typically Dyslipidemia is manifested as High Triglycerides and one other Lipid marker. Dyslipidemia is considered a cardiovascular risk factor particularly for Diabetics and as stated earlier, is not adequately addressed by Statin drugs alone.

Health care professionals, primarily Endocrinologists, are struggling to treat this massive health epidemic facing our country and it is Endocrinologists who are most vocal about this unmet need for therapy beyond merely Statin to treat dyslipidemia in the 26 million Americans with Diabetes.

A placebo-like safety profile; proven efficacy at treating High Triglycerides:
The most promising weapon to fight both High Triglycerides and Dyslipidemia in Diabetics is Vascepa from Amarin Corp. In FDA approved clinical trials Vascepa proved both safe as placebo and effective by meeting and exceeding the study endpoints for both the treatment of Very High Triglycerides (already approved) and High Triglycerides (pending approval).

Vascepa is 96% purified EPA (eicosapentaenoic acid):
It should not be surprising that the safety profile of Vascepa is so strong, or why it's so well tolerated by patients. Vascepa is composed of 96% purified EPA produced to FDA strict pharmaceutical standards. EPA is listed on every bottle of fish oil supplement sold by the millions to unsuspecting consumers as beneficial to cardiovascular health. However, it has been clinically proven that low amounts of either EPA, or DHA, as is contained in these supplements, produce negligible CV benefit. In fact, clinical trials of Vascepa showed that 4 grams of EPA taken daily is required to produce therapeutic benefit and confirming that the health benefits from EPA, as in every other drug, is dependent upon dosage.

Diabetics are being deceived and put at increased CVD risk from unregulated supplementation:
This means that to get 4 grams of EPA daily, a Diabetic would have to consume approximately 20 Fish Oil capsules daily thus exposing them to possible contaminates and excessive DHA levels that is proven to increase bad Cholesterol. Should you speak to any Endocrinologist, you'll hear the stories of Diabetics who unfortunately take fish oil pills to the detriment of their CV health.

The fact that EPA is contained in fish oil mixtures is where the similarity of purified EPA (Vascepa) to fish oil ends and the cost bending effects on health care begin. Recent FDA approved clinical trials conducted with a 4 gram dose of purified EPA achieved the FDA clinical trials endpoints and in doing so indicated a significant therapeutic benefit for Diabetics by lowering key lipid markers including; Triglycerides VLDL-C, non-HDL-C, and even LDL-C. This confirmation led to its initial, albeit limited, approval by the FDA last year for only treating patients with Very High Triglycerides (greater than 500 mg/dL) whereas the Anchor indication pending FDA approval would expand that label to include the treatment or High Triglycerides (greater than 200 mg/dL). It should be noted that it's estimated 40 million Americans have High Triglycerides and this is especially concerning for Diabetics with High Triglycerides because of their added risk of developing CVD.

The United States lags behind other nations who use pharmaceutical grade EPA:
To illustrate the potential of Vascepa to reduce costs by reducing the risk of CVD events, consider a large study conducted in Japan of over 18,000 people using the same purified EPA agent, but at only half the dose of Vascepa (1.8g vs. 4g). The results were astounding. Among the cohort group with Triglycerides over 150 mg/dL and on a Statin drug there was a 53% reduction in cardiovascular events versus those on a Statin drug alone. I am not a statistician, but I think most Americans can intuitively extrapolate the potential for massive reductions of health care costs among Diabetics if we can come close to the reduction rates found in the Japanese study. Should this be realized, the impact on the success of the Affordable Care Act would be very large. And of course, the improvement to the health and well-being of millions of Americans with Diabetes immeasurable.

Despite proven efficacy and a remarkable safety profile it appears Vascepa will not be approved for High Triglycerides and denied to millions of Americans with Diabetes:

Unfortunately, there appears to exist today a bias by the FDA towards not approving Vascepa for the expanded Anchor indication for the treatment of High Triglycerides and Dyslipidemia. This, despite the fact that an approval would provide access to safe treatment for a critical lipid disorder known to increase the risk of cardiovascular disease among the millions of Americans with Diabetes.

If in fact my research is valid, then common sense should dictate a rapid approval for an expanded label for Vascepa. However, incredibly this is not the case. The primary obstacle to approval by the FDA is their stated position that studies of other non-EPA drugs that lowered Triglycerides did not lower the risk for CVD events. And since the other non-EPA drugs failed in outcomes studies, the FDA is concluding the same to likely to be true for Vascepa. Therefore it appears certain the FDA plans to deny approval of Vascepa for an expanded population by December 20, 2013. This would mean that the 26 million

Diabetics and their attending physicians will be denied access to a safe, effective drug. A drug that is proven to reduce the very lipids associated with increased CVD risk in Diabetics. And instead millions of Diabetics will have to wait four years or more for the completion of an outcomes trial for a drug as safe as placebo. I am not a doctor, but from a practical point this does not make sense to me. This means while waiting for the outcomes study, tens of millions of patients with Diabetes will be denied access and reimbursement by health insurers for this safe and proven preventive drug.

Considering risk consequences versus reward consequences:

An important question is how many Diabetics will become increasingly ill or worse, die as a result of untreated and uncontrolled lipid disorders beyond bad cholesterol? I am not alone in my concerns in this regard. During the FDA Advisory meeting on October 16th many leading practicing physicians spoke on public record endorsing the approval of Vascepa citing their patient needs, clinical data, the unmet need among Diabetics, the increased risks of CVD that Dyslipidemia puts on Diabetics, the strong safety profile of Vascepa , the endpoint proving efficacy of this drug, and the risks of over the counter self-treatment with unregulated, ineffective self-prescribed supplements. One by one, these Physicians took to the podium and gave compelling testimony to support expanded approval of Vascepa All spoke of the large unmet need of Diabetics with mixed Dyslipidemia and on the efficacy and remarkable safety of Vascepa. So remarkable is the safety profile of EPA that in 2012, EMEA, the European regulatory body pronounced EPA to be safe in doses up to 5 grams daily, an amount 25% greater than currently being considered by the FDA. The fact is Vascepa is safer than aspirin. As previously stated, Vascepa has been approved for Very High Triglycerides and became available in early 2013. Since then, over 100,000 Vascepa prescriptions have been written and has proven to be very well tolerated as reported by Amarin. The complete list of Physicians who share my view and went on public record at the FDA is included in my attached references.

The FDA advisory meeting was a travesty of manipulation and confusion:

The root cause of this problem concerning the approval of Vascepa reached a critical milestone last week in the FDA controlled advisory committee (recorded) meeting in which a panel of physicians were tasked with voting to guide the FDA in their final decision regarding the expansion of the Vascepa population. However a review of the recorded meeting will show that the voting question crafted and posed by the FDA to the panel was in actuality guided the panelist, not the other way around. The question proved at first confusing and unanswerable as it literally required the panel to admit to being able to predict future events. The panel repeatedly asked the FDA to explain the question but this effort was rebuked by FDA officials. Furthermore, attempts by the panel of physicians to have the question reworded were also rejected by the FDA officials. The resulting control by the FDA of the question put the voting panel in an untenable position of knowing the unknowable and achieved the only possible outcome, a 9-2 vote against approval.

The FDA dealt a fatal blow to Diabetics, but who wins with the decision?

It should be noted that a Special Protocol Assessment (SPA) is in place between the FDA and Amarin Corp for Vascepa. This SPA, which was agreed to by the FDA had no requirement to complete an outcomes study prior to qualifying for approval of the expanded Anchor label. Instead, the SPA noted that the outcomes study was to be significantly enrolled (>50%) prior to acceptance by the FDA of the supplemental New Drug Application (sNDA) for the expanded label for High Triglycerides and dyslipidemia. Amarin met this requirement (and every other requirement) specified by the FDA in late 2012 and submitted the sNDA for Anchor earlier this year Indeed, the fact that Amarin had met all goals was even voiced by one the physicians attending the meeting. But on October 16th the FDA purposefully moved the “goal posts” for approval using a carefully crafted question that could be answered only one possible way, and thereby by forcing a no vote and making the approval contingent upon completion of the outcomes study. The FDA seemingly broke the SPA on October 16th and in doing so changed the requirements for approval Amarin has delivered to the requirements of the SPA. In reviewing the recorded meeting it is clear that steadfast position of the FDA officials in refusing to accommodate the panel brings into question the very purpose of a panel if all you’re going to accomplish is blatantly manipulate them into an answer you personally desire. In essence, the meeting conduced is an embarrassment for the agency and questions the integrity of the process itself.

With its safety profile largely unquestioned, the only remaining obstacle that could be used to prevent this safe effective agent from reaching millions of Americans is the implied opinion by the FDA that the "science" has changed as a result of failed outcomes studies of other drugs used to lower Triglycerides. The other drugs studied and referenced by the FDA included Niacin and Fenofibrate, and not EPA. In one easy to understand example of the misdirection by using these studies as supporting science, each of the other drugs raised bad cholesterol whereas Vascepa (EPA) is proven to be LDL-C neutral and in some cases actually lowers LDL-C. What may be even worse, the FDA is suggesting that the of use a surrogate markers (in this case, triglycerides levels and other lipid markers measurement) are no longer an acceptable target to be used as standard of care. By any measure, this is a both a radical and contrary departure from the accepted standards of care utilized and endorsed by physicians nationwide , especially those that treat Diabetics which are among the highest at risk of CVD.

FDA motivations and agenda is questionable:

Instead of maintaining the integrity of its original agreement, the FDA had coerced the panel to vote no and instead wait 4 years (or more) for the outcomes study on Vascepa to be completed. And in doing so has needlessly put a large segment of Americans at increased risk of CVD despite the drug being safe as placebo and again proven safer than aspirin. It's clear who the losers will be from this decision, but one should consider who the winners would be by keeping a safe, well tolerated drug that improves the health of millions of Americans out of reach. Its obvious healthier Americans need fewer medications and treatments. If Americans received only half the reduction of events seen in the Japanese study, (25% reduction versus 50%), there would be a seismic shift of wealth of epic proportions. Consider for example, the impact that healthier older Americans would have our Health Insurers serving the Affordable Care Act. The Insurers would be far less dependent upon enrolling younger healthy Americans if older Americans required less health care. Clearly the stakes in a population this large are enormous and especially critical, the health of Diabetics Americans, and the success of the Affordable Care Act. And so I implore you to investigate this issue immediately. There remains a limited window of opportunity to take action. The complete history of the Affordable care Act has yet to be written.

There is much more to this story, such as the refusal of the FDA to consider new science:

On September 24th, I personally contacted Stephanie Ramey with an email requesting a new citation on the science of EPA published in September in the Journal of Atherosclerosis and Thrombosis Vol 20, to be submitted for review by the Adcom panel.

It was communicated to me that the new study would be placed into a binder for review by the panel members. On October 10th I received another email from the Stephanie Ramey stating the FDA would not accept the study I submitted, but instead I was free to write a statement and reference the study. As you'd expect, I was more than surprised by the unwillingness of the FDA to allow the panel members access to relevant new science concerning EPA while it considered studies of Drugs composed of completely different chemical formulation to be more relevant to the decision. I found this refusal by the FDA to be truly vexing and suggest to me the need for oversight and investigation. I submitted a statement, and referenced the study but I have no confirmation is read by the panel. A copy of my email and my statement sent to Stephanie Ramey as she instructed is available upon request.

Link to Study I attempted I repeatedly submitted to the FDA:

https://www.jstage.jst.go.jp/article/jat/advpub/0/advpub_18002/_pdf

The most vulnerable are to be adversely affected the most:

The October 16th, 2013 Advisory Committee of the Food and Drug Administration dealt a potentially fatal blow to the life expectancy of minorities in the United States. By a vote of 9-2 the committee rejected broader access of an already approved drug, proven both remarkably safe and effective, that would allow the preventive treatment of Diabetes in its early stages.

The following statistics of Diabetes rates are from the U.S. Department of Health and Human Services who were not represented at the FDA hearing.

• 14.2% of Native Americans
• 12.6% of Black Americans
• 11.8% of American Hispanics and Latinos
• 8.4% of American Asians
• 5.5% of Alaskan Native Americans

I am respectfully requesting that you intercede

Millions of vulnerable Diabetics, many of whom are members of underserved, minority populations, are at increased risk of cardiovascular disease. These Americans are depending upon government leadership to represent their best interests and protect them from the potential harm of special interest groups and lobbyists motivated to preserve the their financial self-interests. To that end I'm respectfully requesting you validate my claims as to the risk/reward benefit of expanding the label of Vascepa to include dyslipidemia for Diabetics. I'm confident you will conclude as I have, and as many physicians and other concerned citizen have, that Vascepa will improve the health of countless Americans and help fight a disease responsible for costing the United States hundreds of billions of dollars each year.

I urge you to contact FDA Commissioner Margaret Hamburg and Curtis Rosebraugh, Director of FDA's Office of Drug Evaluation and request that they review the unusual circumstances and interactions surrounding FDA's undue control of the Advisory Committee and the grave consequences that the negative vote will have.

But most importantly, help us prevent the rejection of the Vascepa expanded label and thus ensure the improved health among millions of our Diabetic citizens.

I would very much appreciate being kept informed of the progress by your office in confirming my assertions not just for myself, but for the millions of Americans who will benefit from improved health and reduced health care costs.

Physicians who spoke publically and on record at the ADCOM hearing

on behalf of Diabetics who need Vascepa

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