UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): January 11, 2021

PLx Pharma Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	001-36351	46-4995704
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

9 Fishers Lane, Suite E, Sparta, New Jersey	07871
(Address of Principal Executive Offices)	(Zip Code)

Registrant's Telephone Number, Including Area Code: (973) 409-6541

(Former Name or Former Address, If Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol(s)	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value	PLXP	The NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

PLx Pharma Inc. ("PLx Pharma") participated in the National Advertising Division ("NAD"), of the Better Business Bureau's voluntary self-regulation process in connection with a review of its plxpharma.com website. On January 6, 2021, NAD issued a press release announcing the results of its review. NAD's review is contained in its Decision, which is attached as Exhibit 99.1 hereto. PLx Pharma's Advertiser's Statement is set forth at page 18 of the Decision.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	National Advertising Division (NAD) of BBB National Programs Decision, dated January 6, 2021, PLx Pharma, Inc., Vazalore, Case #6912.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PLX PHARMA INC.

Dated: January 11, 2021

By: /s/ Natasha Giordano
Name: Natasha Giordano
Title: President and Chief Executive Officer

EXHIBIT INDEX

Exhibit No.	Description
99.1	National Advertising Division (NAD) of BBB National Programs Decision, dated January 6, 2021, PLx Pharma, Inc., Vazalore, Case #6912.

Case #6912 *(12/14/2020)*
PLx Pharma, Inc.
Vazalore
Challenger: *Bayer HealthCare LLC*
Product Type: *Drugs/Health/Health Aids*
Issues: *Superiority Claims; Health & Safety Claims; Comparative Performance Claims*
Disposition: *Modified/Discontinued*

- **Competent and reliable scientific evidence must, in addition to achieving statistical significance, also demonstrate that the results will be meaningful to consumers.**

Basis of Inquiry: Claims made by PLx Pharma, Inc. ("PLx" or the advertiser) in online advertising for its Vazalore product were challenged by Bayer HealthCare LLC ("Bayer" or the challenger), maker of Bayer aspirin products. The following are representative of the claims that served as the basis for NAD's inquiry:

General Superiority Claims

- "The Miracles of Aspirin Fully Realized."
- "[I]t's time for a new scientific advancement that allows aspirin to achieve its full potential to deliver on the cardiovascular benefits so highly sought after."
- "It's about time that there is a new delivery system for this life-saving drug – one that achieves fast, reliable, predictable antiplatelet activity and better gastrointestinal safety."
- "Doing It Right ... Sometimes doing something right requires looking at the problem from a different perspective. It also means we don't have to accept status quo and we're willing to buck common misperceptions. At PLx Pharma we did just that – we took a different approach and engineered a better, more efficient and safer delivery platform for active pharmaceutical ingredients. We saw something good, but had a vision to make it better."

Superior Speed/Absorption/Efficacy Claims:

- "Faster and more predictable antiplatelet response than enteric coated aspirin."
- "Vazalore achieves therapeutic efficacy 4 times faster than EC Aspirin."
- "Vazalore has up to 5X greater absorption than enteric coated aspirin."
- "Vazalore delivers 2X better platelet response than enteric coated aspirin."
- "3-5 times greater antiplatelet benefit than enteric coated aspirin."

Fewer Side Effect Claims:

- "65% lower risk of acute gastric ulcerations than plain aspirin."
- "Vazalore vs. Aspirin: 47% lower risk of erosions or ulcers; 71% lower risk of ulcers."

- "It's a Win-Win for Patients AND Doctors ... If recommended by your doctor, Vazalore may provide: Heart Attack and Stroke Prevention; Predictable Antiplatelet Activity; and Significantly Improved Acute Gastrointestinal Safety.

Evidence Presented:

In support of the challenged claims, the advertiser relied upon:

- A clinical study conducted by Deepak L. Bhatt, MD, MPH et al. (the "Bhatt study") on the comparative pharmacokinetic (PK) and pharmacodynamic (PD) properties of traditional aspirin, enteric coated aspirin, and PL2200 (the premarket name for Vazalore).
- A clinical study conducted by Byron Cryer, MD et al. (the "Cryer study") on the comparative gastrointestinal (GI) damage caused by aspirin and PL2200.
- Expert report of Dr. Dominick Angiolillo.
- Expert report of Dr. James Scheiman.
- Correspondence with FDA and documentation related to the New Drug Application for Vazalore.
- Clinical studies, articles, and FDA guidance related to the safety and efficacy of aspirin

The challenger provided NAD with:

- Two expert declarations from Dr. Rosa Coppolecchia.
- Expert declaration of Michael J. Blaha.
- Two expert declarations from Dr. Andrew Chan.
- Clinical studies, articles, and FDA guidance related to the safety and efficacy of aspirin.

Decision:

I. Background

Both parties to the challenge are makers of aspirin. The first modern products to use the active ingredient in aspirin, acetylsalicylic acid ("ASA"), were developed by Bayer over 120 years ago. In addition to its use as an over-the-counter ("OTC") treatment as a pain reliever, fever reducer, and anti-inflammatory, aspirin may be prescribed by a medical professional to help protect patients at high risk of cardiovascular disease events or stroke.

Heart attacks occur when blood flow in one or several arteries supplying the heart are blocked, leading to the heart muscle being starved of oxygen. If the blood vessels that supply the heart and brain with blood burst, blood clots can form quickly and block the artery, preventing blood flow to the heart and causing a heart attack. A similar problem can occur when clots interrupt blood flow to the brain resulting in an ischemic stroke. Aspirin prevents blood clots by reducing the clumping action of platelets within blood vessels. In doing so, aspirin kicks off a process that eventually results in a reduction of the metabolite, TXB2, which can be measured in blood serum. In short, aspirin suppresses the body's production of TXB2, which helps stop harmful clots from forming and getting bigger, thus helping to keep the blood flowing.[1] The amount of TXB2 in blood serum is a recognized clinical biomarker measured to assess the anti-platelet efficacy of aspirin.

Traditional aspirin comes in two forms, immediate release, or "uncoated," aspirin and enteric coated aspirin, which is also referred to as "EC" aspirin. EC aspirin is a delayed release formulation, that, unlike uncoated aspirin, passes through the stomach without breaking down and begins breaking down in the small intestine. Both coated and uncoated aspirin are well-established as safe and effective drug products.

Aspirin may be prescribed for either primary prevention or secondary prevention. An aspirin regimen for an individual who has not suffered a heart attack or a stroke but is at high risk for such an event, due to family history and other risk factors, is called primary prevention. An aspirin regimen for heart attack or stroke survivors to help prevent another heart attack or ischemic stroke is referred to as secondary prevention. In either case, treatment is not short term, and the individual would likely need to take the prescribed dose in perpetuity. Additionally, it is well-established medical advice that a person suffering from a suspected heart attack can chew an uncoated aspirin tablet during the attack. Recent medical guidance, including that of the American Heart Association, generally recommends against the use of aspirin in the routine primary prevention of cardiovascular disease.[2]

Existing OTC aspirin products are marketed under FDA's Tentative Final Monograph for oral analgesics (the "TFM"). While Vazalore contains the same active pharmaceutical ingredient (aspirin) as OTC products on the market, it is delivered in a novel form and has a different regulatory pathway. Vazalore is a liquid-filled, immediate-release aspirin product that also bypasses the stomach and is absorbed in the intestine. Vazalore is marketed under a New Drug Application, approved by FDA in 2013, allowing it to be marketed for the same indications allowed for aspirin under the TFM. It is also approved for the secondary prevention of heart attacks and strokes.

II. Jurisdiction

As a threshold matter, PLx argued that NAD lacks jurisdiction to hear this case because the challenged statements are not national advertising pursuant to Rule 1.1(A) of the NAD/NARB Procedures, which states that "national advertising" is limited to "any paid commercial message, in any medium (including labeling), if it has the purpose of inducing a sale or other commercial transaction or persuading the audience of the value or usefulness of a company, product or service; if it is disseminated nationally or to a substantial portion of the United States, or is test market advertising prepared for national campaigns; and if the content is controlled by the advertiser." According to the advertiser, while Vazalore has FDA approval, it has never been sold commercially, and has never been advertised to consumers. It contended that the website that formed the basis for Bayer's challenge was a small corporate website, directed at attracting investors, not product sales.

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[1] Aspirin inactivates cyclooxygenase (COX), the enzyme responsible for generation of a potent platelet activator, thromboxane (TX) A2. Consequently, aspirin inhibits formation the stable metabolite of TXA2 (TXB2) in serum.

[2] See 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019;March 17.

Even though Vazalore is not yet available for sale, the advertising has the purpose of "persuading the audience of the value or usefulness of a company, product or service." Accordingly, NAD has jurisdiction under the NAD/NARB Procedures.

Although the advertiser argued that the website is only intended for investors, there is nothing preventing potential consumers from finding the website. Further, the main company page, on which a number of the challenged claims appear, contains statements clearly directed at consumers, such as, "If recommended by your doctor, Vazalore may provide" and "*Consult your healthcare provider before using this product for your heart." Moreover, the fact that the product is not currently available for sale does not preclude NAD's review, as it is undisputed that the product will be at some point offered for sale. The clear purpose of the website is to generate interest in the product with both consumers and health care professionals until that time.

III. NAD's Standard of Review

Advertisers bear the burden of providing a reasonable basis for all the messages reasonably conveyed by their claims.[3] NAD reviews the advertiser's evidence to determine whether it is sufficiently reliable to provide a reasonable basis for the challenge claims. The evidence must also be a good fit for the messages conveyed by the challenged claims.

A. Messages Reasonably Conveyed

It is well-established that advertisers are obligated to support all reasonable interpretations of their claims, not just the messages they intended to convey.[4] In the absence of reliable consumer perception evidence, NAD routinely steps into the shoes of the consumer to determine what implied messages, if any, are conveyed by the advertisement.[5] In analyzing the messages conveyed by a particular advertisement, NAD typically reviews the net impression created by an advertisement as a whole, not merely words or phrases standing alone, and taking into consideration both the words and the visual images.[6]

B. Competent and Reliable Scientific Evidence

All the challenged claims concerning Vazalore are health-related claims, which must be supported by competent and reliable scientific evidence. Competent and reliable scientific evidence, as defined by the Federal Trade Commission (FTC), includes, "tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures

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[3] Mars Petcare US (Pedigree® Dentastix® Chews), Report #5707, *NAD/CARU Case Reports* (April 2014).

[4] Edgewell Personal Care, LLC (Schick® Hydro Razor), Report #5287, *NAD/CARU Case Reports* (February 2011).

[5] The Procter & Gamble Company (Charmin Ultra Strong and Charmin Ultra Soft Products), Report #5960, *NAD/CARU Case Reports* (May 2016).

[6] See Comcast Cable Communications, LLC (XFINITY Television Service), Report #6170, *NAD/CARU Case Reports* (March 2018); Dole Packaged Foods, LLC (Dole Fruit Bowls), Report #5868, *NAD/CARU Case Reports* (July 2015).

generally accepted in the profession to yield accurate and reliable results."[7] While the competent and reliable scientific evidence standard for health-related claims is flexible, when the claims involve the efficacy of a product in the human body, human clinical trials that are methodologically sound and statistically significant to the 95% confidence level are generally required.[8] The features of a sound methodological study are well-known and generally agreed upon by the scientific community.[9] The study's objectives should be clearly described, and the methodology must be appropriate for obtaining the objectives posed by the study.[10] The study's duration should be sufficient to detect an effect on the outcome and the sample size should be large enough to provide sufficient statistical power, with the study population representative of the target population to which the claim is targeted.[11] In evaluating whether evidence constitutes competent and reliable scientific evidence to provide a reasonable basis for a claim, it is relevant to consider the type of claim, the product, the consequences of a false claim, the benefits of a truthful claim, the cost of developing substantiation for the claim, and the amount of substantiation experts in the field believe is reasonable.[12]

NAD has always held that competent and reliable scientific evidence must, in addition to achieving statistical significance, also demonstrate that the results will be meaningful to consumers. Statistically significant differences should also have clinical importance or be large enough to impact therapeutic considerations.[13]

C. Fit of the Evidence to the Claim

Finally, a study must not only be competent and reliable, but also a good fit for the claim at issue. That means that any clinically meaningful results should be related to the specific benefit being claimed and the population being targeted by the claim. For example, if studies are conducted on individuals with certain traits that may cause them to experience the effects of a product differently than the average person targeted by the advertising claim, they may be a poor fit as support for the claim even if they are otherwise competent and reliable.[14]

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[7] FDA, Guidance to Industry: Substantiation for Dietary Supplement Claims Made Under Section 403(r) (6) of the Federal Food, Drug, and Cosmetic Act, available at https://www.fda.gov/regulatory-information/search-fda-guidance- documents/guidance-industry-substantiation-dietary-supplement-claims-made-under-section-403r-6-federal-food).

[8] Avadim Health, Inc. (Theraworx Relief products), Report #6418, *NAD/CARU Case Reports* (October 2020); S.C. Johnson & Son, Inc. (Windex Vinegar Glass Cleaner), Report #6353, *NAD/CARU Case Report* (March 2020).

[9] Good Health Naturally, LLC (Serranol Supplements), Report #5441, *NAD/CARU Case Reports* (March 2012) (citing FDA, Guidance to Industry: Substantiation for Dietary Supplement Claims, supra.

[10] Good Health Naturally, LLC, Report #5441, supra.

[11] Id.

[12] Avadim Health, Inc. (Theraworx Relief products), Report #6418, supra; S.C. Johnson & Son, Inc. (Windex Vinegar Glass Cleaner), Report #6353, supra.

[13] See e.g., Novartis (Extra Strength Excedrin), Report #4973, *NAD/CARU Case Reports* (February 2009)(internal citations omitted).

[14] See e.g., Neogenis, LLC (Neo40 Daily Dietary Supplements), Report #5770, *NAD/CARU Case Reports* (October 2014)(determining study results conducted on people with hypertension could not be extrapolated to the general, healthy population who was the target audience for the advertising).

IV. The Challenged Advertising

Turning to the challenged claims in this matter, the main product page of the adviser's website features various health-related images, including a graphic of a heart with an echocardiogram wave imposed over it, a picture of a doctor in a white lab coat and stethoscope speaking with a patient, and another picture of gloved hands holding a petri dish, which suggests a research facility. The page also contains numerous statements regarding the safety and efficacy of Vazalore:

- "The Miracles of Aspirin Fully Realized" next to a close-up shot of a white and blue pill
- "[I]t's time for a new scientific advancement that allows aspirin to achieve its full potential to deliver on the cardiovascular benefits so highly sought after."
- "It's about time that there is a new delivery system for this life-saving drug – one that achieves fast, reliable, predictable antiplatelet activity and better gastrointestinal safety."
- "Doing It Right ... Sometimes doing something right requires looking at the problem from a different perspective. It also means we don't have to accept status quo and we're willing to buck common misperceptions. At PLx Pharma we did just that – we took a different approach and engineered a better, more efficient and safer delivery platform for active pharmaceutical ingredients. We saw something good, but had a vision to make it better."
- "It's a Win-Win for Patients AND Doctors ... If recommended by your doctor, Vazalore may provide: Heart Attack and Stroke Prevention; Predictable Antiplatelet Activity; and Significantly Improved Acute Gastrointestinal Safety"

Also on this main landing page, the challenged claims, "Faster and more predictable antiplatelet response than enteric coated aspirin." and "65% lower risk of acute gastric ulcerations than plain aspirin." appear under the heading, "Miracles of Aspirin Fully Realized" in a bulleted list containing other performance claims about the product and above a link labeled, "Learn more about the science." A consumer who follows the link is taken to a page containing the challenged claims, "Vazalore achieves therapeutic efficacy 4 times faster than EC Aspirin."; "Vazalore has up to 5X greater absorption than enteric coated aspirin."; and "Vazalore delivers 2X better platelet response than enteric coated aspirin." Each of the latter claims appears below bar or line charts depicting comparisons between PL2200 (the premarket name for Vazalore), plain aspirin, and EC aspirin.

V. Superior Speed/Absorption/Efficacy Claims

The challenger contended that the claims, "Faster and more predictable antiplatelet response than enteric coated aspirin."; "Vazalore achieves therapeutic efficacy 4 times faster than EC Aspirin."; "Vazalore has up to 5X greater absorption than enteric coated aspirin."; and "Vazalore delivers 2X better platelet response than enteric coated aspirin." reasonably convey to consumers that Vazalore is more efficacious than traditional aspirin in the prevention of secondary cardiovascular events. The advertiser argued that the claims simply highlight clinically important differences between the products, but do not convey any messages regarding clinical outcomes.

NAD determined that the claims, in the context in which they appeared, reasonably conveyed messages regarding the comparative performance of each product for the specific properties expressly mentioned in the claims and also that these properties make Vazalore more efficacious as a cardioprotective therapy. In reaching these conclusions, NAD took into consideration the overall context in which the claims are presented, including the other claims made in close proximity – "Unlocking Aspirin's Full Potential" and "it's time for a new scientific advancement that allows aspirin to achieve its full potential to deliver on the cardiovascular benefits so highly sought after" – which serve to distinguish the product from other aspirin products due to promised superior cardioprotective properties.

Further, NAD has noted in many previous cases that quantified performance claims – such as "4 times faster" or "5X greater" – are powerful, and carry great weight with consumers:

> Quantified performance claims have a strong impact on consumers and should closely reflect the test results upon which they are based. It is critical that these types of claims are adequately supported because they convey information that consumers are unable to evaluate for themselves. This is even more important when the quantified performance claims at issue promise consumers they can achieve a specific health-related result by using the advertised product.[15]

Therefore, the strength of the advertiser's evidence must match the strength of its claims.

In support of its claims, the advertiser submitted one human clinical study, the Bhatt study. The Bhatt study was a single-center, randomized, single-blinded, triple-crossover trial that compared the serum antiplatelet activity (blood clotting prevention) after treatment with plain, uncoated aspirin, Vazalore,[16] and a delayed release enteric coated aspirin, at a dose of 325 mg, once a day for 3 days. The study population consisted of 40 participants, aged 21 to 79 years, all of whom were obese (BMI > 30), had been diagnosed with diabetes and no history of heart disease. Each dose of the study drug was administered with 8 ounces of water by a blinded clinic staff member, after an overnight 10 hour fast, and the subjects were fed a standardized meal 2 hours after administration of each dose. After the treatment phase, laboratory assessments continued on days 4 and 7. After a 2-week washout period, the process was repeated for each patient with the next drug. The total treatment time was 3 days.

The primary study endpoint, onset of antiplatelet response, was assessed by time to 99% inhibition of TXB2 generation. According to that metric, Vazalore achieved 99% inhibition at a faster rate than enteric coated aspirin (12.5 hours versus 48.2 hours, $p < 0.0001$). The study also compared the number of patients that reached 99% TXB2 inhibition by 72 hours after the first dose of study drug. 92% of patients had a complete antiplatelet response at the 72-hour time point after taking Vazalore, compared to 47% after taking EC aspirin. Additionally, the study assessed the plasma concentrations of aspirin[17] and the time to maximum plasma concentration after the initial dose of each drug, finding that Vazalore had greater absorption than EC aspirin (2,523 ng x h/ml versus 456 ng x h/ml) and reached its maximum concentration faster than EC aspirin.

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[15] Philips Oral Healthcare LLC. (Sonicare Rechargeable Toothbrushes), Report #6206, *NAD/CARU Case Reports* (August 2018).

[16] The Bhatt study refers to Vazalore as PL2200, its pre-market designation.

[17] Specifically, the concentration of acetylsalicylic acid.

A. "Vazalore achieves therapeutic efficacy 4 times faster than EC Aspirin"; "Faster … antiplatelet response than enteric coated aspirin."

The advertiser's claim that "Vazalore achieves therapeutic efficacy 4 times faster than EC Aspirin" is a powerful, quantitative performance claim that expressly promises faster therapeutic results – that is, results that are meaningful and important to consumers' health. Although not as strong a claim, "faster … antiplatelet response than enteric coated aspirin," also expressly conveys that Vazalore works faster, and, in the context in which it appears (for example, next to claims such as "The Miracles of Aspirin Fully Realized") is the superior cardioprotective choice.

After careful review, NAD determined that the advertiser's evidence was not a good fit for the challenged speed claims. First, the Bhatt study population was comprised of people who were obese, had been diagnosed with diabetes, and had no history of heart disease. However, the advertiser's broad, unqualified claims are targeted at aspirin users generally, a significant portion of which are people who have already experienced a heart attack. When used as advertising claim support, study populations should be representative of the population to whom the claim is targeted, including the health status of the study participants. If the population is not representative, NAD has "no way of knowing whether there may be characteristics of this limited population that might bear upon the reliability of extrapolating test results to the general population" to whom the advertising is directed.[18] While NAD understands that aspirin trials may not be conducted, for ethical reasons, with people with heart disease, it is incumbent on the advertiser to provide evidence sufficient to demonstrate that the results of this study may be reliably extrapolated to Vazalore's target audience.

Here, the advertiser, supported by the expert report of Dr. Angiolillo, asserted that diabetes is a predictor of the risk for future cardiovascular events, such as heart attacks, and that diabetics who have not experienced a prior heart attack have as high of a risk of having a heart attack as do nondiabetic patients who have experienced one. In support of this proposition, Dr. Angiolillo cited guidelines in a report by the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Dr. Angiolillo also cited a clinical study that compared the seven- year incidence of myocardial infarction (fatal and nonfatal) among 1,373 nondiabetic subjects with the incidence among 1,059 diabetic subjects and concluded that diabetic patients without previous myocardial infarction have as high a risk of myocardial infarction as nondiabetic patients with previous myocardial infarction. While it may be true that diabetic patients are at risk for heart disease, this evidence does not support the conclusion that aspirin's pharmacodynamic effect on platelet inhibition speed in diabetics is representative of the results experienced by Vazalore's target audience, i.e. all people suffering from heart disease, both those with diabetes and those with heart disease that is not associated with diabetes.

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[18] Den-Mat Corporation (Rembrandt Whitening Toothpaste), Report #3046, NARB Panel #75 & #76, *NAD/CARU Case Reports* (October 1993); see also Neogenis, LLC (Neo40 Daily Dietary Supplements), Report #5770, NARB Panel #199, *NAD/CARU Case Reports* (October 2014)(determining that a study of one patient with a circulatory disease could not support claims aimed at a general population); FDA, Guidance to Industry: Substantiation for Dietary Supplement Claims.

Second, NAD was concerned that the advertiser had not established that the reported difference between the products in reaching >99% TXB2 inhibition, 12.5 hours versus 48.2 hours,[19] would have a material effect on the performance of the two products that is meaningful to consumers. These products are used for secondary prevention and taken daily, on a long-term basis, to prevent cardiovascular events or stroke. As a result, demonstrating a different length of time to reach a threshold inhibition does not demonstrate a difference in efficacy over the period of time in which consumers use aspirin as a preventative therapy.

Third, NAD was concerned with the advertiser's selection of >99% TBX2 inhibition as its "therapeutic efficacy." Therapeutic efficacy is not a clinical term with a precise, agreed upon definition, but NAD determined that it expressly conveys a powerful message regarding the efficacy of the products as cardioprotective agents. The challenger argued that both the Bhatt study and PLx's claim incorrectly use 99% TBX2 inhibition as a proxy for "complete inhibition" and "therapeutic efficacy." The challenger asserted that FDA's accepted standard for measuring successful platelet inhibition is a >95% reduction of TXB2 and argued that there is no study or recognized learning in the field that would suggest any meaningful difference between 95% inhibition and 99% inhibition. In contrast, the advertiser argued that FDA defines complete inhibition as >99% inhibition, as evidenced in comments made by FDA representatives during a meeting to discuss PLx's NDA application.

Based on the evidence in the record, there was no scientific consensus that 99% TBX2 inhibition equates to "therapeutic efficacy." While the challenger's expert asserts that the correct level, as set by FDA, is >95% reduction of TXB2, there is no evidence offered in support of that conclusion. Expert opinions are most reliable – and therefore most effective at NAD – when the expert's opinion is coupled with competent and reliable evidence demonstrating scientific consensus on an issue. Generally, scientific consensus on an issue is more valuable than the opinion of one individual scientist. On the advertiser's side, comments made by FDA to PLx, specifically about demonstrating the bioequivalence – not superiority – of its product for the purpose of supporting an NDA are not dispositive of the agency's position on this issue.[20] The additional clinical studies provided by the advertiser, such as Cox et al. and Reilly et al., were equally indeterminate, generally supporting the conclusion that achieving greater than 95% inhibition was important but failing to establish any clear delineations beyond that. The lack of consensus on the issue is highlighted in a review cited by the advertiser and authored by Bayer:

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[19] NAD also noted that the time reported for EC aspirin to achieve >99% TXB2 inhibition was not mathematically four times greater than Vazalore's reported time as expressly stated in the claim.

[20] Importantly, while FDA's comments address TXB2 inhibition, they do not specifically address or define "therapeutic efficacy."

> Although ≥95% inhibition of TxB2 is considered necessary for cardioprotection by some investigators, there is currently no standard that defines the optimal percent inhibition of serum TxB2 for prevention of secondary cardiovascular events. Moreover, there is variability in the literature on the appropriate threshold for serum TxB2 inhibition that is associated with adequate platelet inhibition. Some published studies recognized ≥90% TxB2 inhibition as the test threshold for adequate platelet inhibition and to assess an optimal antiplatelet effect of aspirin. … However, other investigators have suggested that 95% inhibition of baseline TxB2 is necessary for adequate cardioprotection, and 95% TxB2 inhibition ex vivo correlates with the inhibition of in vivo TxA2 generation (Reilly, 2017). The variability in these suggested thresholds would seem to imply that a slight decline in TxB2 inhibition is unlikely to have clinical significance. The FDA has previously acknowledged ≥90% TxB2 inhibition as the criterion used by several investigators to assess the clinical significance of drug interaction with aspirin but subsequently requested a 95% threshold in the Kontakt study.[21]

NAD does not dispute that the Bhatt study lends important scientific value to understanding differences in TBX2 inhibition in different aspirin products; however, it is not a good fit for a claim that reasonably conveys a message that Vazalore provides a meaningful, superior long-term cardioprotective benefit in a faster time than EC aspirin. The advertiser did not provide evidence sufficient for NAD to determine that the results from an obese, diabetic population without heart disease could be reliably extrapolated to people seeking to prevent a secondary cardiovascular event. NAD was further concerned that comparing the time to TXB2 inhibition based on three days of data was not a consumer relevant endpoint for a product used long-term (possibly life- long) as a preventative therapy. NAD further determined that the advertiser had not sufficiently demonstrated that the >99% TBX2 inhibition – as opposed to 90% or 95% inhibition – was a consumer relevant threshold sufficient to support a claim of a superior, meaningful benefit to consumers. For all the forgoing reasons, NAD recommended that the advertiser discontinue the claim, "Vazalore achieves therapeutic efficacy 4 times faster than EC Aspirin."

NAD came to a similar conclusion with regard to the advertiser's claim, "faster … antiplatelet response than enteric coated aspirin," because there was insufficient evidence in the record that "faster" – time to 99% TBX2 inhibition – was consumer relevant. NAD also took into consideration that the claim referred to a serious health condition, heart disease; that the nature of the claim is such that consumers (whether they be prescribing doctors or patients) cannot ascertain for themselves whether the claim is accurate; and that the consequences of a potentially false claim is that consumers would invest, long term, in an aspirin product without a superior long-term benefit compared to EC aspirin.[22] For all these reasons, NAD recommended that the advertiser also discontinue the claim "faster … antiplatelet response than enteric coated aspirin." Nothing in this decision prevents the advertiser from making claims about the onset of antiplatelet response for subjects taking Vazalore that is narrowly tailored to fit the evidence provided.

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[21] Bayer HealthCare LLC, Review of Naproxen/Aspirin Pharmacodynamic Interaction Data Including the Results of the Kontakt Study, Joint Meeting of the Arthritis Advisory Committee (AAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM), Submitted on March 23, 2018.

[22] DSE Healthcare, LLC (Prelief Dietary Supplements), Report #5991, *NAD/CARU Case Reports* (August 2016)(enumerating the "Pfizer factors" used to determine the amount of substantiation necessary to constitute a reasonable basis for a particular claim, which include: 1. the product involved; 2. the type of claim being made; 3. the ease of developing substantiation for the claim; 4. the consequences of a false claim; and 5. the amount of substantiation experts in the field would agree is reasonable).

B. "Vazalore delivers 2X better platelet response than enteric coated aspirin."

By stating that Vazalore delivers "better" platelet response than enteric coated aspirin, the advertiser's claim suggests that there is meaningful and persistent difference between the performance of the two products. The advertiser argued that the Bhatt study supports such a conclusion, demonstrating that within 72 hours, 92% of patients had a complete antiplatelet response (>99% TBX2 inhibition) with Vazalore, compared to only 47% for enteric coated aspirin.

In addition its concerns regarding the use of a >99% TBX2 inhibition standard noted above, NAD was concerned that the advertiser had not established that the specific difference in platelet inhibition between the products recorded at three days were clinically relevant for consumers undergoing long term treatments. Evidence in the record suggests that initial differences between platelet inhibition exhibited by EC aspirin and immediate release aspirin may not persist over longer periods of time.[23] Consequently, NAD recommended that the advertiser discontinue the claim, "Vazalore delivers 2X better platelet response than enteric coated aspirin."

C. "Vazalore has up to 5X greater absorption than enteric coated aspirin."

According to the results of the Bhatt study, Vazalore had greater absorption than EC aspirin (2,523 ng x h/ml versus 456 ng x h/ml). In contrast to the other challenged claims involving the results of the Bhatt study, NAD determined that the higher absorption rate of Vazalore represents a material difference between Vazalore and enteric aspirin not necessarily tied to superior cardiovascular outcomes. The erratic absorption of enteric coated aspirin has been well-established and is acknowledged by FDA in the regulations establishing the professional labeling requirements for aspirin products.[24] However, NAD was concerned that the context in which the claim was presented, in conjunction with the line chart from the Bhatt study and under the heading "Implications for Aspirin Efficacy" serves to convey an overbroad and unsupported message to consumers that the product's greater absorption has been demonstrated to provide superior clinical efficacy. NAD was also concerned that the results from such a limited study population, obese diabetic patients without any history of heart disease, may not be representative of the population of consumers requiring aspirin therapy for secondary prevention. Therefore, NAD recommended that the advertiser modify the claim, "Vazalore has up to 5X greater absorption than enteric coated aspirin." to avoid conveying the message that the claimed difference in absorption related to superior clinical efficacy and disclose that the reported results were from a limited study population, diabetic, obese subjects.

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[23] Haastrup PF. Enteric Coating Can Lead to Reduced Antiplatelet Effect of Low-Dose Acetylsalicylic Acid. Basic & Clinical Pharmacology & Toxicology, 2015, 116, 212–215.

[24] See 21 CFR 343.80. See also Levy G., Hollister LE. Failure of USP disintegration test to assess physiologic availability of enteric-coated tablets, N Y State J Med. 1964 Dec 15; 64:3002-5.

D. "… more predictable antiplatelet response than enteric coated aspirin."

The advertiser argued that a critical prerequisite for a predictable drug effect is predictable bioavailability, and that the various PK/PD results of the Bhatt study demonstrate that Vazalore has more predictable bioavailability and, therefore, more predictable antiplatelet response than enteric coated aspirin. However, NAD found the short duration of the Bhatt study rendered it insufficient support for a broad claim regarding the predictability of the two products, a point acknowledged explicitly by the authors, "Limitations of this study include the 3-day duration. It is possible that with more chronic dosing of EC aspirin there would have been less variability in antiplatelet effect." While the advertiser explained that enteric coated aspirin is erratically absorbed, its proffered evidence falls short of establishing that Vazalore's consistent absorption rate in the first three days of treatment translates into more predictable antiplatelet response in the long term.

Consequently, NAD recommended the advertiser discontinue the claim, "… more predictable antiplatelet response than enteric coated aspirin." Nothing in this decision prevents the advertiser from making a claim related to the predictability of Vazalore's antiplatelet response that is narrowly tailored to fit the evidence provided.

VI. Gastric Safety Claims

- "65% lower risk of acute gastric ulcerations than plain aspirin.";
- "Vazalore vs. Aspirin: 47% lower risk of erosions or ulcers; 71% lower risk of ulcers."

While a medical professional may understand the difference between the various types and severities of gastric injuries, such as acute gastric ulceration, erosions, ulcers, and bleeding ulcers, it was unlikely that the average consumer would. Additionally, the chart that appears above the claim, "Vazalore vs. Aspirin: 47% lower risk of erosions or ulcers; 71% lower risk of ulcers." is titled, "Implications of Gastric Ulcer Risk." The chart does not specify the nature of the injuries represented in the chart beyond "erosions and ulcers," adding to the likelihood that consumers can reasonably takeaway the message Vazalore reduces the risk of all types of ulcers generally. As such, NAD determined that one message reasonably conveyed by the gastric safety claims is that Vazalore materially reduces the risk of all types of ulcers, including bleeding ulcers.

According to the advertiser, each of its claims regarding the reduction of GI side effects provided by Vazalore is supported by the Cryer study.

The Cryer Study was a randomized, single blind, multicenter, active controlled study involving 204 participants who were randomized to receive either immediate release aspirin or Vazalore. Participants were healthy volunteers, ages 50-75 years. Subjects were randomized to either immediate release aspirin or Vazalore and who underwent a baseline endoscopy to establish their initial Mucosal Injury Score. The scores reflected the number of petechiae, erosions, and ulcers in the gastric and duodenal mucosae intestinal membranes, which were each evaluated separately. Starting 1-7 days following baseline endoscopy, subjects meeting inclusion criteria took one 325 mg immediate release aspirin tablet or one PL2200 capsule containing 325 mg aspirin once daily for 7 days at least 30 mins before a meal. On Study Day 7, a second endoscopy was performed, 4- 6 hours after final drug dose. The study's primary endpoint was the incidence of participants with gastroduodenal erosions or ulcers (>5 erosions, or 1 or more ulcers ≥3mm) with Vazalore compared to aspirin. Secondary objectives were the incidence of participants with ulcers ≥3 mm, mean number of duodenal erosions, gastric erosions, or erosions in the gastric antrum, body, and fundus.

The study results showed that people that who took Vazalore had a 47.4% lower risk of developing multiple gastroduodenal erosions or an ulcer than those treated with immediate release aspirin for 7 days. Forty-three (42.2%) aspirin treated participants developed six or greater erosions or an ulcer, while twenty-two (22.2%) people treated with Vazalore developed such damage. Additionally, the Vazalore group had a lower mean number of gastric erosions. Further, the Vazalore group had a 71% lower incidence of ulcers than seen with aspirin at the day 7 endoscopy: ulcers developed in 5 people in the Vazalore group and in 18 participants in the aspirin group. All ulcers detected by endoscopy were asymptomatic and predominantly in the stomach.

Although the study reported differences in gastric erosions, it did not demonstrate that the gastric erosions or ulcers were associated with symptoms or that the mucosal damage observed would result in symptomatic injury to subjects as treatment continued. The advertiser argued that the results of the Cryer study are clinically important because of the generalized need to reduce aspirin- induced GI mucosal damage. According to the advertiser's expert, bleeding ulcers start out as gastric erosions and nonbleeding ulcers, and while some the injuries may resolve, some will bleed. The evidence in the record does not establish whether the gastric erosions recorded at 7 days will resolve or result in more serious injury. The advertiser asserted that a reduction in endoscopic lesions in early states of the injury process can act as a surrogate for the reduction of the risk of more significant bleeding. Although the evidence provided by the advertiser and its expert supports an association between the gastric erosions and more severe injuries, it does not demonstrate that the specific reduction in GI mucosal damage exhibited by participants in the Cryer study has a material impact on their risk of more serious bleeding. Thus, the rates of long-term injury or more significant injuries may be similar between the products.

As discussed more fully above, in the consumer-directed advertising challenged here, one message reasonably conveyed by the gastric safety claims is that Vazalore materially reduces the risk of all types of ulcers, including bleeding ulcers. NAD concluded that the Cryer study was not a good fit for the broad message conveyed. Therefore, NAD recommended the advertiser discontinue the claims, "65% lower risk of acute gastric ulcerations than plain aspirin."; and "Vazalore vs. Aspirin: 47% lower risk of erosions or ulcers; 71% lower risk of ulcers." Nothing in this decision precludes the advertiser from making a narrower claim based on the results of the Cryer study that conveys the limited message that Vazalore causes fewer erosions and ulcers in the first week of treatment than traditional immediate release aspirin.

VII. General Superiority Claims

Bayer argued that numerous statements made on the main Vazalore product page convey misleading messages regarding the superior efficacy and safety of the product in comparison to traditional aspirin, including:

- "The Miracles of Aspirin Fully Realized"
- "[I]t's time for a new scientific advancement that allows aspirin to achieve its full potential to deliver on the cardiovascular benefits so highly sought after."
- "It's about time that there is a new delivery system for this life-saving drug – one that achieves fast, reliable, predictable antiplatelet activity and better gastrointestinal safety."

- "Doing It Right ... Sometimes doing something right requires looking at the problem from a different perspective. It also means we don't have to accept status quo and we're willing to buck common misperceptions. At PLx Pharma we did just that – we took a different approach and engineered a better, more efficient and safer delivery platform for active pharmaceutical ingredients. We saw something good, but had a vision to make it better."
- "It's a Win-Win for Patients AND Doctors ... If recommended by your doctor, Vazalore may provide: Heart Attack and Stroke Prevention; Predictable Antiplatelet Activity; and Significantly Improved Acute Gastrointestinal Safety."

The challenger argued that the core message conveyed by these claims is that Vazalore has dramatically superior efficacy and safety in comparison to aspirin. The challenger contended that through phrases such as, "The miracles of aspirin fully realized" and "Win-Win for patients AND Doctors," along with the advertising's overall emphasis of Vazalore's supposed superiority over other aspirin products, particularly regarding gastrointestinal safety, PLx promotes Vazalore's use for primary prevention by implying a significant change to the risk/benefit calculation.

Bayer also alleged statements like, "Doing it Right," "we're willing to buck common misperceptions" and "it's about time" falsely denigrate Bayer aspirin products by implying that Bayer aspirin has dragged its feet, is "doing it wrong" and is somehow harboring "misperceptions" about the science related to prevention of cardiovascular events. The challenger argued that, in the context in which it appeared, the "doing it right" claim reasonably conveyed the message that Bayer aspirin is an outdated and ineffective product for achieving cardiovascular health.

NAD agreed that several of the claims reasonably conveyed the message that Vazalore is objectively superior, including, "The Miracles of Aspirin Fully Realized"; "a new scientific advancement that allows aspirin to achieve its full potential"; "a better, more efficient and safer delivery platform for active pharmaceutical ingredients." Each of these claims is accompanied by additional text touting objective, measurable product attributes, such as "fast, reliable and predictable antiplatelet activity and better gastrointestinal safety."

In contrast, NAD did not find a message of false denigration implied by the statements, "Doing It Right … Sometimes doing something right requires looking at the problem from a different perspective. It also means we don't have to accept status quo and we're willing to buck common misperceptions ... We saw something good, but had a vision to make it better." Additionally, NAD did not find that the phrases, "The miracles of aspirin fully realized" and "It's a Win-Win for Patients AND Doctors." state or imply that Vazalore can safely be prescribed more often for primary prevention.

A. "The Miracles of Aspirin Fully Realized."

The advertiser argued that in the claim, "The Miracles of Aspirin Fully Realized," the word "miracles" was puffery and a non-specific term commonly used to describe aspirin. Additionally, the advertiser argued that "fully realized" is supported by the results of the Bhatt study, showing the superior speed, absorption, and anti-platelet activity of Vazalore.

NAD determined that while referring to aspirin's general therapeutic properties as "miracles" was indeed fanciful, it was an obvious reference to aspirin's cardioprotective abilities. When coupled the term with "fully realized," the advertising conveys a message that Vazalore provides a therapeutic benefit beyond that of its predecessors or competitors. Because the advertiser did not provide evidence supporting the conclusion that its product provides superior cardiovascular benefits or gastrointestinal safety, NAD recommended that the advertiser discontinue the claim, "The Miracles of Aspirin Fully Realized."

B. Other General Superiority Claims

NAD reviewed the remaining general superiority claims in turn.

The advertiser explained that while all aspirin products use the same active pharmaceutical ingredient, once launched, Vazalore will be the only liquid filled aspirin capsule product on the market and makes use of a novel delivery system, which the challenger did not dispute. Therefore, NAD was satisfied that the advertiser had provided a reasonable basis for the claims, "new delivery system for this lifesaving drug" and "we took a different approach."

As for the claims, "achieves fast, reliable, predictable anti-platelet activity and better gastrointestinal safety" and "a better, more efficient and safer delivery platform," the advertiser argued that the results of the Bhatt and Cryer studies, as well as a bioequivalence study conducted by Angiolilio et al.,[25] support these general statements of superiority.

NAD determined that the advertiser had provided a reasonable basis for the monadic claim, "fast, reliable, predictable antiplatelet activity." This claim is supported by data on Vazalore collected during the Bhatt study. The PK and PD data collected in the bioequivalence study also supports claims that the product provides "fast, reliable, and predictable anti-platelet activity." However, with both studies, NAD had concerns regarding the representativeness of their respective test populations – diabetic, obese subjects in the Bhatt study and healthy subjects in the bioequivalence study. Without evidence tying the results in these populations to the target population, NAD recommended that the advertiser modify the claim to disclose that it is based on testing of diabetic, obese subjects and healthy subjects.

NAD determined that the comparative claims, "better gastrointestinal safety" and "a better, more efficient and safer delivery platform for active pharmaceutical ingredients. We saw something good, but had a vision to make it better." were unsupported. This claim, in the context of advertising for Vazalore reasonably conveys the message that Vazalore is "better, more efficient and safer," and was not a message limited to the delivery platform.[26] As discussed above, NAD was concerned that the Cryer study's duration was too short to support an unqualified claim regarding Vazalore's comparative gastrointestinal safety to traditional aspirin, particularly for more significant issues, such as bleeding ulcers.

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[25] Angiolillo DJ et al., Pharmacokinetic/pharmacodynamic assessment of a novel, pharmaceutical lipid-aspirin complex: results of a randomized, crossover, bioequivalence. J Thromb Thrombolysis. 2019 Nov;48(4):554-562. doi: 10.1007/s11239-019-01933-7. PMID: 31420787; PMCID: PMC6800884.

[26] NAD's analysis of the claim, "a better, more efficient and safer delivery platform for active pharmaceutical ingredients." is limited to the applicability of the claim as a delivery platform for Vazalore. To the extent the advertiser may intend to make claims concerning its PLxGuard Delivery System alone or in conjunction with other pharmaceutical products, those claims (which would require support) were not reviewed by NAD here.

Similarly, NAD determined that claims that Vazalore's patented PLxGuard Delivery System allows for an experience with aspirin that is safer, more efficient, and objectively "better" than traditional aspirin were not supported by the Bhatt study. In reaching this conclusion, NAD considered but was not persuaded by the advertiser's argument that the overall superiority of Vazalore and its delivery system is established by the PK/PD markers tracked in the Bhatt study. The advertiser argued that the therapeutic benefit of drugs of this type are the result of a specific biological effect that leads to a risk modification and improved clinical outcomes. It likened the relationship between the PK/PD markers tracked in the Bhatt study with other established surrogates that help clinicians assess the effectiveness of therapeutics, such as blood pressure measurements in the treatment of hypertension, cholesterol measurements for hyperlipidemia, and glycosylated hemoglobin levels in the treatment of diabetes.

However, the issue before NAD is not whether there is a correlation between thromboxane production and aspirin's ability to suppress this production on a macro level. Rather, the pertinent question is whether the difference in inhibition between the products as measured at three days is meaningful. Although the advertiser and its expert repeatedly assert that PD measurements of antiplatelet effects are a meaningful surrogate for clinical outcomes, nothing in the record establishes that degree of difference expressed in the advertiser's claims – 5x greater absorption, 2x greater platelet response, or the achievement of >99% TXB2 inhibition 4 times faster than aspirin – have been shown to have an effect on the ability of the product to reduce the risk of future cardiovascular events. Extrapolating evidence that aspirin therapy influences cardiovascular outcomes to conclude that Vazalore will provide superior outcomes based on PK/PD markers is not sufficient to support a claim that Vazalore is safer, more efficient or objectively "better" than traditional aspirin. Although the results are promising, superior efficacy in improving cardiovascular outcomes has not been established by clinical study, nor has the advertiser offered any additional evidence sufficient to support a reasonable basis for treating the PD measurements as a proxy for health outcomes.[27]

For these reasons, NAD recommended that the advertiser modify the claim, "fast, reliable, predictable antiplatelet activity" to disclose that it is based on testing of diabetic, obese subjects and healthy subjects. NAD further recommended the advertiser discontinue the claims, "better gastrointestinal safety" or modify it to convey the limited message that Vazalore causes fewer erosions and ulcers in the first week of treatment than traditional immediate release aspirin. Finally, NAD recommended that the advertiser discontinue the claim, "a better, more efficient and safer delivery platform for active pharmaceutical ingredients. We saw something good, but had a vision to make it better." as well as claims that Vazalore's delivery system allows for an experience with aspirin that is safer, more efficient, and objectively "better" than traditional aspirin.

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[27] Prevention Pharmaceuticals, Inc. (Omax3 Ultra Pure Dietary Supplement), Report #5966, *NAD/CARU Case Reports* (July 2016)(noting that not every aspect of an advertising claim must be contained in one study and gaps in substantiation may be addressed with additional, reliable and relevant information).

VIII. Discontinued Claim

During the course of the proceeding, the advertiser voluntarily permanently discontinued the claim, "3-5 times greater antiplatelet benefit than enteric coated aspirin." The voluntarily discontinued claim will be treated, for compliance purposes, as though NAD recommended its discontinuance and the advertiser agreed to comply.

Conclusion:

NAD recommended that the advertiser discontinue the claims, "Vazalore achieves therapeutic efficacy 4 times faster than EC Aspirin."; "Faster … antiplatelet response than enteric coated aspirin"; and "Vazalore delivers 2X better platelet response than enteric coated aspirin." Nothing in this decision prevents the advertiser from making claims about the onset of antiplatelet response for subjects taking Vazalore that is narrowly tailored to fit the evidence provided.

NAD recommended that the advertiser modify the claim, "Vazalore has up to 5X greater absorption than enteric coated aspirin." to avoid conveying the message that the claimed difference in absorption related to superior clinical efficacy and disclose that the reported results were limited to diabetic, obese subjects.

NAD recommended the advertiser discontinue the claim, "… more predictable antiplatelet response than enteric coated aspirin." Nothing in this decision prevents the advertiser from making a claim related to the predictability of Vazalore's antiplatelet response that is narrowly tailored to fit the evidence provided.

NAD recommended the advertiser discontinue the claims, "65% lower risk of acute gastric ulcerations than plain aspirin."; "Vazalore vs. Aspirin: 47% lower risk of erosions or ulcers; 71% lower risk of ulcers." Nothing in this decision precludes the advertiser from making a narrower claim based on the results of the Cryer study that conveys the limited message that Vazalore causes fewer erosions and ulcers in the first week of treatment than traditional immediate release aspirin.

NAD recommended that the advertiser discontinue the claim, "The Miracles of Aspirin Fully Realized."

NAD was satisfied that the advertiser had provided a reasonable basis for the claims, "new delivery system for this lifesaving drug" and "we took a different approach." However, NAD recommended that the advertiser modify the claim, "fast, reliable, predictable antiplatelet activity" to disclose that it is based on testing of diabetic, obese subjects and healthy subjects. NAD further recommended the advertiser discontinue the claims, "better gastrointestinal safety" or modify it to convey the limited message that Vazalore causes fewer erosions and ulcers in the first week of treatment than traditional immediate release aspirin. Finally, NAD recommended that the advertiser discontinue the claim, "a better, more efficient and safer delivery platform for active pharmaceutical ingredients. We saw something good, but had a vision to make it better." as well as claims that Vazalore's delivery system allows for an experience with aspirin that is safer, more efficient, and objectively "better" than traditional aspirin.

Finally, during the course of the proceeding, the advertiser voluntarily permanently discontinued the claim, "3-5 times greater antiplatelet benefit than enteric coated aspirin." The voluntarily discontinued claim will be treated, for compliance purposes, as though NAD recommended its discontinuance and the advertiser agreed to comply.

Advertiser's Statement:

PLx Pharma Inc. will comply with NAD's recommendations. PLx Pharma Inc. is pleased that NAD recognized that VAZALORE™ is an immediate-release (IR) aspirin that delivers the life- saving drug aspirin in a novel liquid-filled capsule. NAD acknowledged that VAZALORE is designed to bypass the stomach and be absorbed in the intestine. NAD recognized the validity of the VAZALORE peer-reviewed, published clinical studies that can be used to support advertising messages tailored to consumers and healthcare professionals. The clinical study results show that VAZALORE liquid-filled capsules caused fewer erosions and ulcers than IR aspirin tablets during the first week of treatment, as well as fast, reliable, predictable, antiplatelet activity consistent with IR aspirin. NAD also acknowledged the erratic absorption of enteric coated aspirin tablets that has been well established and required as part of aspirin professional labeling. PLx Pharma Inc. believes these findings will be meaningful to consumers and healthcare professionals alike when VAZALORE is introduced to the market in 2021.

PLx Pharma Inc. respects NAD's self-regulatory process and will incorporate NAD's recommendations as it updates its company website and develops VAZALORE's marketing campaign. **(#6912 LCS, closed 12/14/2020)**