

1 **COMPLAINT**

2 **COMES NOW** Plaintiff, RAYMOND N. RAYES by and through undersigned
3 counsel, and hereby brings this action for damages against Defendants, Novartis
4 Pharmaceuticals Corporation; Novartis AG; Novartis Pharma AG; Novartis Institutes for
5 Biomedical Research, Inc.; Novartis Pharmaceuticals UK Limited; and Alcon Research,
6 LLC f/k/a Alcon Research, Ltd., and alleges as follows:

7
8 **INTRODUCTION**

9
10 1. This is an action for damages due to Plaintiff relating to Defendants'
11 development, testing, manufacture, packaging, preparation, labeling, marketing, supply
12 and/or sale of the dangerous and defective pharmaceutical product Beovu®.

13
14 2. Defendants misrepresented that Beovu was a safe and effective treatment for
15 age-related macular degeneration when in fact the drug causes serious medical problems
16 including intraocular inflammation, retinal vasculitis, retinal vascular occlusion, and
17 other serious vision problems.

18
19 3. Defendants failed to warn physicians and the public about Beovu's
20 propensity to cause vision related adverse events including, but not limited to, ocular
21 inflammation, retinal vasculitis, retinal vascular occlusion, and other serious and
22 permanent eye injuries.

23
24 4. Consumers and physicians alike have been misled about Beovu's safety and
25 efficacy, and as a result consumers, including Plaintiff, have suffered serious and
26 permanent eye injuries including ocular inflammation, retinal vasculitis, retinal vascular
27 occlusion, and other serious eye injuries.

PARTIES

1
2
3 5. Plaintiff, **RAYMOND N. RAYES** is and was at all times relevant hereto, a
4 resident of Riverside County, California. Plaintiff used Beovu, and was treated for his
5 Beovu related injuries, in this judicial District.
6

7 6. Defendant, Novartis Pharmaceuticals Corporation, a subsidiary of Novartis
8 AG, is and was at all times relevant hereto, a corporation organized under the laws of the
9 State of Delaware with its principal place of business at One Health Plaza, East Hanover,
10 New Jersey 07936. Defendant, Novartis Pharmaceuticals Corporation is the current
11 sponsor of the Biologics License Application for Beovu, and thus maintains primary
12 responsibility and control over the drug and all activities and materials relating thereto.
13 Upon information and belief, Defendant, Novartis Pharmaceuticals Corporation has also
14 been substantively involved in the design, funding, authoring, conduct and/or publication
15 of medical research related to Beovu.
16

17 7. Defendant, Novartis AG is and was at all times relevant hereto, a foreign
18 corporation organized and existing under the laws of Switzerland with its principal place
19 of business at Lichtstrasse 35, CH-4056 Basel, Switzerland. Defendant, Novartis AG is
20 the ultimate global parent corporation to Defendants, Novartis Pharmaceuticals
21 Corporation, Novartis Pharma AG, Novartis Institutes for Biomedical Research, Inc., and
22 Novartis Pharmaceuticals UK Limited. Upon information and belief, Defendant, Novartis
23 AG has been substantively involved in the design, funding, authoring, conduct and/or
24 publication of medical research related to Beovu.
25

26 8. Defendant, Novartis Pharma AG, a subsidiary of Novartis AG, is and was at
27 all times relevant hereto, a foreign corporation organized and existing under the laws of
28 Switzerland with its principal place of business at Lichtstrasse 35, CH-4056 Basel,

1 Switzerland. Upon information and belief, Defendant, Novartis Pharma AG developed
2 the commercial formulation of Beovu, and has been substantively involved in the design,
3 funding, authoring, conduct and/or publication of medical research related to Beovu.

4 9. Defendant, Novartis Institutes for Biomedical Research, Inc., a subsidiary of
5 Novartis AG, is and was at all times relevant hereto, a corporation organized under the
6 laws of the State of Delaware with its principal place of business at 250 Massachusetts
7 Avenue, Cambridge, Massachusetts 02139. Upon information and belief, Defendant,
8 Novartis Institutes for Biomedical Research, Inc. has been substantively involved in the
9 design, funding, authoring conduct, and/or publication of medical research related to
10 Beovu.

11
12 10. Defendant, Novartis Pharmaceuticals UK Limited, a subsidiary of Novartis
13 AG, is and was at all times relevant hereto, a foreign corporation organized and existing
14 under the laws of the United Kingdom with its principal place of business at Frimley
15 Business Park, Frimley, Camberley, Surrey, GU16 7SR, United Kingdom. Upon
16 information and belief, Defendant, Novartis Pharmaceuticals UK Limited has been
17 substantively involved in the design, funding, authoring, conduct and/or publication of
18 medical research related to Beovu.

19
20 11. Defendant, Alcon Research, LLC, formerly known as Alcon Research, Ltd.,
21 is and was at all times relevant hereto, a corporation organized under the laws of the State
22 of Delaware with its principal place of business at 6201 South Freeway, Fort Worth,
23 Texas 76134. Upon information and belief, Defendant, Alcon Research, LLC, formerly
24 known as Alcon Research, Ltd., was the entity which maintained primary responsibility
25 for the design and conduct of the Phase I, II, and III clinical trials for Beovu, filed the
26 original Investigational New Drug Application for Beovu with the FDA on April 20,
27 2011, and sponsored the Biologics License Application for Beovu until October 16, 2018.
28 Additionally, Defendant, Alcon Research, LLC, formerly known as Alcon Research,

1 Ltd., has been substantively involved in the design, funding, authoring, conduct and/or
2 publication of medical research related to Beovu.

3
4 12. Defendants, Novartis Pharmaceuticals Corporation; Novartis AG; Novartis
5 Pharma AG; Novartis Institutes for Biomedical Research, Inc.; Novartis Pharmaceuticals
6 UK Limited; and Alcon Research, LLC f/k/a Alcon Research, Ltd., shall hereinafter be
7 referred to collectively as “Defendants” or “Novartis”.

8
9 13. Defendants were jointly engaged in the business of designing, developing,
10 manufacturing, testing, packaging, promoting, marketing, distributing, labeling, and/or
11 selling Beovu, and controlling the Investigational New Drug Application and Biologics
12 License Application for Beovu.

13
14 14. At all times relevant hereto, Defendants include and have included any and
15 all parent companies, subsidiaries, affiliates, divisions, franchises, partners, joint
16 venturers, and organizational units of any kind, their predecessors, successors and assigns
17 and their officers, directors, employees, agents, representatives and any and all other
18 persons acting on their behalf.

19
20 15. At all times relevant hereto, Defendants were engaged in the business of
21 developing, designing, licensing, manufacturing, distributing, selling, marketing, and or
22 introducing into interstate commerce throughout the United States, and in the state of
23 California, either directly or indirectly, through third-parties, subsidiaries and/or related
24 entities, the pharmaceutical product Beovu.

25
26 **JURISDICTION & VENUE**

27
28 16. The jurisdiction of this Court over the subject matter of this action is

1 predicated on 28 U.S.C. § 1332. The amount in controversy exceeds \$75,000.00,
2 exclusive of interest and costs and complete diversity of citizenship exists between the
3 parties.

4 17. Venue in this Court is proper pursuant to 28 U.S.C § 1391 in that a
5 substantial part of the events or omissions giving rise to the claims asserted herein
6 occurred in this District, and Defendants are subject to personal jurisdiction in this
7 District.

8
9 **GENERAL ALLEGATIONS**
10

11 18. This action is for damages brought on behalf of Plaintiff, RAYMOND N.
12 RAYES, who was prescribed and supplied with and who has taken the prescription drug
13 Beovu, as tested, studied, researched, evaluated, endorsed, designed, formulated,
14 compounded, manufactured, produced, processed, assembled, inspected, distributed,
15 marketed, labeled, promoted, packaged, advertised for sale, or otherwise placed in the
16 stream of commerce by Defendants.

17
18 19. Plaintiff, RAYMOND N. RAYES, brings this action against Defendants to
19 recover damages for the injuries suffered as a result of his ingestion of Beovu and to
20 recover for his individual economic and non-economic damages which he sustained as a
21 result therefrom.

22
23 20. Defendants' wrongful acts, omissions, and fraudulent misrepresentations
24 caused Plaintiff's injuries and damages.

25
26 21. At all times relevant, Defendants were engaged in the business of
27 researching, licensing, designing, formulating, compounding, testing, manufacturing,
28 producing, processing, assembling, inspecting, distributing, marketing, labeling,

1 promoting, packaging and/or advertising for sale the prescription drug Beovu for use by
2 physicians in treating their patients, including Plaintiff.

3
4 22. At all times relevant, Defendants were authorized to do business within
5 Plaintiff's state of residence and did conduct such business.

6
7 23. At times relevant, the officers and directors of Defendants participated in,
8 authorized, and directed the production and promotion of Beovu when they knew, or with
9 the exercise of reasonable care should have known, of the hazards and dangerous
10 propensities of Beovu and thereby actively participated in the tortious conduct which
11 resulted in the injuries suffered by Plaintiff discussed herein.

12
13 **FACTS COMMON TO ALL COUNTS**

14
15 24. Beovu® (brolucizumab) is a human vascular endothelial growth factor
16 ("VEGF") inhibitor indicated for the treatment of Neovascular (Wet) Age-Related
17 Macular Degeneration ("AMD" or "nAMD") in adults.

18
19 25. Wet AMD, also referred to as exudative AMD ("eAMD"), is characterized
20 by the presence of choroidal neovascularization, a pathologic form of angiogenesis that
21 results in the leakage and accumulation of fluid within the retina. In general, the primary
22 goal of treatment for wet AMD is to maintain visual acuity, which requires drying the
23 retina through the inhibition of new blood vessel growth and reduction of fluid leakage.

24
25 26. The Beovu molecule, formerly known as ESBA1800 and/or RTH258, was
26 originally developed by Switzerland-based ESBA Tech AG. ESBA Tech AG was acquired
27 by Alcon, Inc. in September 2009, after which Alcon, Inc. and its subsidiaries, including
28 Alcon Research, LLC f/k/a Alcon Research, Ltd., assumed ownership and all future

1 marketing rights to Beovu. Novartis Pharmaceuticals Corporation subsequently acquired
2 Alcon, Inc. in April 2011, and with it, ownership and all future marketing rights to
3 Beovu. During the premarketing development process, Beovu was regulated under
4 Investigational New Drug Application number 112023 in the United States.

5
6 27. Novartis announced that the United States Food and Drug Administration
7 (“FDA”) accepted the Biologics License Application (“BLA”) for Beovu on April 15,
8 2019. At that time, Novartis noted that it had used a priority review voucher to expedite
9 review of Beovu in the U.S. in order to “make brolocizumab available as quickly as
10 possible”. This is despite the fact that safe and efficacious drugs for the treatment of wet
11 AMD were already on the market in the United States.

12
13 28. Beovu received FDA approval on October 7, 2019 under BLA number
14 761125.

15
16 29. Approval of Beovu was based on the results of two prospective, randomized,
17 double-blind, multicenter Phase III studies, HAWK (NCT02307682) and HARRIER
18 (NCT02434328), which, based on the data as characterized to the FDA by Defendants,
19 met the primary endpoint of non-inferiority to aflibercept in mean change in best-
20 corrected visual acuity (“BCVA”) from baseline to week 48.

21
22 30. Beovu is administered as an intravitreal injection and is intended to treat
23 AMD by inhibiting the binding of VEGF to the VEGFR1 and VEGFR2 receptors,
24 thereby suppressing the growth of abnormal blood vessels and reducing the potential for
25 fluid leakage into the retina.

26
27 31. Beovu is the third VEGF inhibitor to receive FDA approval for the treatment
28 of wet AMD. Other VEGF inhibitors approved for the treatment of wet AMD include

1 Lucentis® (ranibizumab) by Genentech, which was approved June 30, 2006, and Eylea®
2 (aflibercept) by Regeneron Pharmaceuticals, which was approved November 18, 2011.
3 Unlike Beovu, Lucentis and Eylea “have been well established as effective and safe anti-
4 VEGF therapies for nAMD”.

5
6 32. Although not approved by the FDA for this indication, Avastin®
7 (bevacizumab) by Genentech is another VEGF inhibitor routinely utilized by
8 ophthalmologists in the treatment of wet AMD. Avastin has been on the market since
9 February 26, 2004.

10
11 33. Clinical treatment guidelines published by the American Academy of
12 Ophthalmology currently state “intravitreal injection therapy using anti-vascular
13 endothelial growth factor (VEGF) agents (e.g., aflibercept, bevacizumab, and
14 ranibizumab) is the most effective way to manage neovascular AMD and represents the
15 first line of treatment”.

16
17 34. Novartis sought to acquire and develop a new drug for the treatment of wet
18 AMD that they could promote as requiring less frequent injections than other VEGF
19 inhibitors. This would be accomplished by creating a drug composed of a smaller
20 molecule that would allow for delivery of a greater molar dose with more effective tissue
21 penetration and greater durability, thereby allowing for longer intervals between
22 injections.

23
24 35. According to the published article titled *Retinal vasculitis and intraocular*
25 *inflammation after intravitreal injection of brolocizumab* by Baupal et al., Beovu’s
26 “molecular mass of 26 kDa is less than that of other commercially available anti-VEGF
27 agents, allowing for a higher molar concentration with potential for greater anti-VEGF
28 therapeutic performance per intravitreal injection. Increased molar concentration

1 combined with a high binding affinity for VEGF have been postulated to account for its
2 potential for increased durability, and brolocizumab is the first agent in this class
3 approved for a dosing interval range of 8 to 12 weeks after 3 loading doses.”

4 36. Since receiving FDA approval, Novartis has encouraged ophthalmologists to
5 switch their patients to Beovu by marketing it as requiring less frequent injections than
6 other VEGF inhibitors used in the treatment of AMD, thereby purporting to offer greater
7 convenience and reduce patient non-adherence.

8
9 37. While Novartis’ marketing of Beovu has been primarily directed towards
10 convincing doctors to switch patients who have previously been treated with other VEGF
11 inhibitors to Beovu, none of the patients included in the premarket clinical trials had ever
12 received prior treatment with other VEGF inhibitors. Instead, the study protocols for the
13 HAWK and HARRIER clinical trials required all enrolled patients to be treatment-naïve.
14 Therefore, Novartis failed to perform any testing in the very patient population to which
15 it intended, and indeed did, specifically market Beovu to after it received FDA approval.

16
17 38. The instant matter involves injuries of retinal vasculitis, retinal vascular
18 occlusion, and other acute eye injuries associated with the administration of Beovu.

19
20 39. Retinal vasculitis is characterized by inflammation of the vessels of the
21 retina typically leading to a decrease in vision. Retinal vascular occlusion is characterized
22 by an obstruction of the venous system of the retina, usually by a thrombus or embolus,
23 causing vision loss which can be severe and permanent. In many cases patients can
24 present with concomitant retinal vasculitis and retinal vascular occlusion.

25
26 40. Retinal vasculitis and retinal vascular occlusion are injuries unique to Beovu
27 use. These injuries have been widely reported in patients taking Beovu, but are not
28 considered to be a risk with other VEGF inhibitors.

1
2 41. Data from the HAWK and HARRIER Phase III clinical trials were published
3 in January 2020. In their publication titled *HAWK and HARRIER: phase 3, multicenter,*
4 *randomized, double-masked trials of brolocizumab for neovascular age-related macular*
5 *degeneration*, Dugel et al. reported no cases of retinal vasculitis in any treatment group,
6 two (0.6%) serious cases of retinal artery occlusion in the Beovu 3mg group, no serious
7 cases of retinal artery occlusion in the Beovu 6mg groups, and one (0.3%) serious case of
8 retinal artery occlusion in the aflibercept 2mg group. These events were simply listed in a
9 table in the publication and were not discussed by authors in the text of the manuscript.
10 Additionally, as noted below, these events were significantly underreported in this
11 publication.

12
13 42. It should further be noted that Defendant, Novartis Pharma AG funded and
14 “participated in the design of the study; management, analysis, and interpretation of the
15 data; preparation, review, and approval of the manuscript” for this publication by Dugel
16 and colleagues. Additionally, two of the authors of this study, James Warburton, MBBS
17 and Andreas Weichselberger, PhD, were employees of Defendant, Novartis Pharma AG,
18 and were noted to have contributed to the conception and design, data collection, analysis
19 and interpretation, and maintained overall responsibility for the study. These two authors
20 are also inventors of the brolocizumab molecule as reflected on United States Patent
21 number US 2016/0130337 A1. Accordingly, at all times Defendant maintained control
22 over the study data and manuscript, and thus had the ability to edit, revise, or correct any
23 false or misleading information contained therein, however it chose not to do so.

24
25 43. On February 23, 2020, the American Society of Retina Specialists (“ASRS”)
26 issued an alert to its members in which it noted that it had received 14 reported cases of
27 vasculitis following Beovu injections, 11 of which were designated as occlusive retinal
28 vasculitis.

1
2 44. On March 30, 2020, ASRS issued an update noting the number of cases of
3 retinal vasculitis following intravitreal injections of Beovu it had received had risen to 25,
4 with 21 such cases involving retinal occlusion.

5
6 45. Subsequent to the first ASRS communication in February 2020, Novartis
7 announced it was “conducting a comprehensive review of a limited number of reported
8 cases of severe vision loss, inflammation and potential retinal vasculitis in patients
9 treated with Beovu” and that it would commission an external Safety Review Committee
10 to conduct safety evaluations for Beovu.

11
12 46. Following their review of safety data, on April 8, 2020 Novartis confirmed
13 the existence of a safety signal involving rare adverse events of “retinal vasculitis and/or
14 retinal vascular occlusion that may result in severe vision loss” for Beovu.

15
16 47. On June 4, 2020, ASRS issued a report containing the external Safety
17 Review Committee’s initial findings regarding cases of retinal vasculitis and retinal
18 vascular occlusion occurring during the Phase III HAWK and HARRIER trials.

19
20 48. According to the report, out of a total 1,088 patients in premarket clinical
21 trials assigned to Beovu treatment arms, the committee found that 36 (3.3%) experienced
22 retinal vasculitis, 23 (2.1%) of which experienced concomitant vascular occlusion. Risk
23 of ≥ 3 line vision loss and ≥ 6 line vision loss over two years in patients with retinal
24 vasculitis was 22% (8/36) and 14% (5/36), respectively, and in those with occlusive
25 retinal vasculitis was 30% (7/23) and 22% (5/23), respectively.

26
27 49. In comparing the external Safety Review Committee’s findings to the Beovu
28 Phase III clinical trial data as originally reported by Novartis to the FDA, ASRS

1 commented, “the [Safety Review Committee] found that their observed incidences of
2 both retinal vasculitis and retinal vascular occlusion were higher than the incidences
3 reported by the investigators”.

4 50. Published ahead-of-press on June 20, 2020, just 16 days after the
5 preliminary Safety Review Committee’s report was issued, in a publication titled *HAWK*
6 *and HARRIER: Ninety-Six-Week Outcomes from the Phase 3 Trials of Brolocizumab for*
7 *Neovascular Age-Related Macular Degeneration*, Dugel et al. (2020) reported on 96-
8 week outcomes from the HAWK and HARRIER Phase III clinical trials. In this updated
9 data set, retinal vasculitis was simply noted to have occurred during the trials, and the
10 treatment assignments and number of patients affected were not reported. Four retinal
11 arterial occlusive events were reported in the Beovu 3mg group and six retinal arterial
12 occlusive events were reported in the Beovu 6mg groups. Total retinal arterial occlusive
13 events occurring in the aflibercept 2mg group were not reported, but one case of retinal
14 artery occlusion coded as a serious adverse event was listed in a table.

15
16 51. Dugel and colleagues did make a passing reference to postmarketing cases
17 of intraocular inflammation, vasculitis, and retinal occlusive vasculitis as reported by
18 ASRS, and noted that such reports are currently being investigated by Novartis and an
19 external safety review committee. However, there was no mention by the authors that the
20 safety review committee was reanalyzing the HAWK and HARRIER data and had
21 already found numerous unreported cases of retinal vasculitis and retinal vascular
22 occlusion. It should be noted that while this manuscript was originally submitted for
23 publication in December 2019, it was last revised on June 4, 2020, the same day the
24 Safety Review Committee report was issued, prior to its being accepted for publication
25 by *Ophthalmology* on June 12, 2020.

26
27 52. Similar to the earlier publication by Dugel et al. discussed above, Defendant,
28 Novartis Pharma AG funded and “participated in the design of the study; management,

1 analysis, and interpretation of the data; and preparation, review, and approval of the
2 manuscript” for this updated publication by Dugel and colleagues. Again, two of the
3 authors of the study, Georges Weissgerber, MD and Kinfemichael Gedif, PhD, were
4 employees of Defendant, Novartis Pharma AG, and one or both were noted to have
5 contributed to the conception and design, data collection, analysis and interpretation, and
6 maintained overall responsibility for the study. Accordingly, at all times Defendant
7 maintained control over the study data and manuscript, and thus had the ability to edit,
8 revise, or correct any false or misleading information contained therein, however it chose
9 not to do so.

10
11 53. Following its confirmation of a safety signal, Novartis revised the United
12 States product labeling for Beovu on June 9, 2020 to include a new warning regarding the
13 risk of “Retinal Vasculitis and/or Retinal Vascular Occlusion” (§5.2), which reads as
14 follows:

15 Retinal vasculitis and/or retinal vascular occlusion,
16 typically in the presence of intraocular
17 inflammation, have been reported with the use of
18 BEOVU [*see Contraindications (4.2) and Adverse
19 Reactions (6.1)*]. Patients should be instructed to
20 report any change in vision without delay.

21 54. It is yet unclear when this new warning was widely disseminated to
22 physicians utilizing Beovu with their patients.

23 55. Prior to June 2020, no warnings regarding the risk of retinal vasculitis or
24 retinal vascular occlusion were present in the United States product labeling for Beovu.

25
26 56. Data further supporting the causal relationship between administration of
27 Beovu and retinal vasculitis and retinal vascular occlusion injuries have been documented
28 in the peer-reviewed medical literature. Several publications have detailed these adverse

1 health outcomes following Beovu administration since its approval in 2019.

2
3 57. For example, in a publication titled *Retinal vasculitis and intraocular*
4 *inflammation after intravitreal injection of brolocizumab*, Baupal et al. presented a
5 retrospective case series of retinal vasculitis and intraocular inflammation in 15 eyes from
6 12 patients following administration of Beovu. All eyes had received previous intravitreal
7 injections of one or more anti-VEGF agents including aflibercept, bevacizumab, and
8 ranibizumab. The diagnosis of retinal vasculitis and intraocular inflammation in this
9 series was made at a mean of 35.5 days (range 14-56 days) in 10 eyes after receiving the
10 first Beovu injection and 20 days (range 7-25 days) in five eyes after receiving more than
11 one Beovu injection. The most severely affected eyes in the series featured occlusion of
12 larger retinal arteries at the optic nerve or branches proximal to the fovea, and
13 demonstrated severe visual loss at 20/200 or worse when vasculitis was diagnosed and
14 showed limited improvement at the most recent follow-up. Authors noted that a history of
15 recent Beovu intravitreal injection combined with examination demonstrating the
16 spectrum of features observed in the case series likely rules out a systemic event, which
17 otherwise could occur in this age group. Baupal and colleagues found that “retinal
18 vasculitis after brolocizumab was typically occlusive and could involve the retinal
19 arteries, veins, and potentially capillaries, with a range in the severity of findings” and
20 declared, “Brolocizumab is the first FDA-approved anti-VEGF agent associated with
21 noninfectious retinal vasculitis after intravitreal therapy”.

22
23 58. In another retrospective case series by the ASRS Research and Safety in
24 Therapeutics (“ReST”) Committee titled *Occlusive retinal vasculitis following*
25 *intravitreal brolocizumab*, Witkin et al. analyzed the characteristics of 26 post-marketing
26 cases of retinal vasculitis following intravitreal Beovu administration in 25 patients
27 which were reported to ASRS through April 1, 2020. In this study, retinal vasculitis
28 presented after one Beovu injection in 11 (42%) eyes, after two injections in 11 (42%)

1 eyes, and after three injections in four (16%) eyes. Authors noted that 22 (85%) eyes
2 were reported by the treating physician as having occlusive vasculitis, with a mean time
3 to presentation of 26 days (range, 3-63 days) from the most recent Beovu injection, and
4 46 days (range, 15-146 days) from the first Beovu injection. All patients had previously
5 been treated with other anti-VEGF agents with no history of anti-VEGF-associated
6 inflammation, and no Beovu injections were given in the presence of intraocular
7 inflammation according to the reporting physicians. Of note, 20 (77%) patients included
8 in this case series were stated to have switched from other VEGF inhibitors to Beovu for
9 the purpose of “Extend[ing] treatment interval”, consistent with Novartis’ marketing
10 efforts. Authors also noted that they found no identifiable associations with product lot
11 numbers, as these events were reported with Beovu from eight different lots administered
12 by 20 different physicians, and expressed that there was no indication of an association
13 with any ocular disorders, autoimmune diseases, drug allergies, or other medical
14 disorders, ruling out alternative causation.

15
16 59. Despite the clear risk of post-injection retinal vasculitis and vascular
17 occlusion, the 13-member ReST Committee, five of whom have stock ownership in,
18 receive fees or research support from, or serve as consultants to Novartis, did not
19 recommend against continued use of Beovu. However, they did advise, “Because of the
20 potentially severe nature of the consequences of retinal vasculitis secondary to
21 brolocizumab, caution is advised when considering injection of brolocizumab in
22 monocular patients or when bilateral injections are being contemplated”.

23
24 60. The findings of the external Safety Review Committee, previously discussed
25 above, were formally published in November 2020 in an article titled *Risk of*
26 *Inflammation, Retinal Vasculitis and Retinal Occlusion-Related Events with*
27 *Brolocizumab: Post-Hoc Review of HAWK and HARRIER*. In addition to reiterating the
28 data previously disclosed in the June 2020 report, Mones et al. provided additional detail

1 and context to the events of retinal vasculitis and retinal vascular occlusion that occurred
2 in the clinical trials for Beovu. The authors took care to emphasize that their review was
3 limited only to the 60 patients for whom investigators reported intraocular inflammation
4 and did not include all patients enrolled in the clinical trials. As such, they noted
5 “Additional cases may have been identified if the SRC had applied the conservative
6 review to all patients in the two studies” and stated “The actual event rate may have been
7 higher than reported by the investigators, particularly if some of the cases were minimally
8 symptomatic or asymptomatic”. Based on the data that was made available to the
9 committee, there were eight cases of at least moderate visual acuity loss (≥ 15 ETDRS
10 letters) among eyes with definite or probable intraocular inflammation, five of which
11 were severe (≥ 30 ETDRS letters), and seven of these cases occurred in eyes with definite
12 or probable intraocular inflammation with concomitant retinal vasculitis and retinal
13 vascular occlusion. In eyes with definite or probable intraocular inflammation, the
14 incidence of retinal vasculitis was 72.0%; in eyes with intraocular inflammation and
15 retinal vasculitis, the incidence of retinal occlusion was 63.9%. Approximately three
16 quarters of cases of each event occurred within six months of the first Beovu injection,
17 and half of cases occurred within the first three months following the first Beovu
18 injection. Mones et al. discussed some of the limitations of the imaging performed by the
19 study investigators and made available for their review, commenting that “fluorescein
20 angiograms were usually not widefield and limited in number, preventing the assessment
21 of peripheral vasculitis signs and retinal blood flow”. Authors concluded, “this rigorous
22 analysis of cases of definite/probable IOI that occurred in the phase 3 HAWK and
23 HARRIER clinical trials identified a number of cases with signs of retinal vasculitis with
24 or without signs of retinal vascular occlusion, and such events were associated with
25 increased risk of visual acuity loss”.

26
27 61. Case reports describing patients who experienced retinal vasculitis and/or
28 retinal vascular occlusive events following intravitreal administration of Beovu have also

1 been published in the peer-reviewed medical literature.

2
3 62. In an article titled *Retinal arterial occlusive vasculitis following intravitreal*
4 *brolocizumab administration*, Haug et al. presented a published report of vascular
5 occlusion with vasculitis after intravitreal injection of Beovu for wet AMD. The patient,
6 who had received multiple intravitreal ranibizumab treatments previously in both eyes
7 without complication, reported loss of vision with light sensitivity in both eyes four
8 weeks after bilateral intravitreal Beovu injection. After excluding other potential
9 etiologies, and given the temporal relationship with administration of Beovu, the patient
10 in this case was diagnosed with “possible delayed or type IV hypersensitivity to
11 brolocizumab”.

12
13 63. In a publication titled *Severe vision loss secondary to retinal arteriolar*
14 *occlusion after multiple intravitreal brolocizumab administrations*, Jain et al. reported on
15 a patient who presented with sudden blurry vision and floaters without pain or redness
16 following her third injection of Beovu. The patient had previously received treatment
17 with bevacizumab, ranibizumab, and aflibercept without incident. Upon examination the
18 patient was found to have multiple retinal arteriolar occlusions which caused “severe loss
19 of vision”. After a thorough work-up and exclusion of other potential causal factors, the
20 patient was ultimately diagnosed with “retinal arteriolar occlusion associated with
21 repeated intravitreal brolocizumab administrations”.

22
23 64. In their discussion, Jain et al. pointed out that data from the HAWK and
24 HARRIER clinical trials as presented at the 43rd Annual Meeting of the Macula Society
25 indicated six cases of retinal artery occlusion (including terms of retinal artery
26 thrombosis, retinal artery occlusion, and retinal artery embolism) occurred in the
27 brolocizumab 6mg patients. They then made the observation that these data were
28 “different than the published Phase 3 data of the HAWK and HARRIER studies which

1 reported only 3 cases of retinal artery occlusion/thrombosis”.

2
3 65. In a publication titled *Retinal Vasculitis After Administration of*
4 *Brolucizumab Resulting in Severe Loss of Visual Acuity*, Kondapalli et al. reported on a
5 patient who experienced immediate blurry vision with clinically-significant boxcarring of
6 the retinal arteries following her second injection of Beovu. This patient had previously
7 been treated with bevacizumab and aflibercept without experiencing any intraocular
8 inflammation or other complications. The patient was noted to have no visual
9 improvement at her most recent follow-up, approximately five weeks post-injection.
10 Fungal and viral etiologies were ruled out, and the patient was diagnosed with “occlusive
11 retinal vasculitis associated with intravitreal administration of brolucizumab in the setting
12 of neovascular age-related macular degeneration”.

13
14 66. In a publication titled *Brolucizumab-related retinal vasculitis with*
15 *exacerbation following ranibizumab retreatment: A clinicopathologic case study*, Iyer et
16 al. described a case involving a patient who was found to have retinal vasculitis and
17 intraocular inflammation after presenting with pain, ocular aches, floaters and decreased
18 visual acuity one week following her third injection of Beovu. As with other reports, this
19 patient had previously received regular intravitreal treatments with bevacizumab,
20 aflibercept, and ranibizumab without incident. In discussing the matter, authors
21 commented, “Retinal occlusive vasculitis with intraocular inflammation has been a
22 devastating adverse event for brolucizumab, leading to blinding visual outcomes for
23 many patients. Although intraocular inflammation has been seen with other anti-VEGF
24 medications, severe vision loss due to retinal occlusive vasculitis has not been reported.”

25
26 67. Based on the significant safety issue related to retinal vasculitis and retinal
27 artery occlusion, Rosenfeld & Browning explained in their recent editorial titled *Is This a*
28 *737 Max Moment for Brolucizumab?*, “[w]e have stopped using brolucizumab because of

1 the associated inflammation. Our patients have alternatives without incurring this risk”.
2 Making note of the unusual nature of the inflammation in that it is associated with
3 “occlusive vasculitis and irreversible severe vision loss”, they pointed out that “[t]he
4 retinal community had not reported this type of vision-threatening occlusive retinal
5 vasculitis after intravitreal injections of other commonly used anti-VEGF drugs”. Finally,
6 the authors stressed, “[I]t is our view that intravitreal injections of brolocizumab should
7 stop. Brolocizumab is not the only drug that can be used for the treatment of eAMD. In
8 the face of the known risk, its use is unwarranted.”

9
10 68. In response to the Rosenfeld & Browning editorial, Kayath & Sauer (two
11 Novartis employees) used a public platform to attempt to defend Novartis’ handling of
12 the matter and made clear that Novartis did not appreciate independent ophthalmologists
13 shedding light on the undisclosed safety issues with Beovu and advising against its
14 further use. The authors noted, “we believe the choice of treatment should ultimately be
15 left to individual treating physicians and their patients, after appropriate evaluation of the
16 benefit-risk profile of the product” and “[a]t Novartis, we support individual physicians,
17 who we believe, whether or not they choose to use brolocizumab, are able to make the
18 best treatment choices for their patients”. At no point in this published response did these
19 Novartis employees take responsibility or apologize for their failure to present accurate
20 data concerning adverse events in clinical trials or for putting patients at risk for severe
21 vision loss that otherwise could have been prevented had they not been exposed to
22 Beovu.

23
24 69. Rosenfeld & Browning subsequently issued a reply criticizing the published
25 response letter by Kayath & Sauer. The authors pointed out that “Their letter fails to
26 disclose the recent clarifications in the HAWK and HARRIER trial data, and by doing so
27 they fail to reveal the true risks and benefits for the patients who might be given
28 brolocizumab”. Noting that the external Safety Review Committee found that incidences

1 of retinal vasculitis and retinal vascular occlusion were higher in the HAWK and
2 HARRIER trials than previously reported, Rosenfeld & Browning commented, “[t]hese
3 data, and the discrepancy from the previously released results, in addition to the cases
4 arising from the community use of brolocizumab, raise red flags”. In response to
5 Novartis’ contention that the overall rate of vision loss was comparable between Beovu
6 and aflibercept groups in the clinical trials, the authors noted that “this comparison is
7 flawed”, and such an assessment must instead be “based on the risk of vision loss from
8 the drug and not from the natural history of disease progression after anti-vascular
9 endothelial growth factor injections”. Mirroring their statements in the original editorial,
10 Rosenfeld & Browning commented “we believe that the benefits of brolocizumab are not
11 worth the risks compared with similarly effective therapies that do not have the same risk
12 of an occlusive vasculitis” and stated “we reiterate our recommendation that a
13 moratorium be imposed on the use of brolocizumab until the cause is discovered for these
14 inflammatory side effects and until remedies are devised”. The authors finally declared,
15 “It comes down to a simple question for Novartis and the vitreoretinal community: how
16 many more patients need to lose vision before this moratorium is implemented?”
17

18 70. Echoing the concerns expressed by Rosenfeld & Browning, other retinal
19 practices have also made the decision not to use Beovu in light of the significant safety
20 issues involving retinal vasculitis and retinal vascular occlusion. For example, California-
21 based The Retina Partners explained in a recent article, “Given that other safe and
22 effective therapies exist for neovascular AMD, and that we currently have no way of
23 predicting who will be affected by occlusive vasculitis, we have elected to avoid Beovu
24 until safety can be demonstrated”. They further noted, “many retina specialists, including
25 our group, believe that odds of 1 in 50 that an injection could result in vascular occlusion
26 is unacceptable – especially when some of these patients will end up with severely and
27 permanently reduced visual acuity, and/or scotoma”.

1 71. Researchers have identified biologically plausible mechanisms through which
2 Beovu can cause retinal vasculitis and/or retinal vascular occlusion events.

3
4 72. Various hypotheses have been proposed, including that the pathogenic
5 mechanism involves the formation of local antibodies, or patient factors such as prior
6 anti-VEGF treatment use, human leukocyte antigens, immune status, and causative
7 comorbidities are potential culprits.

8
9 73. According to Novartis, “The proprietary innovative structure results in a
10 small molecule (26 kDa) with potent inhibition of, and high affinity to, all VEGF-A
11 isoforms. Beovu is engineered to deliver a high concentration of drug, thus providing
12 more active binding agents.”

13
14 74. Given these unique attributes, certain researchers have proposed that the
15 distinct molecular structure of Beovu is responsible for the events of retinal vasculitis and
16 retinal vascular occlusion. As noted by Jain et al. in *Severe vision loss secondary to*
17 *retinal arteriolar occlusion after multiple intravitreal brolocizumab administrations*, “[i]t
18 could be theorized that the observed adverse event is attributed to the more potent VEGF
19 blockade, owing to the properties of the brolocizumab molecule.” Similarly, in *Occlusive*
20 *retinal vasculitis following intravitreal brolocizumab*, Witkin et al. stated “[i]t is possible
21 that because of its more potent anti-VEGF effect, brolocizumab may have a high enough
22 anti-VEGF effect to cause retinal arteriolar constriction and occlusive vasculopathy
23 compared with other anti-VEGF agents.”

24
25 75. In a publication titled *Brolocizumab-related retinal vasculitis with*
26 *exacerbation following ranibizumab retreatment: A clinicopathologic case study*, Iyer et
27 al. also discussed the potential for the unique characteristics of Beovu to confer greater
28 immunological effects than other VEGF inhibitor products, as they postulated

1 “Brolucizumab may be more immunogenic than other anti-VEGF agents by virtue of its
2 relative small size and consequent ability to unfold which exposes epitopes that may not
3 be recognized by the immune system. Alternatively during the post-translational
4 modification process of protein fragments like brolucizumab, structural changes such as
5 cleavage and cross-linking of the protein may result in the creation of new protein
6 epitopes. These new protein structures could lead to formation of aggregates, which can
7 significantly enhance immunogenicity.”
8

9 76. Several researchers have also proposed that the retinal vasculitis and/or
10 retinal vascular occlusion observed following exposure to Beovu is potentially a result of
11 a type III or type IV hypersensitivity reaction.
12

13 77. A hypersensitivity reaction is an inappropriate or over-reactive immune
14 response to an antigen resulting in undesirable effects in the human body. In a type III
15 hypersensitivity reaction, an abnormal immune response is mediated by the formation of
16 antigen-antibody aggregates called immune complexes, which can precipitate in various
17 tissues and trigger the classical complement pathway. Complement activation leads to the
18 recruitment of inflammatory cells that release lysosomal enzymes and free radicals at the
19 site of immune complexes, causing tissue damage. A type IV hypersensitivity reaction,
20 also referred to as a delayed hypersensitivity reaction because it takes more than 12 hours
21 to develop, is mediated by T cells that provoke an inflammatory reaction against
22 exogenous or endogenous antigens. After antigen exposure, an initial local immune and
23 inflammatory response occurs that attracts leukocytes. Then the antigen, engulfed by
24 macrophages and monocytes, is presented to T cells, which then becomes sensitized and
25 activated. Type IV drug hypersensitivity occurs when various drug particles bind to a T
26 cell receptor, even if not metabolized by antigen-presenting cells or presented by major
27 histocompatibility complex molecules.
28

1 78. Pathologic findings in patients presenting with retinal vasculitis and/or
2 retinal vascular occlusion following Beovu administration that support the plausibility of
3 a type III or type IV delayed hypersensitivity reaction include the presence of anti-drug
4 antibodies and elevated T cells and B cells.

5
6 79. According to Iyer et al., “Among findings favoring type III hypersensitivity
7 are frequent demonstration of anti-drug antibodies in the Hawk and Harrier trials, delayed
8 onset retinal vasculitis, and some clinical overlap with hemorrhagic occlusive retinal
9 vasculitis which is also postulated to involve type III hypersensitivity.” The case reported
10 by Iyer and colleagues also demonstrated the presence of both T cells and B cells in
11 vitreous sample staining.

12
13 80. Regarding the Phase III clinical trials for Beovu, the FDA also found,
14 “Among subjects with treatment-emergent antibodies, a higher number of intraocular
15 inflammation events were observed”.

16
17 81. Novartis has also commented on anti-drug antibodies observed during
18 clinical trials, noting “In a post-hoc unmasked assessment of the Phase III HAWK and
19 HARRIER data, there was an observed trend toward increased incidence of [retinal
20 vasculitis and/or retinal vascular occlusion] in patients with treatment emergent
21 (boosted/induced) anti-drug antibodies (ADAs)”.

22
23 82. Beovu is a monoclonal antibody, which are complex, laboratory-made
24 proteins that mimic the body’s immune system in order to fight off infections or suppress
25 disease processes, and may cause immunogenicity. As pointed out by Sharma et al. in
26 their publication *Brolucizumab and immunogenicity*, “Type III hypersensitivity reactions
27 (HSR) to the [monoclonal antibodies] including anti-VEGF agents used for oncological
28 indications have been reported to cause vasculitis”.

1
2 83. The case of abicipar pegol also serves as a strong analogy to the instant
3 matter. Abicipar pegol is an investigational anti-VEGF therapy currently under joint
4 development by Allergan and Molecular Partners for the treatment of patients with wet
5 AMD. Similar to Beovu, abicipar pegol has a small molecular weight of 32 kDa, has been
6 shown to have high affinity for binding with its cellular targets, and has demonstrated a
7 longer period of effectiveness when compared with older VEGF inhibitors at equal molar
8 doses, allowing for longer dosing intervals. Drawing a comparison between Beovu and
9 abicipar pegol, in a publication titled *Brolucizumab-related retinal vasculitis: emerging*
10 *disconnect between clinical trials and real world*, Sharma et al. (2020) noted, “[t]he
11 common aspect of these molecules is the low molecular weight, a different structure
12 compared to the previous anti-VEGF molecules, and the occurrence of an emerging
13 phenomenon of retinal vasculitis in the phase 3 trials.”
14

15 84. On June 26, 2020 Allergan and Molecular Partners announced that the FDA
16 had issued a Complete Response Letter concerning the BLA for abicipar pegol in which
17 the agency indicated “the rate of intraocular inflammation observed following
18 administration of Abicipar pegol 2mg/0.05 mL results in an unfavorable benefit-risk ratio
19 in the treatment of neovascular (wet) age-related macular degeneration (AMD)”.
20 Incidence of intraocular inflammation adverse events in the two Phase III pivotal trials
21 for abicipar pegol, CEDAR and SEQUOIA, was 15.4%, 15.3%, and 0.3% in the abicipar
22 Q8, abicipar Q12, and ranibizumab Q4 groups, respectively.
23

24 85. A review of the safety data from CEDAR and SEQUOIA demonstrates a
25 similar trend to Beovu whereby a significantly greater number of adverse events
26 involving retinal vasculitis and retinal arterial occlusion were reported in the abicipar
27 pegol-treated group compared to the active comparator group treated with ranibizumab.
28 Retinal vascular occlusion (coded as retinal artery occlusion or retinal vein occlusion)

1 was reported in eight patients assigned to abicipar pegol groups in CEDAR and
2 SEQUOIA while only one patient assigned to ranibizumab experienced retinal vasculitis.
3 Retinal vasculitis was reported in 17 patients assigned to abicipar pegol groups in
4 CEDAR and SEQUOIA while no patients assigned to ranibizumab experienced retinal
5 vasculitis.

6
7 86. Given the significant underreporting of retinal vasculitis and retinal vascular
8 occlusion by Novartis from its clinical trials it remains questionable whether the FDA
9 would have even approved Beovu had these rates been properly reported to the agency at
10 the time the drug was being evaluated for approval.

11
12 87. In addition to misreporting the safety data from the HAWK and HARRIER
13 clinical trials as demonstrated by the external Safety Review Committee reanalysis,
14 Novartis has misled healthcare providers and the public by consistently downplaying the
15 frequency at which retinal vasculitis and/or retinal vascular occlusion adverse events
16 have occurred in patients treated with Beovu.

17
18 88. On March 2, 2020, Novartis issued a press release regarding “reported cases
19 of severe vision loss, inflammation and potential retinal vasculitis in patients treated with
20 Beovu” in which it stated, “[w]e believe the incidence of these events remains consistent
21 with or below the package insert”.

22
23 89. Again, on March 11, 2020, Novartis issued a press release in which it stated
24 “[t]he rate of the reported post-marketing events remains consistent with or below the
25 approved prescribing information”. However, during March 2020 the United States
26 prescribing information cited an incidence rate of 1% for retinal artery occlusion
27 occurring in the HAWK and HARRIER clinical trials and cited no incidence rate for, nor
28 made any reference to retinal vasculitis.

1
2 90. In April 2020, Novartis' Chief Executive Officer Vas Narasimhan, citing the
3 incidence of these adverse events, was quoted as stating they are "very rare, with about 1
4 to 2 cases in 10,000 injections". Despite this statement citing an incidence rate even
5 lower than Novartis had cited just the month prior, Novartis nonetheless issued another
6 press release on April 8, 2020 in which it stated that it was initiating an update to the
7 prescribing information for Beovu after it "concluded that there is a confirmed safety
8 signal of rare adverse events of 'retinal vasculitis and/or retinal vascular occlusion that
9 may result in severe vision loss'".

10
11 91. Also wildly inconsistent with Novartis' earlier statements, as reported by
12 BioPharma Dive on April 9, 2020, after a review of Beovu postmarketing data "Novartis
13 found retinal artery occlusion, inflammation of blood vessels in the eye — known as
14 vasculitis — or severe vision loss occurred in 8.75 to 10.08 out of 10,000 injections for
15 five weeks spanning Feb. 28 to March 27".

16
17 92. Following the emergence of the safety issues discussed herein, Novartis
18 created a webpage which provides data on the incidence of events of retinal vasculitis and
19 retinal vascular occlusion which have been reported in the postmarketing setting since
20 October 2019. By reviewing the data presented on this website, it can be seen that
21 Novartis has consistently downplayed and continues to downplay the frequency with
22 which these adverse events have actually occurred in patients treated with Beovu, and
23 that the frequency at which these events are occurring continues to rise.

24
25 93. As of July 24, 2020, Novartis' postmarketing data website for Beovu cited
26 the following incidence rates for the adverse events of interest: 2.73 reports of retinal
27 vasculitis per 10,000 injections; 2.64 reports of retinal vascular occlusion per 10,000
28 injections; 4.76 reports of concomitant retinal vasculitis and retinal vascular occlusion per

1 10,000 injections; and when all categories are combined, 10.13 reports of retinal
2 vasculitis, retinal vascular occlusion, or retinal vasculitis with retinal vascular occlusion
3 per 10,000 injections.

4 94. As of September 25, 2020, Novartis' postmarketing data website for Beovu
5 cited the following incidence rates for the adverse events of interest: 4.50 reports of
6 retinal vasculitis per 10,000 injections; 3.00 reports of retinal vascular occlusion per
7 10,000 injections; 6.14 reports of concomitant retinal vasculitis and retinal vascular
8 occlusion per 10,000 injections; and when all categories are combined, 13.64 reports of
9 retinal vasculitis, retinal vascular occlusion, or retinal vasculitis with retinal vascular
10 occlusion per 10,000 injections.

11
12 95. As of October 23, 2020, Novartis' postmarketing data website for Beovu
13 cited the following incidence rates for the adverse events of interest: 5.13 reports of
14 retinal vasculitis per 10,000 injections; 3.22 reports of retinal vascular occlusion per
15 10,000 injections; 6.12 reports of concomitant retinal vasculitis and retinal vascular
16 occlusion per 10,000 injections; and when all categories are combined, 14.50 reports of
17 retinal vasculitis, retinal vascular occlusion, or retinal vasculitis with retinal vascular
18 occlusion per 10,000 injections.

19
20 96. As of November 20, 2020, Novartis' postmarketing data website for Beovu
21 cited the following incidence rates for the adverse events of interest: 5.08 reports of
22 retinal vasculitis per 10,000 injections; 3.24 reports of retinal vascular occlusion per
23 10,000 injections; 7.16 reports of concomitant retinal vasculitis and retinal vascular
24 occlusion per 10,000 injections; and when all categories are combined, 15.47 reports of
25 retinal vasculitis, retinal vascular occlusion, or retinal vasculitis with retinal vascular
26 occlusion per 10,000 injections.

27
28 97. As of June 30, 2020, the same month the Beovu product labeling was

1 revised to add a warning regarding retinal vasculitis and/or retinal vascular occlusion, 85
2 cases of retinal vasculitis and 3 cases of ocular vasculitis had been reported to FAERS
3 wherein Beovu was identified as the suspect product. Beovu was also identified as the
4 suspect product in 43 cases of retinal artery occlusion, 38 cases of retinal vascular
5 occlusion, and 3 cases of retinal vein occlusion reported to FAERS as of June 30, 2020.
6 These numbers have been reported, although based on well-established reporting
7 principles, these numbers vastly underestimate the true number of these events occurring
8 in Beovu users. Further, as specifically noted by Mones et al. in their publication
9 regarding Beovu-related retinal vasculitis and retinal vascular occlusion, when it comes
10 to postmarketing adverse event data, there is a “considerable possibility of
11 underreporting”.

12
13 98. Consistent with the large and growing body of evidence demonstrating a
14 causal relationship between Beovu and retinal vasculitis and retinal vascular occlusion,
15 and that Beovu confers a greater risk of vision-threatening inflammatory adverse effects
16 than alternative anti-VEGF treatments, Novartis has itself admitted to such an
17 association. In a Novartis-funded and authored review titled *Brolucizumab: evolution*
18 *through preclinical and clinical studies and the implications for the management of*
19 *neovascular age-related macular degeneration*, Nguyen et al. admit to the causal
20 relationship between Beovu and the injuries complained of herein, stating, “Amidst the
21 reports of ocular inflammation, including occlusive retinal vasculitis with significant
22 visual loss, ***that is associated with brolucizumab administration*** in eyes with
23 neovascular AMD” (emphasis added).

24
25 99. As a direct and proximate result of the dangerous and defective nature of
26 Beovu as described herein, Plaintiff suffered severe bodily injury, and resulting pain and
27 suffering, disability, disfigurement, mental anguish, loss of capacity for the enjoyment of
28 life, expense of hospitalization, medical and treatment. The losses are permanent and

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Plaintiff will continue to suffer the losses in the future.

FIRST CAUSE OF ACTION

STRICT LIABILITY – FAILURE TO WARN

1
2
3 100. Plaintiffs incorporate by reference herein each of the allegations heretofore
4 set forth in this Complaint as though fully set forth herein.
5

6 101. At all times relevant hereto, Beovu was defective and unreasonably
7 dangerous when it left the possession of Defendants in that it failed to contain warnings
8 of an adequate or sufficient nature as to alert consumers and physicians, including
9 Plaintiff and Plaintiff’s healthcare providers, to the dangerous risks associated therewith,
10 including, but not limited, to its propensity to cause serious and permanent eye injuries
11 including those which Plaintiff sustained. These risks and dangers were known and/or
12 reasonably knowable by Defendants prior to and during the time which Plaintiff was
13 prescribed and ingested Beovu.
14

15 102. At all times relevant hereto, Defendants failed to provide sufficient warnings
16 and instructions that would have put the general public, including Plaintiff and Plaintiff’s
17 physicians, on notice of the dangers and adverse effects caused by ingestion of Beovu,
18 including, but not limited to intraocular inflammation, retinal vasculitis, retinal vascular
19 occlusion, and other serious vision problems.
20

21 103. Defendants failed to provide warnings of such risks and dangers to Plaintiff
22 and Plaintiff’s healthcare providers as described herein, and further, concealed the known
23 risks and dangers and failed to warn of known or scientifically knowable risks and
24 dangers associated with Beovu from patients, the medical community, and consumers,
25 including Plaintiff, and Plaintiff’s healthcare providers.
26

27 104. Plaintiff was prescribed and did ingest Defendants’ Beovu in a manner
28 consistent with and as intended by Defendants.

1 105. Ordinary patients and consumers, such as Plaintiff, could not have
2 discovered or recognized any relevant potential risks and dangerous defects in
3 Defendants' Beovu through the exercise of reasonable care within their capacity.
4

5 106. Defendants, as entities materially involved in the development, testing,
6 manufacture, sale and/or distribution of Beovu, are held to the level of knowledge of an
7 expert in the field.
8

9 107. Plaintiff individually, and through his prescribing physician, reasonably
10 relied upon the skill, superior knowledge, and judgment of Defendants.
11

12 108. Despite their possession of knowledge regarding these risks and a their duty
13 to adequately warn of severe and dangerous adverse events associated with use of Beovu,
14 Defendants failed to properly warn the medical community and consumers, including
15 Plaintiff and Plaintiff's healthcare providers, that use of Beovu was associated with an
16 increased risk of serious vision problems including intraocular inflammation, retinal
17 vasculitis, retinal vascular occlusion, and other serious vision problems.
18

19 109. Beovu was designed, manufactured, distributed, sold and/or supplied by
20 Defendants, and was marketed while defective due to inadequate warnings, instructions,
21 labeling and/or inadequate testing in light of Defendants' knowledge of Beovu's innate
22 risks and dangers and attributable serious vision related adverse events.
23

24 110. As a direct and proximate result of the dangerous and defective nature of
25 Beovu, Plaintiff suffered Central Retinal Artery Occlusion, and resulting pain and
26 suffering, disability, disfigurement, mental anguish, loss of capacity for the enjoyment of
27 life, expense of hospitalization, and medical treatment. The losses are permanent and the
28 Plaintiff will continue to suffer the losses in the future.

1 **SECOND CAUSE OF ACTION**

2 **NEGLIGENCE**

3 111. Plaintiff incorporates by reference herein each of the allegations heretofore
4 set forth in this Complaint as though fully set forth herein.

5
6 112. At all times relevant hereto, Defendants were under a duty to exercise
7 reasonable care in advertising, analyzing, assembling, compounding, designing,
8 developing, distributing, formulating, inspecting, labeling, manufacturing, marketing,
9 packing, producing, promoting, processing, researching, selling, and testing Beovu to
10 ensure that use of Beovu did not result in avoidable injuries.

11
12 113. At all times relevant hereto, Defendants owed a duty to consumers,
13 physicians, and the general public to assess, manage, and communicate the risks, dangers,
14 and adverse effects of Beovu, and to warn consumers and the medical community,
15 including Plaintiff and Plaintiff's healthcare providers, of those risks, dangers, and
16 adverse effects.

17
18 114. Defendants' duties include, but are not limited to, carefully and properly
19 advertising, analyzing, assembling, compounding, designing, developing, distributing,
20 formulating, inspecting, labeling, manufacturing, marketing, packing, producing,
21 promoting, processing, researching, selling, and testing Beovu, which was placed in the
22 stream of commerce, and providing adequate information regarding the appropriate use
23 of Beovu.

24
25 115. Defendants negligently breached the above-described duties to Plaintiff by
26 committing negligent acts and/or omissions, including, but not limited to the following:

- 27
28 a. failing in their obligation to provide consumers and the medical community,

1 including Plaintiff and Plaintiff's healthcare providers, with accurate,
2 adequate and clinically relevant information, data and warnings regarding
3 the adverse health risks associated with use of Beovu, and/or that there
4 existed safer alternative pharmaceutical drugs to treat AMD;

5
6 b. failing to continually monitor, test, and analyze data regarding safety,
7 efficacy, and the prescribing practices for Beovu;

8
9 c. failing to review all adverse drug event information and to report any
10 information bearing upon the adequacy and/or accuracy of its warnings,
11 efficacy, or safety, including the risks and/or prevalence of side effects
12 caused by Beovu to consumers and the medical community, including
13 Plaintiff and Plaintiff's healthcare providers;

14
15 d. failing to provide adequate post-marketing warnings and instructions after
16 Defendants knew or should have known of the significant risks of, among
17 other things, adverse vision-related events and/or reactions, including, but
18 not limited to an increased risk for intraocular inflammation, retinal
19 vasculitis, retinal vascular occlusion and other severe vision problems
20 associated with use of Beovu;

21
22 e. failing to review all medical literature regarding Beovu and failing to report
23 data regarding the adequacy and/or accuracy of its warnings, efficacy, or
24 safety of Beovu;

25
26 f. failing to disclose the results of the testing and other information in their
27 possession regarding the potential for Beovu to cause vision-related adverse
28 events including, but not limited to, an increased risk for intraocular

1 inflammation, retinal vasculitis, retinal vascular occlusion and other severe
2 vision problems;

3
4 g. representing that Beovu was safe for use when, in fact, Defendants knew or
5 should have known that it was unsafe for use and that Beovu use was
6 associated with vision-related events and/or reactions, including, but not
7 limited to an increased risk for intraocular inflammation, retinal vasculitis,
8 retinal vascular occlusion and other severe vision problems;

9
10 h. promoting and marketing Beovu for use despite the fact that Defendants
11 knew or should have known that Beovu use was associated with vision-
12 related adverse events and/or reactions, including, but not limited to an
13 increased risk for intraocular inflammation, retinal vasculitis, retinal
14 vascular occlusion and other severe vision problems;

15
16 i. promoting and marketing Beovu as safe and effective for use when, in fact,
17 it was unsafe, especially as compared to other available therapies to treat
18 AMD;

19
20 j. failing to act as reasonably prudent drug manufacturers in advertising,
21 analyzing, assembling, compounding, designing, developing, distributing,
22 formulating, inspecting, labeling, manufacturing, marketing, packaging,
23 producing, promoting, processing, researching, selling, and testing Beovu;

24
25 k. failing to exercise ordinary care in advertising, analyzing, assembling,
26 compounding, designing, developing, distributing, formulating, inspecting,
27 labeling, manufacturing, marketing, packing, producing, promoting,
28 processing, researching, selling, and testing Beovu so as to reveal and

1 communicate the risk of vision-related adverse events and/or reactions,
2 including, but not limited to, an increased risk for intraocular inflammation,
3 retinal vasculitis, retinal vascular occlusion and other severe vision problems
4 to consumers and the medical community, including Plaintiff and Plaintiff's
5 healthcare providers;

6
7 l. failing to conduct adequate post-marketing studies, non-clinical and clinical
8 testing, and post-marketing surveillance and analyses to determine and
9 subsequently communicate the safety profile and side effects associated with
10 the use of Beovu;

11
12 m. continuing to promote the safety and effectiveness of Beovu while
13 downplaying its risks, even after Defendants knew or should have known of
14 the significant risks of Beovu use;

15
16 n. failing to provide consumers and the medical community, including Plaintiff
17 and Plaintiff's healthcare providers, with scientific data which indicated that
18 Beovu was unreasonably dangerous due to its propensity to cause vision-
19 related adverse events including, but not limited to, an increased risk for
20 intraocular inflammation, retinal vasculitis, retinal vascular occlusion and
21 other severe vision problems;

22
23 o. negligently and carelessly over-promoting Beovu in a zealous and
24 unreasonable manner, without regard for the potential dangers which it
25 posed to users; and/or

26
27 p. failing to adequately test Beovu on patients that had a prior history of VEGF
28 use especially in light of the plan to market precisely to that population of

1 patients.

2
3 116. Although Defendants knew or should have known that Beovu causes
4 unreasonably dangerous side effects, including an increased risk for intraocular
5 inflammation, retinal vasculitis, retinal vascular occlusion and other severe vision
6 problems, they continue to market Beovu, despite the fact there are safer and more or
7 equally effective alternative therapies to treat AMD.

8
9 117. Defendants knew or should have known that failure to exercise ordinary
10 care, as described herein, would result in serious injury to patients, such as Plaintiff.

11
12 118. As a direct and proximate result of the dangerous and defective nature of
13 Beovu Plaintiff suffered Central Retinal Artery Occlusion, and resulting pain and
14 suffering, disability, disfigurement, mental anguish, loss of capacity for the enjoyment of
15 life, expense of hospitalization, and medical care and treatment. The losses are
16 permanent and the Plaintiff will continue to suffer the losses in the future.

17 **THIRD CAUSE OF ACTION**

18 **FRAUDULENT MISREPRESENTATION**

19 119. Plaintiff incorporates by reference herein each of the allegations heretofore
20 set forth in this Complaint as though fully set forth herein.

21
22 120. Defendants' fraudulent, intentional and material misrepresentations and
23 omissions regarding the safety and efficacy of Beovu and of Beovu's side effects,
24 including that concerning an increased risk for intraocular inflammation, retinal
25 vasculitis, retinal vascular occlusion and other severe vision problems were
26 communicated to Plaintiffs directly through promotional materials, advertising, product
27 inserts, and the product monograph with the intent that Plaintiff use Beovu. The safety
28 and efficacy of Beovu was also fraudulently and intentionally misrepresented to

1 Plaintiff's healthcare providers with the intent that such misrepresentations would result
2 in Beovu being prescribed and administered to Plaintiff.

3
4 121. Defendants knew that the material representations they were making
5 regarding the safety, efficacy, and side effects of Beovu were false.

6
7 122. Defendants fraudulently and intentionally made misrepresentations and/or
8 actively concealed, suppressed, or omitted this material information with the intention
9 and specific desire to induce consumers and the medical community, including Plaintiff
10 and Plaintiff's healthcare providers, to use, prescribe, and purchase Beovu.

11
12 123. Defendants fraudulently and intentionally knew that Plaintiff and/or
13 Plaintiff's healthcare providers would rely upon such material misrepresentations and/or
14 omissions in selecting Beovu for the treatment of Plaintiff.

15
16 124. Defendants made these material misrepresentations and/or omissions and
17 actively concealed adverse information at a time when they, their agents and/or their
18 employees knew that Beovu had certain defects, dangers, and characteristics that differed
19 from what had been represented to the medical community and the consuming public,
20 including Plaintiff's healthcare providers and Plaintiff. Those misrepresentations and
21 omissions include, but are not limited to, the following:

- 22
23 a. Defendants failed to disclose or actively concealed the fact that their
24 preclinical and premarket clinical testing, and post-marketing surveillance
25 was inadequate to sufficiently determine the safety and side effects of
26 Beovu;
- 27
28 b. Defendants failed to disclose or actively concealed data demonstrating that

1 Beovu increased the risk of vision-related adverse events including, but not
2 limited to, intraocular inflammation, retinal vasculitis, retinal vascular
3 occlusion and other severe vision problems;

4
5 c. Defendants failed to include or provide adequate warnings along with Beovu
6 regarding potential and established risks, and the nature, scope, severity, and
7 duration of any serious side effects of Beovu use, including, but not limited
8 to, an increased risk of intraocular inflammation, retinal vasculitis, retinal
9 vascular occlusion and other severe vision problems, when compared to
10 other available therapies to treat AMD;

11
12 d. Defendants concealed and misrepresented, and continue to conceal and
13 misrepresent, past and present facts of which Defendants were aware, and
14 concealed their knowledge of a link between the use of Beovu and
15 dangerous side effects, including the increased risk of intraocular
16 inflammation, retinal vasculitis, retinal vascular occlusion and other severe
17 vision problems, to consumers and the medical community, including
18 Plaintiff and Plaintiff's healthcare providers;

19
20 e. Defendants misrepresented the number of retinal vasculitis, retinal vascular
21 occlusion, and intraocular inflammation adverse events suffered by patients
22 in the Beovu clinical trials; and/or

23
24 f. Defendants promoted Beovu as a safe and effective treatment for patients
25 with a prior history of using other anti-VEGF therapies despite the fact that
26 the Defendants had not properly studied Beovu in that patient population.

27
28 125. Defendants' material misrepresentations and/or active concealment,

1 suppression, and omissions were perpetuated directly and/or indirectly by Defendants,
2 their sales representatives, employees, distributors, agents and/or detail persons, through
3 databases, printouts, monographs, product labeling and other information drafted,
4 prepared, marketed, sold, and supplied by Defendants, their sales representatives,
5 employees, distributors, agents and/or detail persons.

6
7 126. Defendants' material misrepresentations and/or active concealment,
8 suppression, and omissions constitute a continuing tort.

9
10 127. Through its product inserts and other public statements, Defendants continue
11 to misrepresent the serious potential vision-related risks and complications associated
12 with use of Beovu.

13
14 128. Defendants had a post-sale duty to timely warn physicians including
15 Plaintiff's healthcare providers, and consumers, such as Plaintiffs, about the potential
16 risks and complications associated with use of Beovu.

17
18 129. Defendants fraudulently and intentionally misrepresented the safety and
19 efficacy of Beovu in their labeling, advertising, product inserts, promotional materials, or
20 other marketing resources and materials.

21
22 130. If Plaintiff's healthcare providers and Plaintiff had known the true facts
23 concerning the risks of Beovu use, in particular, the risk of vision-related adverse events
24 and/or reactions, including, but not limited to an increased risk for intraocular
25 inflammation, retinal vasculitis, retinal vascular occlusion and other severe vision
26 problems, they would not have prescribed or used Beovu and would have instead
27 prescribed and used a safer alternative pharmaceutical drug or no drug at all.

1 131. Plaintiff and Plaintiff's healthcare providers' reliance upon Defendants'
2 material misrepresentations were justified, among other reasons, because said
3 misrepresentations and omissions were made by individuals and entities who were in a
4 position of knowledge of the true facts concerning Beovu, while Plaintiff and Plaintiff's
5 healthcare providers were not in a position to know the true facts concerning Beovu, and
6 because Defendants overstated the benefits and safety of Beovu, and concomitantly
7 downplayed the risks of its use, including, but not limited to, an increased risk for
8 intraocular inflammation, retinal vasculitis, retinal vascular occlusion and other severe
9 vision problems, thereby inducing Plaintiff's healthcare providers to prescribe and
10 Plaintiff to use Beovu, in lieu of other safer alternatives, or no drug at all.

11
12 132. As a direct and proximate result of the dangerous and defective nature of
13 Beovu Plaintiff suffered Central Retinal Artery Occlusion, and resulting pain and
14 suffering, disability, disfigurement, mental anguish, loss of capacity for the enjoyment of
15 life, expense of hospitalization, and medical care and treatment. The losses are
16 permanent and the Plaintiff will continue to suffer the losses in the future.

17 **FOURTH CAUSE OF ACTION**
18 **NEGLIGENT MISREPRESENTATION**

19 133. Plaintiff incorporates by reference herein each of the allegations heretofore
20 set forth in this Complaint as though fully set forth herein.

21
22 134. Defendants' negligent material misrepresentations and omissions regarding
23 the safety and efficacy of Beovu and of Beovu's side effects, including that concerning
24 an increased risk for intraocular inflammation, retinal vasculitis, retinal vascular
25 occlusion and other severe vision problems were communicated to Plaintiffs directly
26 through promotional materials, advertising, product inserts, and the product monograph
27 with the intent that Plaintiff use Beovu. The safety and efficacy of Beovu was also
28 negligently misrepresented to Plaintiff's healthcare providers with the intent that such

1 misrepresentations would result in Beovu being prescribed and administered to Plaintiff.
2

3 135. Defendants either knew or should have known that the material
4 representations they were making regarding the safety, efficacy, and side effects of
5 Beovu were false.
6

7 136. Defendants negligently made misrepresentations and/or actively concealed,
8 suppressed, or omitted this material information with the intention and specific desire to
9 induce consumers and the medical community, including Plaintiff and Plaintiff's
10 healthcare providers, to use, prescribe, and purchase Beovu.
11

12 137. Defendants negligently knew or should have known that Plaintiff and/or
13 Plaintiff's healthcare providers would rely upon such material misrepresentations and/or
14 omissions in selecting Beovu for the treatment of Plaintiff.
15

16 138. Defendants made these material misrepresentations and/or omissions and
17 actively concealed adverse information at a time when they, their agents and/or their
18 employees knew or should have known that Beovu had certain defects, dangers, and
19 characteristics that differed from what had been represented to the medical community
20 and the consuming public, including Plaintiff's healthcare providers and Plaintiff. Those
21 misrepresentations and omissions further include, but are not limited to, the following:

- 22 a. Defendants failed to disclose or actively concealed the fact that their
23 preclinical and premarket clinical testing, and post-marketing surveillance
24 was inadequate to sufficiently determine the safety and side effects of
25 Beovu;
26
27 b. Defendants failed to disclose or actively concealed data demonstrating that
28 Beovu increased the risk of vision-related adverse events including, but not

1 limited to, intraocular inflammation, retinal vasculitis, retinal vascular
2 occlusion and other severe vision problems;

3
4 c. Defendants failed to include or provide adequate warnings along with Beovu
5 regarding potential and established risks, and the nature, scope, severity, and
6 duration of any serious side effects of Beovu use, including, but not limited
7 to, an increased risk of intraocular inflammation, retinal vasculitis, retinal
8 vascular occlusion and other severe vision problems, when compared to
9 other available therapies to treat AMD;

10
11 d. Defendants concealed and misrepresented, and continue to conceal and
12 misrepresent, past and present facts of which Defendants were aware, and
13 concealed their knowledge of a link between the use of Beovu and
14 dangerous side effects, including the increased risk of intraocular
15 inflammation, retinal vasculitis, retinal vascular occlusion and other severe
16 vision problems, to consumers and the medical community, including
17 Plaintiff and Plaintiff's healthcare providers;

18
19 e. Defendants misrepresented the number of retinal vasculitis, retinal vascular
20 occlusion, and intraocular inflammation adverse events suffered by patients
21 in the Beovu clinical trials; and/or

22
23 f. Defendants promoted Beovu as a safe and effective treatment for patients
24 with a prior history of using other anti-VEGF therapies despite the fact that
25 the Defendants had not properly studied Beovu in that patient population.

26
27
28 139. Defendants' material misrepresentations and/or active concealment,

1 suppression, and omissions were perpetuated directly and/or indirectly by Defendants,
2 their sales representatives, employees, distributors, agents and/or detail persons, through
3 databases, printouts, monographs, product labeling and other information drafted,
4 prepared, marketed, sold, and supplied by Defendants, their sales representatives,
5 employees, distributors, agents and/or detail persons.

6
7 140. Defendants' material misrepresentations and/or active concealment,
8 suppression, and omissions constitute a continuing tort.

9
10 141. Through its product inserts and other public statements, Defendants continue
11 to misrepresent the serious potential vision-related risks and complications associated
12 with use of Beovu.

13
14 142. Defendants had a post-sale duty to timely warn physicians including
15 Plaintiff's healthcare providers, and consumers, such as Plaintiffs, about the potential
16 risks and complications associated with use of Beovu.

17
18 143. Defendants negligently misrepresented the safety and efficacy of Beovu in
19 their labeling, advertising, product inserts, promotional materials, or other marketing
20 resources and materials.

21
22 144. If Plaintiff's healthcare providers and Plaintiff had known the true facts
23 concerning the risks of Beovu use, in particular, the risk of vision-related adverse events
24 and/or reactions, including, but not limited to, an increased risk for intraocular
25 inflammation, retinal vasculitis, retinal vascular occlusion and other severe vision
26 problems, they would not have prescribed or used Beovu and would have instead
27 prescribed and used a safer alternative pharmaceutical drug or no drug at all.

1 145. Plaintiff and Plaintiff's healthcare providers' reliance upon Defendants'
2 material misrepresentations were justified, among other reasons, because said
3 misrepresentations and omissions were made by individuals and entities who were in a
4 position of knowledge of the true facts concerning Beovu, while Plaintiff and Plaintiff's
5 healthcare providers were not in a position to know the true facts concerning Beovu, and
6 because Defendants overstated the benefits and safety of Beovu, and concomitantly
7 downplayed the risks of its use, including, but not limited to, an increased risk for
8 intraocular inflammation, retinal vasculitis, retinal vascular occlusion and other severe
9 vision problems, thereby inducing Plaintiff's healthcare providers to prescribe and
10 Plaintiff to use Beovu, in lieu of other safer alternatives, or no drug at all.

11
12 146. As a direct and proximate result of the dangerous and defective nature of
13 Beovu Plaintiff suffered Central Retinal Artery Occlusion, and resulting pain and
14 suffering, disability, disfigurement, mental anguish, loss of capacity for the enjoyment of
15 life, expense of hospitalization, and medical care and treatment. The losses are
16 permanent and the Plaintiff will continue to suffer the losses in the future.

17 **FIFTH CAUSE OF ACTION**

18 **PUNITIVE DAMAGES**

19 147. Plaintiff incorporates by reference herein each of the allegations heretofore
20 set forth in this Complaint as though fully set forth herein.

21
22 148. As discussed herein, Defendants have intentionally misrepresented the
23 clinical trial data for Beovu to FDA, healthcare providers, and the general public in order
24 to mask the true risk of retinal vascular occlusion, retinal vasculitis, intraocular
25 inflammation, and other severe eye injuries related to Beovu use. Those
26 misrepresentations continue to the present.

27
28 149. Defendants have engaged in marketing efforts seeking to induce healthcare

1 providers to switch their patients from other anti VEGF agents to Beovu despite lacking
2 the necessary evidence to demonstrate that Beovu is safe and effective in this population
3 and despite affirmative evidence that the drug is not safe in this patient population.
4

5 150. Defendants have intentionally misled healthcare providers and the general
6 public in making non-inferiority claims for Beovu as compared to other anti VEGF
7 agents despite possessing the knowledge that these claims are false.
8

9 151. Defendants have intentionally failed to properly warn healthcare providers
10 about the true risk of retinal vasculitis, retinal vascular occlusion, intraocular
11 inflammation, and other severe eye injuries related to Beovu use despite possessing
12 knowledge that Beovu causes these serious adverse events.
13

14 152. Defendants' actions were willful and malicious in that Defendants' conduct
15 was carried on with a conscious disregard for the safety and rights of Plaintiff.
16 Defendants' unconscionable conduct thereby warrants an assessment of exemplary and
17 punitive damages against Defendants in an amount appropriate to punish Defendants, and
18 deter similar conduct in the future.
19

20 153. As a direct and proximate result of the dangerous and defective nature of
21 Beovu Plaintiff suffered Central Retinal Artery Occlusion, and resulting pain and
22 suffering, disability, disfigurement, mental anguish, loss of capacity for the enjoyment of
23 life, expense of hospitalization, and medical care and treatment. The losses are
24 permanent and the Plaintiff will continue to suffer the losses in the future.
25

26 WHEREFORE, Plaintiff prays for judgment against Defendants, as follows:
27

- 28 a. For general damages in an amount to be proven at the time of trial;

