Stargardt Disease (STGD1)

FDA Patient-led Listening Session

Minutes of the June 30, 2022, Meeting

Background

Stargardt disease is a rare, genetic condition that affects the retina, the light-sensing layer in the back of the eye. Stargardt disease leads to irreversible, progressive vision loss, causing challenges in the performance of activities of daily living, such as driving, reading, writing, or recognizing faces. Although rare, Stargardt disease is most common form of inherited juvenile macular degeneration. No treatment currently exists, and the disease progresses to legal blindness in almost all patients.

Overview

On June 30, 2022, six patients and four caregivers representing a total of 11 Stargardt patients, along with one retina specialist addressed the Food and Drug Administration (FDA) in a virtual FDA Patient Listening Session and provided first-hand accounts of what it is like living and caring for someone with this devastating condition. Numerous members from the FDA attended the meeting, representing 16 offices/divisions.

This document contains a summary of the topics covered, and of the patient and caregiver testimonies.

Key Points presented by speakers

1. Stargardt Disease is a rare, genetic disease caused by mutations on the ABCA4 gene.
2. Stargardt causes progressive and irreversible vision loss, leading to legal blindness, which has a severe and devastating impact on daily life.
3. Most patients experience onset of symptoms of vision loss during their teenage years.
4. The patient journey to proper diagnosis can take years, despite advances in genetic testing.
5. Patients rapidly lose the ability to read, drive, and recognize faces, leading to difficulty in school, work, social situations, and loss of independence.
6. No FDA-approved treatment exists. Potential drugs and therapies, including cell and gene therapies, have been explored for over 20 years.
7. As of June 2022, one potential treatment, ALK-001, has shown positive efficacy. Several of the listening session speakers have been involved in that trial.
8. Patients have challenges identifying clinical trials in which they could qualify. Clinical trials take many years to conduct due to the progressive nature of the disease requiring long treatment periods, as well as the small patient population and even smaller number of correctly diagnosed patients. Recently completed trials have taken over five years.

9. Time is of the essence for patients, as the only potential treatment with efficacy has shown an ability to slow disease progression but is not expected to restore vision already lost.
10. Early treatment is critical to preserve vision for as long as possible.

Objectives of session

- Share personal experiences of patients and caregivers living with Stargardt disease
- Share priorities for future treatments and clinical trials as there are no approved treatments
- Further inform FDA's understanding of this condition beyond what can be found in the medical literature, or what may be prioritized by researchers or drug developers
- Open a dialogue between the FDA and the Stargardt community to enable the FDA to take our voices into consideration as they review new drugs/treatments that could benefit patients

Summary of topics discussed

Topic: What is Stargardt Disease?

- Genetic disease that causes retinal degeneration leading to blindness, which is caused primarily by mutations in the ABCA4 gene
- ABCA4-related retinopathies also include a broader range of phenotypes including fundus flavimaculatus, pattern dystrophy, and cone-rod dystrophy. This means that treatments for ABCA4-related retinopathy would encompass a greater number of individuals than those diagnosed with Stargardt Disease alone. An effective treatment for Stargardt disease could also be effective for other ABCA4-related diseases.
- Patients with Stargardt Disease primarily lose their central vision, which severely impacts or eliminates a person's ability to read, recognize faces, and drive a car, among other things.
- Stargardt Disease is the 3rd largest monogenic recessive disease. Monogenic means that it is caused by a single gene.
- Of the 6 most common monogenic recessive diseases, Stargardt is the only one that remains without treatment.

Topic: Prevalence of Stargardt Disease

- Stargardt disease is a rare condition: Commonly reported estimate of 1 in 10,000 was published in the 1980s, based on empirical information, before the gene for Stargardt was identified
- Number of people actually diagnosed is estimated to be significantly smaller
- No precise U.S. data exists, but data from countries with centralized healthcare systems suggest a diagnostic prevalence of ~1 in 20,000 (Netherlands) and ~1 in 15,000 (U.K.)
- U.S. diagnostic prevalence is likely significantly lower due to noncentralized system, lack of specific diagnostic code, disparities in access to healthcare
- A small number of diagnosed cases makes conducting clinical trials challenging. Clinical trials can take a long time to enroll even a small number of patients.

- Because of these challenges and the severity, irreversible and progressive nature of Stargardt Disease, it was suggested that the FDA take into consideration the challenges of conducting multiple trials when reviewing treatments for approval.

Topic: Age of Onset

- Symptoms can begin in early childhood
- Average age is in one's teenage years
- Most people live with visual impairment for most of their lives
- Late onset can occur in middle-aged people

Topic: Symptoms and Treatment

- Causes devastating irreversible vision loss that affects all aspects of life, characterized by progressive degeneration of the retina
- Typically leads to legal blindness
- No treatment exits

Topic: Diagnosis and Progression

- The road to diagnosis is long and winding, with high costs of time, emotion, and money
- Patients experience misdiagnosis (~ 40%)
- Delayed diagnosis (4 years)
- Numerous visits to doctors
- Barriers to access genetic testing
- Time is of the essence to obtain treatment for the patient to maintain vision
- Speed of progression is associated with the age at symptom onset/diagnosis
- The younger the age of diagnosis, the quicker legal blindness

Topic: Impact on Daily Life

- Relationships and social life greatly impacted due to inability to recognize faces, communication becomes difficult because patients cannot see facial expressions or emotions of others, many withdraw from previously enjoyed activities and social events, anxiety and depression sometimes occur as daily life and personal interactions become harder
- Considerable accommodations required for school and work
- Inability to drive
- Difficulty reading and writing
- Difficulty recognizing faces
- Loss of independence
- Caregivers are necessary
- Depending on when patients reach legal blindness, career goals and aspirations may have to be altered
- Many patients expressed the loss of long-held personal dreams including pursuing particular careers and playing sports. Many also reported changes in personality due to severely limited ability to interact with others in ways that require sight. Anxiety and

depression were also discussed by some patients as the reality of losing their vision set in and their way of life deteriorated

Topic: Treatments and Therapies Under Investigation

- Presenters provided a brief overview about the state of clinical trials/investigational medical products and their preferences for potential treatment.
- No FDA approved treatment exists.
- Therapies under investigation include oral products (multiple trials ongoing, one product has positive efficacy data), injections in the eye (data expected 2022), gene therapy (no efficacy data to date), stem cell therapy (no efficacy data to date).
- Oral products include: ALK-001 (Phase 2, granted breakthrough therapy designation by FDA), Emixustat (Phase 3), STG-001 (Phase 2), LBS-008 (Phase 2)
- There is a clinical trial involving injections in the eye with data expected in 2024 using Zimura (Phase 2).
- Gene therapy and stem cell therapy appear to be in the works; however, no efficacy data to date.
- Early treatment is paramount, as the disease is progressive and vision loss is irreversible
- Patients are seeking at a minimum a treatment option that will slow or stop the progression. Any rate of slowing would be acceptable to the patients, and even a small percentage could have a dramatic impact given the severity of the symptoms.

Patients Represented

Summary: 6 patients and 4 caregivers represented a total of 11 Stargardt patients spoke specifically about age of onset, path to diagnosis, treatment received and pursued, impact on daily life, personal struggles with the disease, and treatment preferences and priorities. The following summarizes personal testimonies from the patients and the caregivers.

Speaker 1: Adriann Keve

- Current age: 40
- Age of Diagnosis: 12
- Preference for Treatments: Gene therapy, stem cell therapy

Summary of Adriann's Patient Testimony:

- Symptoms first presented as a young child having trouble reading, needing to sit very close to board in classrooms, holding books very close to face, and sitting in the front row at school. Taken to optometrist as a child and was accused of staring at the sun or lying about vision loss. The doctor dismissed the problem and said, "There's nothing wrong with her eyes. She's clearly making it up for attention, and what she really needs is a psychiatrist." Her parents continued to pursue answers to the vison problems she was experiencing, and Adriann was later diagnosed with Stargardt Disease at the University of Iowa at the age of 12. Adriann participated in a research study at the University of Iowa where she learned about the gene mutation.
- Middle School and High School were a struggle for her as she was already shy. Fell behind academically, feared being called on to read or solve math problems, skipped extracurricular activities. Overcame these challenges and managed to make honor roll every semester.
- Pursued getting a driver's license and was granted restricted use permit at the age of 18.
- Went to college but fell behind first semester, ended up on academic probation, and dropped out freshman year.
- Got a job that required minimal paperwork and computer time to hide vision impairment.
- Desire to go to college remained and she ended up going back.
- Significant incident occurred driving to class on a narrow, two-lane road, speed limit 45 when she almost hit a jogger that she didn't see until she was parallel with her. This caused her to give up her driver's license.
- Adriann's visual acuity is now 20/280, central vision is lost and cannot recognize faces or read standard print, she has extreme light sensitivity, poor depth perception, and blinding flashes of light from retina misfiring. She carries a cane to assist with walking.
- Physical and mental fatigue occur as the daily challenges of not being able to see mount.
- Uses technology to assist with vision loss, but it's expensive, quickly becomes obsolete, and is not sustainable for most people.
- Would love to see gene therapy or some other treatment to slow or even halt progression in people in the early stages. For patients with advanced progression, she would love to see a complete cure.

Speaker 2: Tara, mother/caregiver of Vivian and Emmett:

Vivian:

- Current age: 15
- Age of diagnosis: 15
- Preference for treatment: Involved in a clinical trial, hope is for this to restore all lost vision, and/or halt the progression

Summary of Tara's (mother) Patient Testimony for Vivian:

- Diagnosed in November 2021, Tara mentioned missing her diagnosis because 85% of--the time the older sibling presents with symptoms first
- Vivian has central vision loss, blind spots, double vision, and uses one of the strongest bifocal prescriptions left available to her.
- The past year her vision has declined to 20/60.
- Vivian was an avid reader and has had to give that up due to her vision loss.
- She has trouble identifying friends, seeing the board at school.
- Vivian takes mostly honors classes, and her mental health has suffered because of additional struggle of seeing her work. Tara has found her crying in her room on many occasions as Vivian struggles to keep up with her schoolwork.
- Vivian misses reading and playing the piano and being able to read music.
- Vivian describes her blind spots as annoying and described them as TV static or seeing stars when you get up too quickly from lying down.
- Vivian is currently enrolled in clinical trial and hopes to have her vision restored or at least halt vision loss.

Emmett:

- Current age: 14
- Age of diagnosis: 12
- Preference for treatment: Involved in a clinical trial, hope is for this to restore all lost vision, and/or halt the progression

Summary of Tara's (mother) Patient Testimony for Emmett:

- 3 years before diagnosis on January 27, 2021, Emmett started to show signs of a vision impairment as he could not see the board at school. Emmett was taken to a doctor and was told he did not need glasses. As other patients mentioned in the listening session, the doctor did not believe they had a problem with their eyesight and that Emmett was faking symptoms to get glasses.
- During COVID-19, Emmett's family hired a retired schoolteacher to help teach 6 boys while school was not in session. The teacher contacted Emmett's mother and texted a photo of Emmett sitting with his face a few inches from his laptop screen.
- Emmett recognized his impairment and expressed he would not be able to attend school because he could not see anything.
- The appointment with an optometrist gave a diagnosis of macular dystrophy. A scan of the eyes was required to make the full diagnosis of Stargardt Disease. Emmett was 12 years old.

- Emmett eventually gave up his passion for hip hop dance due to the intense workload, exposure to stage lights that he fears may cause additional vision loss, and interference from his blind spots that makes following choreography difficult.
- Emmett suffers from significant central vision loss, corrected vision of 20/100.
- Emmett cannot see the board at school, identify his friends in the hallways, read books, see faces, and will likely never obtain a driver's license.
- Drastic psychological and emotional impact and has been bullied at school and called the "blind boy"
- Tara was recently confronted with one of the saddest days of her life when Emmett revealed he could no longer recognize her face from 4 feet away.
- Emmett suffers from sensitivity to light, spends most of time in very dim lighting
- Family time no longer includes watching TV together or attending shows or attending sporting events
- Emmett worries everyday about losing more of his vision and struggles with all of life being more difficult because he cannot see.
- His blind spots appear as a bunch of colorful dots in the middle of his vision.
- Currently enrolled in a clinical trial and hopes this will preserve what vision he has left and achieve full restoration of his sight.

Speaker 3: Lucas Carmo

- Current age: 27
- Age of Diagnosis: 8
- Preference for Treatment: Stopping the progression of the disease, regeneration for lost cells, restoring visual acuity

Summary of Lucas Carmo's Patient Testimony:

- Diagnosed at age 8, signs that prompted visits to the ophthalmologist included not being able to read the blackboard from 4th row of chairs in the classroom, mother noticed Lucas needed to sit closer to the TV.
- Three visits to the ophthalmologist were attended before the doctor realized something was wrong with Lucas's eyes. Lucas was unable to read the eye charts and needed a picture of the retina to see what was wrong with his eyes.
- Stargardt disease was diagnosed, and Lucas was told there was no treatment, and he would eventually be legally blind. No genetic testing was available at that time. He did get genetic testing in 2017 that confirmed the diagnosis.
- Lucas discussed growing up with Stargardt stating that a year after diagnosis his vision really started to change. He needed to be in the first row at school, he began to be bullied, he was no longer able to play with friends, his night vision got worse, had problems with bumping into things and hurting himself.
- At the age of 14 his vision was no longer functional as he could no longer read the board at school or read books. At 14 his classmates began to read aloud to him, he needed help crossing streets, and a blind spot appeared in his central vision (which got larger with age and appeared as lights and dots constantly moving). Lucas described the blind spot as TV static. Today the blind spot covers 80% of his visual field.
- Today Lucas struggles with daily challenges of regular tasks taking longer to complete, inability to see people's faces which makes socializing difficult, inability to read social cues from others facial expressions; he has no friends or a girlfriend, spends most days at home, unable to go out alone on most occasions, has had to give up playing sports, and finds it very difficult to find a job.
- Lucas was able to graduate high school in 2011 but did not start college until 2019 due to depression and feelings of uselessness. His dream of becoming a medical doctor came to an end when he was told by a school advisor that he shouldn't mention his visual impairment.
- Lucas has also dealt with people accusing him of lying about his impairment because he does not use a walking cane.
- Mental health has been a struggle for Lucas. He struggles specifically with depression and anxiety. He has addressed that with medication and counseling. Weight gain, difficulty sleeping, panic attacks have resulted from the depression. His posture has also suffered.
- Lucas seeks a treatment that stops the disease progression as well as restores lost vision. Restoration of some functional vision would give Lucas the freedom to live and accomplish his goals. It would give him the ability to regain some independence and quality of life.

Speaker 4: Evie Baxter

- Current Age: 17
- Age of Onset: 11
- Preference for Treatment: Continue taking oral investigational drug ALK-001 after the conclusion of the clinical trial.

Summary of Evie's Patient Testimony:

- Short clip from her documentary, *The Sightseers*[1], was played highlighting the travels of Evie and her mother, Victoria, as they go see all they can before Evie loses her sight.
- Evie's testimony recounted the difficult 6-8 hours of constant eye testing that revealed she had Stargardt Disease.
- Since Evie's diagnosis she struggles with doing little things that were previously easy such as reading a menu at a restaurant, walking into a dark room, walking home when it is dark, finding herself standing in a bus section in London because she couldn't see it.
- Evie has lived with Stargardt Disease for 6 years. She cannot see her own facial features in a mirror. She described it as, "Melting and blurring into her skin tone". Sharp features of her family can no longer be seen.
- Her passion for art has been affected deeply. As she realized her ability to draw and create became stagnant or worse in some cases, she described this time as "a part of her soul dying". As a result, Evie spends many days crying in bed.
- Every time Evie adapted to a new level of vision loss her eyesight would worsen even further and she would have to repeat the adaptation process again.
- Evie describes her reaction to this disease as heartbreaking, making her want to hide from the world.
- Evie has gained some hope and happiness as she participates in a clinical trial for an investigational medical product (ALK-001) for Stargardt Disease.. She describes her experience with the investigational medical product as giving her the ability to enjoy her passions again, hope for her disease to stop progressing, and hope for future restoration of her vision.

[1] https://doclandfilms.com/portfolio/the-sightseers/

Speaker 5: Victoria Smurfit (Evie's mother/caregiver)

- Victoria describes her experience since Evie's diagnosis as banging on doors and asking questions. She took Evie to see the top clinicians in both the US and Europe and inquired about the clinical trials available. Every doctor responded that in their opinion, should the patient be their child, that they would choose the oral investigational drug ALK-001 for their family.
- ALK-001 has for Evie had no side effects and since receiving it, she has not ended up in Victoria's arms on the kitchen floor crying because what she could vaguely see yesterday, she cannot see today.
- Victoria's dream is for Evie to see her future child's face.
- Victoria commented on Stargardt Disease "taking your sight, your confidence, focus, and at times your hope."

Speaker 6: Brady

- Current Age: 26
- Age of Diagnosis: 19.5
- Preference for Treatment: Stopping and/or slowing the progression. Ultimately a cure to reverse effects.

Brady also spoke on behalf of her brother Chase.

- Current Age: 23
- Age of Diagnosis (asymptomatic at the time): 16.5
- Preference for Treatment: Slow and/or stop the progression. Ultimately a cure to reverse effects.

Summary of Brady's Patient Testimony:

- Brady provided a tearful testimony of her great loss and described her life before the diagnosis, and life now with declining vision and the realities of how that has changed her dreams and plans for her future.
- Brady had a long-time dream of becoming a pediatrician but had to stop her education in medical school due to her visual acuity declining.
- Her path to diagnosis at the age of 19 included visiting an ophthalmologist who identified her inability to read the eye chart. The doctor wondered if Brady had hit her head or had some sort of accident.
- Brady was referred to 3 specialists before confirming with genetic testing that she had Stargardt Disease. Brady's brother, Chase, was diagnosed through genetic testing at age 16 but is not symptomatic at this time.
- Brady described her life before Stargardt Disease as good and normal.
- Brady's life now is marked by decreased visual acuity, difficulty reading and recognizing faces from a distance.
- Eyeglasses have not been assistive for Brady. Through college Brady worked with the adaptive department to help her with testing, seating in the classroom, visual aids, and font.
- Brady finds herself making excuses to not participate in things she previously enjoyed such as games or large group gatherings. It is overwhelming because she cannot recognize people. Brady also doubts her ability to be a mother one day and questions if that will be a right decision for her.
- Brady discussed side effects from Stargardt Disease. She fell into a deep depression and has developed social anxiety.
- Brady mentioned that being born blind would be easier than having your vision being slowly taken from you.
- As for trials or treatments Brady would like to slow and/or stop the progression of the disease. Ultimately wants a cure to reverse the effects.

Brady's Summary of Chase (her brother):

- Diagnosed at 16.5, current age 23 works as a paramedic. Chase has just been accepted into the fire department as a paramedic firefighter.
- Chase was diagnosed as a means to help his sister enter a Stargardt clinical trial.
- No visual effects are suffered by Chase: he was diagnosed before the onset of symptoms.

- Because of his unique circumstances of being diagnosed with Stargardt before the onset of symptoms, he was placed into an open label arm of the ALK-001 clinical trial., At that time, there was no clinical trial of ALK-001 for which Brady qualified, and so she could not be enrolled.
- Chase still has no degradation in his vision. He has perfect vision, and they believe it is related to the investigational medical product.
- Chase's preference for trials and/or treatment are the same as Brady's.

Speakers 7 and 8: Mother and Father (caregivers to Son and Daughter)

Son:
Current Age:20
Age of Diagnosis: 15
Preference for Treatment: Stopping and/or slowing progression. Reversing damage to macula and restoring vision loss.

Daughter (early onset with minimal vision impairment):
Current Age: 17
Age of Diagnosis: 12
Preference for Treatment: Stopping and/or slowing the progression to maintain vision.

Summary of Mother's Testimony on behalf of her children:

- Son showed early signs of visual problems in 7th grade when he got an iPhone for his 13th birthday. His parents noticed that he held his phone closer to his eyes than most people.
- Mother took him to an optometrist that took images of Son' eyes and referred them to a specialist for more tests. This appointment resulted in a misdiagnosis, and he was fitted for glasses.
- Son was blowing off standardized tests at school, claiming his glasses didn't work and was labeled a "gifted underachiever" that hated school.
- Vision problems for Son continued another year and he was taken to an ophthalmologist that was highly recommended. More tests and scans again resulted in a misdiagnosis with a condition called amblyopia, which was treated with patching the stronger eye to strengthen the weaker eye.
- Visual problems for Son continued as his family went on with their lives. While visiting a museum, Son was asked to read a plaque three feet in front of him and he could not read it.
- Three years of misdiagnosis resulted in a visit to Bascom Palmer Eye Institute in Miami. Son received a full day of tests and scans. It was at this appointment they learned the devastating news that Son had Stargardt Disease. They were told Son would almost certainly be legally blind in his 20s.
- Son is a very talented basketball player that has been recruited since he was in the 9th grade with an offer for a full scholarship. His parents fear this would all be taken away from him.
- Following Son's diagnosis, his sister, Daughter, was also diagnosed with Stargardt Disease through genetic testing. This was terrible news in obvious ways, but even more concerning as Daughter is already dealing with Type 1 Diabetes. Daughter's symptoms have not progressed yet.
- Mother and Father researched the disease and learned about possible clinical trials. They learned of promising clinical trials but concluded that FDA approval is a long and timely process. Mother noted that patients with Stargardt Disease do not have time to wait as their vision gets worse and worse over time.
- Son continued to play basketball, receiving many Division 1 offers to play in college. Father and Mother struggled with this because they knew his vision would get worse.

- Stargardt impacted his ability to see his basketball coach from across the court, he couldn't see the score board, etc.
- They made the choice to not tell anyone about Son having Stargardt Disease because they were afraid that Son would not be considered for a scholarship, and that he would be looked at differently. They wanted Son to have an opportunity to reach his goals.
- Currently Son signed with a division 1 basketball school and just finished his freshman year. He is struggling due to Stargardt Disease.
- Son is suffering due to lack of a social life because he cannot recognize anyone. He believes most people think he is a jerk because he doesn't say hello or waive to them because of his inability to recognize them.
- Son is at a point where his vision impairment is more noticeable now that he is competing with greater speed and talent at the college level.
- Son must have special equipment to transform textbooks into audio as there is not enough time in the day for him to read required materials.
- Son stated to his mother that he could read better in 3rd grade than he can now.
- Son spends a lot of time studying to make up for what he can't see on the written board in class. Son receives accommodations for test taking at school.
- According to his mother, Son is in a fragile and life changing point in his life due to the progression of his disease. They worry about his future career and his dreams to have a family. They also realize that once the disease progresses just a little more, he will no longer be able to drive.
- Their hope is for a drug that will at least slow down the progression. It would be life changing for Son.
- Daughter is a rising senior and has already obtained a full scholarship to play volleyball. She is now starting to have symptoms.
- Mother reiterated that it is so difficult to see Stargardt Disease progress in your children at such a young age and see the irreversible damage it does to their lives.

Father (caregiver to Son and Daughter) Testimony of behalf of his children:

- Father spoke about doctors at Bascom Palmer telling them not to worry because there was a lot of research and clinical trials going on with Stargardt and that there would be treatment soon.
- After researching all the available trials, they requested participation in the clinical trial involving one of the investigational medical products known as ALK-001, which is designed to slow the progression of the disease.
- Factors that influenced their decision to choose this clinical trial were Son's and Daughter's visual acuity at the time, it seemed safe as it is a Vitamin A replacement, and their ophthalmologist recommended this trial as she was involved in the research and stated she would have her own children participate in it.
- Daughter was enrolled in the trial right away. She was placed in the open label category of the patients to be monitored better since her disease progression was very little.
- Son (2 years older than Daughter) already had visual impairments and was not enrolled at that time.

- Daughter was on the investigational medical product for 4 years. They were amazed at her lack of progression during this time. Her visual acuity remained near 20/20 and her OCT scans showed little if any changes.
- Son was accepted into this open label trial 2 years later. During his participation in the trial, he also had little if any changes in his vision.
- Daughter and Son both stopped taking the investigational medical product this past February due to the FDA protocol expiring for them, and Daughter has just started to make comments about her vision getting worse.
- Father stated they found this trial to be beneficial and it was not much of a burden given that it only involved a once per day pill taken at night before bed. There were no side effects during this 4-year period.
- Father also noted trials for Stargardt Disease take a long time and enroll slowly because of a low number of Stargardt patients. Father stated, “Unfortunately, our kids do not have that time. Time is of the essence for them to get treatment before their vision gets worse.”

Speaker 9 and 10: Bryan and Bradford Manning (Brothers, both have Stargardt Disease)

Bryan:
Current Age: 31
Age of Diagnosis: 5
Preference for Treatment: Stopping and/or slowing progression. Find a cure for disease.

Bradford:
Current Age: 36
Age of Diagnosis: 7
Preference for Treatment: Stopping and/or slowing progression. Find a cure for disease.

Summary of Bryan's Patient Testimony:

- Bryan shared experiences of childhood in which he pretended to be the "dumb kid" in class because it was better than the reality of being labeled "blind kid"
- Diagnosed at an early age he and his brother, Bradford, decided to fight their way through academics and getting a job. 6 years ago, founded Two Blind Brothers clothing brand. They make luxury casualwear and donate 100% of their profits to retinal researchers working to find cures for blindness. Bryan and his brother, Bradford, believe a cure is coming.
- Side effects Bryan noted as he has interacted with the blind community through patient advocacy and organizations searching for a cure included depression of individuals as their symptoms of Stargardt increase.
- Bryan shared the importance of extending the time people have functional vision.
- Bryan mentioned that genetic testing before couples have babies can now see if they are carriers of Stargardt Disease. He noted that 5-10% of people in the US population are a carrier.

Summary of Bradford's Patient Testimony:

- Bradford highlighted that he has had the opportunity to hear and interact with many Stargardt patients and their stories are always consistent. He gave a specific example of a 19-year-old kid that wrote to him and shared he was choosing to sleep more than be awake because dreams were 20/20 vision.
- It is a regular occurrence for Bradford to hear suicidal thoughts and the term "long sleep" from the community of those suffering with Stargardt Disease.
- Bradford remarked on the cruel aspects of degenerative diseases. Although humans are adaptive and resilient, the challenges of degenerative diseases never stop as the progression of the disease gets worse with every passing, day, year or month. Bradford referred to this as "psychological torment". He finds himself asking, "Will I be able to handle the next impact of this?"
- Bradford and Bryan have fought through school, academics, got good jobs, got married, and now Bradford has a 10-month-old, and Bryan has a 6-month-old. Bradford said, "Now the question is, Will I have enough eyesight to make sure my 10-month-old is safe?"
- Bradford shared an experience of meeting a man at a conference in Orlando. The man was a Stargardt patient who used a cane and a seeing eye dog. It occurred to Bradford

that this man had a very different level of independence than he did, which made him realize that this could get much worse for him. Bradford was happy his wife was not there to see this because he wasn't sure of her response to Bradford possibly losing his independence. What would this look like for his wife and daughter?

- Bradford and Bryan both reiterated the importance of stopping the progression of this disease. The level of mental stress and lack of clarity of how bad it will get is hard to deal with.
- Bradford believes treatment and cures are coming down the pipeline.
- Bradford thanked the participants of this meeting and believes this will help further the search for effective treatment and a cure.

Open Discussion

FDA thanked speakers for sharing their stories. FDA Director of the Division of Ophthalmology (DO) made a statement and asked a question and was given a response.
The following description will outline the discussion.

FDA Response to Patients and Caregivers Testimonies**:**

- Statement made that the FDA absolutely recognizes that slowing or stopping the progression of this disease is a legitimate endpoint without question. Mentioned having been on a podium multiple times saying he wants a cure, but that doesn't mean they wouldn't approve an investigational therapy that at least slows the disease down to give people more time.
- FDA asked why the son and daughter for Speakers 7 and 8 that have been on the investigational medical product therapy stopped taking the investigational medical product given the fact that they believed it was helping?

Father (Caregiver of 2 Stargardt children) Response:

- Father responded by stating that his 2 children had to stop because the FDA trial protocol for their use ended. From Father's understanding, his daughter was permitted to participate 2 years and it got extended for 2 years. There was no longer an approved protocol for his children, but they would like to get them back on the investigational medical product treatment right away as they believed the investigational treatment was beneficial. It was Father's understanding that the FDA would need to approve a different protocol for them to be allowed the extended use of the investigational prior to FDA approval.

FDA Response:

- FDA would permit expanded access to the investigational medical product to the Stargardt patient that believed that he or she was receiving a benefit from a treatment that is currently under investigation. FDA also stated that extended use of an investigational medical product under clinical trial may be beneficial to the FDA's review of the investigational medical product. However, FDA clarified that the drug company must also approve expanded access to this product for a patient. He encouraged patients to speak to their clinicians.

Father's Response:

- Father asked if there is anything the patient community can do to help facilitate drug development and FDA review of those drugs?

FDA Response:

- The FDA does not develop products and does not have control over that. He would encourage patients to not necessarily look for approvals of drugs, but to have products that makes a difference and slows the progression down, reverses the disease, or improves acuity. If the product is reasonably safe the FDA will allow use and encourage continuation of studying the therapy. Patients need to find products and people to develop treatments that work.

Partner Organizations:

- Stargardt Network, patient advocacy group
- Hyman, Phelps & McNamara, P.C., Consultant to Stargardt Network

FDA Divisions Represented

Office of the Commissioner (OC) – 2 *offices*

- OC/OCPP/PAS – Office of Clinical Policy and Programs/Patient Affairs *(organizer)*
- OC/OCPP/OOPD – Office of Clinical Policy and Programs/Office of Orphan Products Development

Center for Biologics Evaluation and Research (CBER) – 2 *offices/divisions*

- CBER/OCD – Office of the Center Director
- CBER/OTAT/DCEPT/GMBII – Office of Tissues and Advanced Therapies/Division of Clinical Evaluation and Pharmacology/Toxicology/General Medicine Branch II

Center for Drug Evaluation and Research (CDER) – 6 *offices/divisions*

- CDER/OCD/DSS – Office of the Center Director/Drug Shortages Staff
- CDER/OND/ORDPURM/DRDMG – Office of New Drugs/Division of Rare Diseases and Medical Genetics
- CDER/OND/OSM – Office of New Drugs/Office of Specialty Medicine
- CDER/OND/OSM/DO – Office of New Drugs/Office of Specialty Medicine/Division of Ophthalmology
- CDER/OTS/OB/DAI – Office of Translational Sciences/Office of Biostatistics/Division of Analytics and Informatics
- CDER/OTS/OB/DBIV - Office of Translational Sciences/Office of Biostatistics/Division of Biometrics IV

Center for Devices and Radiological Health (CDRH) – 6 offices/divisions

- CDRH/OPEQ/OHTI – Office of Product Evaluation and Quality/ Office of Health Technology I
- CDRH/OPEQ/OHTI/DHTIA – Office of Product Evaluation and Quality/ Office of Health Technology I /Division of Health Technology 1 A
- CDRH/OPEQ/OHTI/DHTIC - Office of Product Evaluation and Quality/ Office of Health Technology I /Division of Health Technology 1C)
- CDRH/OPEQ/OHTIII/DHTIIIC Office of Product Evaluation and Quality/ Office of Health Technology III/Division of Health Technology IIIC
- CDRH/OSPTI/DAHRSSP- Office of Strategic Partnership & Technology Innovation/Division of All Hazards Response, Science and Strategic Partnerships

- CDRH/OSPTI/DAHRSSP/PSE - Office of Strategic Partnership & Technology Innovation/Patient Science & Engagement

Patients and Community Members Represented

- Adriann Keve, person living with Stargardt
- Tara, mother/caregiver of Vivian and Emmett, two children with Stargardt
- Lucas Carmo, person living with Stargardt
- Evie Baxter, person living with Stargardt
- Victoria Smurfit, mother/caregiver of Evie Baxter
- Brady, person living with Stargardt, also speaking on behalf of her brother Chase, person living with Stargardt
- Mother and father, caregivers of a son and daughter with Stargardt
- Bryan and Bradford Manning, two brothers living with Stargardt

Financial Disclosures

Participants/caregivers have no financial relationships with drug developers. None of the participants/caregivers received compensation from drug developers for their participation in the Listening Session.

Disclaimer

Discussions in FDA Patient Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects the Stargardt Network's account of the perspectives of patients and caregivers who participated in the Patient Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of Stargardt Disease, health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire Stargardt patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report