Online Comments

X-Linked Retinitis Pigmentosa (XLRP) Externally Led Patient-Focused Drug Development Meeting

The Foundation Fighting Blindness hosted the XLRP Externally-Led Patient Focused Drug Development (EL-PFDD) meeting on June 7, 2022. This EL-PFDD meeting was modeled after the work of the FDA's Patient-Focused Drug Development (PFDD) initiative. PFDD is a systematic way of gathering patient and caregiver perspectives on their condition and on available treatments. The information gathered at the meeting is presented in the *Voice of the Patient* report, which may be used to guide therapeutic development and inform the FDA's benefit-risk evaluations when assessing therapies to address X-linked retinitis pigmentosa.

The Foundation has provided this report on behalf of the XLRP community, and it is publicly available for the many stakeholders in the XLRP community including the FDA, other federal agencies, academics, clinicians, advocacy and professional organizations, biopharmaceutical companies, and universities from across the world. The *Voice of the Patient* report, the meeting transcript, a recording of the meeting, as well as this document, can be found at: https://www.fightingblindness.org/xlrp-pfdd.

An online comment submission portal was open for one week before and four weeks after the XLRP EL-PFDD meeting in order to allow as many voices as possible to be heard. The submitted comments are presented in this document. Respondents are identified by their first name only, and comments were sorted

so that the comments from each individual are presented together. Comments were edited only slightly for grammar, spelling and punctuation.

Comments that did not address the Meeting Discussion Questions from **Appendix 4** of the *Voice of the Patient* report were not included as were any comments that were perceived to be disrespectful to individuals, companies or organizations or comments promoting commercial products or organizations. Selected comments and excerpts are included in the main body of the *Voice of the Patient* report.

<u>One comment submitted by the Foundation Fighting Blindness on behalf of an individual affected with XLRP</u>

I was diagnosed with RP at age 17 and am now 61. My vision has degraded fairly slowly over the years from still driving to age 22 on to now only having light perception.

How does x-linked retinitis pigmentosa (XLRP) impact the daily life of affected individuals?

For me, it started with night blindness soon after I started driving at age 16.

I was diagnosed with RP at age 17.

My night driving diminished to a point where I was very dependent upon the painted lines on the road in order to stay in my lane. It was quite difficult when meeting cars on a two lane road at night.

My driver's license was taken away after I had an accident at age 22 when the state found out I was legally blind. I had to rely on friends, family, and public transportation thereafter.

I also had problems going from light to dark. Hence if I went from outside to inside a restaurant or bar, I couldn't see to get around, and would bump into things or people.

I did have a folded cane I'd carry at night, but rarely used it until a few years later.

Being diagnosed with RP, I was encouraged to pick a career compatible with going blind. I chose computer programming. I used Zoomtext screen reader and a CCTV to read papers & books, as well as fill out paperwork from age 18 to age 43, at which time making things bigger wasn't working anymore, and I took disability.

I relied on following people to get where I was going. At first, I didn't need to hold on to them, then by age 43, I asked to put my hand on their shoulder, and still do today at age 61.

I had bad stress leading to heart attacks & panic attacks from going blind & trying to continue my career, although I did try to learn to work audibly, instead of visually, it was just such a big change, and added to my stress. Ended up staying on disability instead of returning to work.

With my progressive disease, I had to keep giving things up, hence, driving @Age22, tennis @age30, golf @age55 (of which I painted my clubs white & could line up the white ball with the head of the club and could see well enough to hit the ball, then get help to get to it.)

@age55, I could still see lights on the ceiling of most stores & had an idea of how big the store was. As the years passed, I could see fewer lights. Today, I can, but barely can see a light on the ceiling at all.

One thing kind of interesting, I can't see the sun, but I can see the moon.

I can navigate my home without a cane due to being familiar with its layout. However, I'd never leave the house without a white cane. Been this way probably the last 15 years.

Also, have been using Jaws screen reader on the computer & voiceover on my phone, which greatly help with my independence.

Much thanks to my sighted wife for all her help and support as well as to the various doctors, and blind organizations.

What expectations do affected individuals have of the treatments under development for XLRP?

This is an easy answer for me, in order of my preferred priority. 1. Vision restored, 2. Vision enhanced, 3. Vision stabilized, and in all cases without a big risk to health & adverse side effects.

Paul 1 – One comment submitted online

Hi! I am an artist and illustrator with XLRP. I am 31-years old and have lost most of my vision (I have about 15 degrees remaining).

I am grateful to have the little bit of central vision I have today. With corrective lenses I have 20/50 acuity in both eyes and I'm able to make a living as a visual artist. When people inevitably ask, "How do you paint and draw without sight?" I am quick to remind them that blindness is a spectrum, and my vision is sort of like "looking through a straw."

With my "straw vision" I am still able to do what I love most: Making art. It might take me a little longer to do, but it brings me so much joy.

Of course, I often wonder about the future and worry about losing my ability to paint and draw. While I remind myself that complete blindness is a very real possibility, I am also hopeful that science will develop a treatment.

Even if that treatment were to halt the progression of my disease, I would feel as though I'd won the lottery. While my blindness today is a challenge, it's a challenge I know I can handle.

I have an amazing supporting spouse, a beautiful guide dog, and a life that is filled with love and community.

I am a strong believer in things happening for a reason, and I believe in my heart that --no matter what the future holds-- I am going to be fine.

Why? Because despite how I felt the day I was diagnosed with RP, today I know I'm not alone.

The blind community is strong, resourceful, compassionate, and resilient. And I mean it when I say that I am proud to be part of it; I am proud to be blind.

Adam – One comment submitted online

I have X-linked RP caused by mutation in the *RPGR* gene. I was diagnosed at age 10 and was legally blind with less than 20% visual field by age 15. I am 50 years old now and have lost the majority of my usable sight. I have never had a driver's license. After years of "faking it to make it" I embraced my vision-loss in my mid-30s, and I now fully identify as a person with blindness.

RP is an evergreen and ever-changing experience. Each day you wake up knowing you see a little less than the day before. As the lights dim, you learn through all of the harrowing, painful and humiliating experiences associated with sight-loss that your life is change in motion and you have to constantly adjust to that dynamic. In my case, night blindness came swiftly and completely at a young age. The peripheral vision loss was a bit more gradual but certainly impactful by my mid-20s.

While vision loss and night blindness are the major symptoms of RP, the trauma produced by dealing with these symptoms is the most challenging symptom of all. All of the bumps and bruises (or worse) from spills and accidents leave leaves on the body and spirit. I have had multiple concussions for hitting my head in any

number of ways. My toes have all been broken multiple times (save for the big toe on my left foot - the "magic toe."). I have developed amazing recovery skills from all of the stumbles and falls over the years. Last month I walked off a sidewalk ledge with about a 3 ft drop in NYC. I landed perfectly on both feet with knees bent and kept my balance and avoided serious injury. Sometimes the mobility cane misses something, it is not a perfect solution. I got lucky in this case, but that is not always the outcome. Your body really takes a beating when you bounce around the world as a person with blindness.

It was liberating for me when I attended adjustment to blindness training and learned essentially how to be a blind person in the world. Once I knew how to use a mobility cane and assistive technology with confidence, I knew that I could carve my own path in life and still be successful in my career. It was invaluable and life-affirming. But we must remember that no matter what the advancement (short of a cure or effective treatment), folks with RP are on a march to blindness that makes their journey unique unto itself. Every person that experiences it has unique inputs and outputs that make the journey their own. What we all suffer is ignorance, discrimination, and exhaustion from having to constantly re-learn how to navigate a society that is not designed to support us.

On my best days, I am using assistive technology effectively, traveling confidently, navigating independently, and feeling like I have value in the world. On my worst days, my head aches from stress, my shins ache from running into something for the millionth time, my heart hurts from the acute loneliness that drags my spirit down and my mind shuts down from the stress of too many moments where I am reminded that things are only getting tougher. I have my fair share of both bad and good days. Most days are a mix of both.

What I know is this - I am living an alternative experience. I have a disability because the world tells me I am disabled. I believe I am just living a different way than folks with working retinas. My vulnerability is empowering because it helps me find grace in the way we all live with each other. I would not change a thing about my life, but I would love to have known what it would have been like if the progression of my retinal degeneration could have been halted or treated when I was younger. We owe it to ourselves to develop therapies and treatments that might help the younger version of me find out.

Ben - One comment submitted online

Symptoms with most impact:

1. Peripheral vision constricted

2. Night blindness

XLRP affect on worst days:

1. Social isolation

2. Mundane activities can be a challenge, ie. going into dark bathroom at a restaurant

3. Anxiety and lack of confidence to participate in crowded social functions

4. Anxiety gong to any nighttime activity

5. Always worried about lighting conditions

XLRP affect on best days:

1. Not much affect when staying at home and just being around family.

Specific Activities Restricted:

1. Cannot drive

2. Evening events restricted

3. Cannot go to movies

4. Cannot go into dark restaurants

5. Cannot go to crowded sporting events or parties without bumping into people

6. Cannot see when people want to shake my hand

Coping over Time:

Trying to build confidence to ask for assistance in crowded or low light situations

Elizabeth – One comment submitted online

Tunnel vision/lack of peripheral vision is the most serious symptom, followed by dark/light adaptation and night blindness, then light sensitivity & glare. Best days include sunshine & longer daylight hours.

Worst days are those where eyes are impacted further by allergies, dry eye, cloudy conditions or the requirement to travel for my work. When combined the "worst day" symptoms result in reduced activities of daily living [ADLs], work performance, social activities, independence and overall health due to limited ability to get healthy food quickly and difficulty in getting cardiovascular exercise.

Changes- inability to navigate in dark places; cannot read a menu to eat out; navigating stairs and uneven terrain is diminished; increased falls and injuries (this year have fallen 3 times); necessity for cane to alert others; use of a sighted guide often; loss of facial recognition of others; diminished work functioning; increased usage of assistive technology.

Experience frustration/anxiety/tend to stay at home/isolate and must stay resilient and self-motivated; difficulty educating others constantly - "you don't look blind".

Note - XLRP can impact women as well as affected carriers.

Rod – One comment submitted online

Continual progression of blindness requires lots of ongoing adjustment to cope & perform. For example, losing one's driver's license takes away major independence of ones life. Not being able to read normal sized print requires technology, which works, but takes time & training. Adjusting from using LARGE PRINT to audio, was extremely difficult for me, causing me to have to take disability. Technology is great, and helps with independence, but certainly doesn't compare to having vision.

Oh yes, taking disability, meant leaving the work force, taking a cut in pay, and ending up reversing the roles of me & my wife. She had to go to work to help us get by.

Even though I have the apps & screen readers & know how to use them, reading "snail mail" & paying bills is not something I can do anymore. I fortunately have a

sighted wife who can. I can't imagine having to scan through all the "junk mail" to find the "bills" and get to the "details" to "make a payment".

Good days are when I'm in a familiar environment. Bad days are when I'm not, especially depending on what, if any, people are around to help.

Fortunately, the slow progression of the disease helps ease adjustment with coping. I've gone from driving until age 22, to taking a bus & using a white cane at night, to learning technology to read and write. To placing my hand on one's shoulder to get me somewhere. Learning to give things up & accept it is a big part of having RP.

Paul 2 – One comment submitted online

The most significant symptoms of my condition and the impact of the condition on daily life.

Massachusetts Eye and Ear confirmed in 2018 I have the RP GR gene mutation. I was diagnosed with RP at the age of four due to my mother observing my difficulty seeing at night. For years I wore corrective lenses due to astigmatism and near sightedness, and my corrected vision was 20-40, with restricted fields and night blindness. I had a daylight only driving license until 33, although drove sparingly. I was a participant in Dr. Eliot Berson's Vitamin A / E trial during the 1980s before being declared legally blind at the age of thirty-six. My central vision was the initial cause of legal blindness. I adjusted first by wearing prism magnifying glasses to read with directed light which lasted for a decade followed by about another decade using video magnification (CCTV). Since about the age of sixty-two, my access to information has been entirely digital using JAWS screen reader and my iPhone with Voiceover. I didn't use a cane for a decade after being declared legally blind, and for the last 21 years my primary mobility aide has been three German Shepherd guide dogs.

Continued access to information has been especially important professionally and now as an active volunteer. I consider myself fortunate to live in the digitized era and have worked hard transitioning from a visual to auditory learner.

Current approaches to management or treatment.

I am now sixty-seven, and over the last several years begun the end stage of RP with only light perception. While access to information and mobility remain good, I have become more reliant on my wife for certain activities such as organizing clothing, medication and financial management. While I can get around my home independently without a cane, I use that now outside of my home when not working with my guide dog.

Aaron – One comment submitted online

The most significant impact of XLRP on my life is the loss of peripheral vision. The most significant affect of that is not being able to drive. This is a big loss of freedom. I did drive for a time and I enjoyed both the experience and the freedom of it. Now my wife does all of our driving. Fortunately, I am able to work from home (one benefit of the pandemic) and so I don't need to drive to work. On my best days, I don't even think about my RP - I still have decent central vision and can do most things I want to do. My worst days are when I feel embarrassed because I knock over and/or break something, or miss another person going for a handshake or showing me something, or I miss out on something fun because of my vision (playing a sport with my friends). My wife has been very supportive of me and understanding of my condition, which I am very grateful for. As I mentioned, she does all our driving and she never complains about that. She guides me in the dark and points out obstacles to me when she sees them. It was difficult for her at first to understand what I could and could not see, but she is learning more over time.

Bryson – Once comment submitted online

I'm about to be 28 and am doing really well over all. My night vision is not great and I'll catch myself dropping things and taking a minute to find them at times but overall I'm doing well. The hardest thing for me has been the anxiety of anticipating vision loss in the future. While that's given me a great deal of anxiety it has also set my life in a direction that I would not change for the world. Though scary I'm blessed to have XLRP and will do my best to make the best of it and I am so grateful for people like you all who are trying to find a cure for this disease thank you guys :)

Tom – Two comments submitted online

Comment 1

I was diagnosed with RP in my late teens (I am now 69) and with genetic testing 5 or 6 years ago found it was the X-linked with the *RPGR* gene. I don't say these things to have someone feel sorry for me, but to give you actual day to day living experiences. One of the most significant symptoms for me is the loss of my central vision...no detail, fuzziness...like being in a white fog or a blizzard.

It was progressive for me...and as the changes came about so did the losses...loss of driving at night, loss of not being able to drive at all, loss of not being able to go where I want when I want, loss of not being able to see my wife's face, my children's faces, and my grandchildren's faces, loss of reading, loss of not being able to see wonderful sunsets but only gray...so many losses.

As far as coping for my loved one/caretaker...when my wife and I married it was expected that we would share the responsibilities and day to day life; that has changed for my wife as she has had to take on more and more of the everyday life "things". It can be very tiring for her. We don't always see eye to eye on things due to the fact that I cannot see things as they are.

This disease has robbed me of a part of my life that I hopefully can get back with new clinical trials or new drug applications.

Comment 2

I participated in a stem cell clinical trial about 6 years ago. Initially it seemed to have helped. Follow up tests consisting of dilating the eye and shining painfully bright lights in my eyes to take pictures seemed to increase my vision loss rapidly to where I feel I lost 5 years of vision in 6 months.

Jeffrey – Six comments submitted online

Comment 1

Q1 - Of all the symptoms of X-Linked Retinitis Pigmentosa (XLRP) which 1-3 symptoms have the most significant impact on you or your loved one's life?

A1 - I would say my loss of night vision, trouble distinguishing colors, and inability to process images. Losing my night vision has made it very hard for me to function

in dimly lit situations. Having trouble distinguishing colors and processing images makes it very hard for me to see pictures, watch TV, or recognize faces.

Q2 - How does XLRP affect you or your loved one on best and on worst days? Describe your best days and your worst days.

A2 - I have set up my living situation and my life to function very well on my best days. I don't use my eyes to do a lot of daily activities. So when I am in a comfortable environment, I function very well and live a happy life. My worst days come when I am in different environments that may require me to travel. I have to rely on Uber or Lyft to travel that can be very unreliable (leading to frustrating situations). When in unfamiliar environments, I may bump into things, get lost, need help from others, and I often get myself into embarrassing situations.

Q3 - Are there specific activities that are important that you or your loved one cannot do at all or as fully as you would like because of XLRP?

A3 - Driving. I can't underestimate how difficult it is to be an adult and not be able to drive. I have to rely on others to do any of my errands. I have to rely on Uber or Lyft to get places, and this can be very frustrating. Not being able to drive limits my job opportunities, and it dictates where I can live.

Q4 - How has your loved one's ability to cope with the symptoms changed over time?

A4 - I have gotten much much better. In my early 20's, I don't think I realized how much my visual impairment was affecting my life. Over time, I started using assistive technology. This has helped me cope much better. I have also developed a better attitude about my visual impairment.

Comment 2

Question: What do you fear the most as you or your loved one gets older? What worries you most about your or your loved one's condition?

Answer: Honestly, I don't really worry about the progression of my condition. I get most worried about my career. As a telemedicine doctor, my work flow is in constant flux. My clients are very unstable. But, my visual impairment really

limits my options in the field of medicine. My biggest fear is complete career change because of the limitations my visual impairment puts on me.

Comment 3

Question: What are you currently doing to manage your or your loved one's XLRP symptoms?

Answer: I take Vitamin A, Fish Oil, and Lutein every day. I use ZoomText to help me operate my computer. I use a CCTV to read letters and paperwork. I use a cane to get around. I enjoy listening to sports on the radio as opposed to watching on TV.

Comment 4

Question: How well do these treatments address the most significant symptoms and health effects of XLRP?

Answer: I am not sure how much the Vitamin A, Fish Oil, and Lutein are helping. But, assistive technology helps me tremendously. I still do have many limitations, and I still ask for help quite frequently. But, with assistive technology, I function very well and I am able to complete nearly all of my daily tasks.

Comment 5

Question: What are the most significant downsides to your or your loved one's current treatments and how do they affect daily life?

Answer: Vitamin A, Fish Oil, and Lutein do not actually improve my vision. There is limited evidence that shows this could slow the progression of XLRP. So, it is a downside that we do not actually know how much it is helping. As for assistive technology: The only downside is that there are inherent limitations. They do not help 100%. Zoom Text has frequent malfunctions. It still has many glitches that need to be worked out. It often crashes my computer. Also, there is no assistive technology to help me drive at this time.

Comment 6

Question: Short of a complete cure, what specific things would you look for in an ideal treatment for XLRP? What factors would be important in deciding whether to use a new treatment?

Answer: Other than a complete cure, I would be happy if the progression of my disease was completely stopped. If I could gain any sight back, I would really like to see faces and people again. When deciding whether or not to use a treatment, I would consider cost, the risk of adverse events, frequency of treatments, duration of treatment, feasibility of treatment.

Polly – Two comments submitted online

Comment 1

Of all the symptoms of X-Linked Retinitis Pigmentosa (XLRP) which 1-3 symptoms have the most significant impact on you or your loved one's life?

My 10-year-old son was diagnosed with RP six months ago. Night blindness is the most significant symptom for him at this point. It has impacted him playing with friends outside at dusk or later in the backyard, navigating a movie theater on his own and feeling safe in his room at night. We have been able to combat these inconveniences with porch lighting, using an iPhone flashlight and adding more nightlights in his room and hallways. But as his mother, I worry about when what are now inconveniences become more. Will he be able to drive at night? Or drive at all since night blindness is the first of more symptoms to come for RP? How do I navigate him spending the night at a friend's house and making sure they are aware without him being labeled? We have not shared his diagnosis beyond immediate family at this point. Each stumble or trip reminds me of the coming changes in our lives and the reality that he has a condition with no cure.

Comment 2

How does XLRP affect you or your loved one on best and on worst days? Describe your best days and your worst days.

I will answer as the mother of a 10-year-old son who was diagnosed with RP six months ago. On my best days, I'm thankful my son lives in a time when a cure for RP is (no pun intended) within sight. Clinical trials are in place that could give him a life of sight that my grandfather, who was legally blind at 20 and completely blind at 40, didn't have. I'm confident that my son will have a different outcome. I'm grateful for FFB for being a resource and a comfort to my family, and for helping us connect with a phenomenal physician scientist to serve as my son's provider. I'm grateful my son's symptoms are manageable and only visible to his

immediate family. On my worst days, I'm consumed with worry. Will a treatment be approved in time to help my son? Will we be able to find a clinical trial accepting new pediatric patients? I'm terrified he will lose his vision before a treatment is available, and then it will be too late. I hear the words of the optometrist who told me, "there is no cure" over and over, and the words of my son leaving the appointment asking, "What's going to happen to my eyes?" I feel like I'm in a car crash and I can't swerve out of the way. I can't stop it. I can only watch it happen, helplessly.

Denise – One comment submitted online

As everyone with this disease does, I struggle daily with normal tasks and my world keeps getting smaller and darker. I have not been able to participate in any trials or research for RP because I also have dry macular degeneration. Will there ever be a chance for me to take advantage of any new developments?

Jamie – Three comments submitted online

Comment 1

Best/worst days

XLRP affects our best days in how I guide my husband through crowds and obstacles and we snuggle close as we walk. He keeps me on track and we work as a team. He never gets angry and disappears for hours. I always feel needed and very loved.

XLRP affects our worst days when I’m the only driver, and the one in charge of all the paperwork. He can’t see the expressions on our son’s face and misunderstandings arise. And worst, he can’t find things and it’s probably my fault they’re lost.

Comment 2

Vision Loss is the main symptom. He can't see his own face in the mirror, hasn't driven since he was 18. Just lately, his field of vision is extremely small in one eye. He is still able to do his job on a computer, but it's getting more difficult.

Comment 3

We have two sons, my husband has RP. We assumed that our boys were safe from XLRP. Surprise! Our eldest son is 47XXY, and we found out he carries the *RPGR* gene. He'll have his first ERG this month, at age 19. It's a huge challenge for his due to his anxiety and sensory issues. No one really knows if he'll exhibit symptoms or if it will be as if he's a female carrier. It's scary and unknown at the moment.

Patricia– One comment submitted online

As a parent of an individual with RP, it is difficult to watch his struggle with simple daily activities… struggling to open a door, to see a glass on a table. Every month these simple activities become more obvious.

Knowing that he is losing his vision, we took a family vacation four years ago. Yes, he could sit on the beach, but a simple hike was too difficult.

It was indeed difficult when he could know longer drive; that loss of independence was devastating. Fortunately, there are food delivery companies and Uber; but they don't replace the personal freedom that he once had.

He is currently employed, but as his ability to read becomes more challenging what will become of his job? He has a graduate degree and a masters degree but I know that blind individuals are among the most underemployed. As parents we obviously worry about his long-term future.

He always made friends so easily, but his college friends now live all over the country. Travel is difficult. It can be done but the logistics are so much more difficult. Making new friends is much more challenging. He is unable to participate in the activities he could do as a teen.

Our son participated in a clinical trial years ago. It was obviously not successful, and worse there are possible detrimental effects.

He had hoped to get into another one, but he did not qualify. Knowing that his "window" of opportunity is closing is difficult. It seems that those with more advanced cases need treatment to preserve what vision he has.

I could go one and on about day-to-day challenges. How does one maintain hope when everything is becoming more and more difficult? One tries to be optimist but that is not always possible.

It seems that blindness is one of the most cruel disabilities. Please help.

Kathy – Three comments submitted online

Comment 1

I'd be interested in hearing about research relating to women affected with XLRP

Comment 2

Is FDA looking at changing the baseline for research benchmarks on the idiosyncratic expressions of symptoms of XLRP making it hard to measure improvements.

Comment 3

I participated in a study at Wilmer Institute and was found to have improved night vision and acuity through acupuncture. I am torn between continuing this therapy which I started 10 years ago, and giving it up all together. My progression seems like it has picked up in the last year or so that I haven't done acupuncture. Is this a coincidence? I just don't know. My retinal specialist is very supportive of me doing whatever I feel like helps. But I'm pretty sure he is just being his kind supportive self. As a practitioner, he has said that he doesn't feel that acupuncture has any impact on my disease.

Lisa– Four comments submitted online

Comment 1

In my X-linked RP family there are more females affected then males but the males are more significantly affected, but by older years (70) the women are fully blind too. I know of three other X-linked RP families and all of them have affected females. I had a 30% reduction of photo receptor cells by 22 years old. I am 50 now and currently receiving cane training.

Comment 2

I take higher levels of DHA, lutein and zeaxanthin daily, general liquid vitamins (easily absorbed) and eat mostly organic food, drinking a lot of filtered water. I get daily exercise, at least 7 hours of sleep, otherwise I can't see my best the next day. I wear prescription sunglasses, a visor and protective shoes so I don't stub my toes. I keep my regular glasses handy in case the light levels dip down and I need them quickly, especially while driving. I know my day driving only days are numbered. I use Lyft/Uber if I need to go somewhere at night with my (minor) daughters, one is adopted and blind due to LCA. The lights in our home are LED and everywhere, we modified the lighting when we moved in and put in a sola-tube in the kitchen where I cook. (We bought a one level home w/ no steps intentionally.) I only see where there is light!

We adopted two girls from India to prevent the speeding up of my vision loss going thru a pregnancy and to prevent passing the genetic disease down. My girl cousins all chose to biologically have children so now we have another fresh young generation of 'going blind' young men (and women.)

Comment 3

I wanted to second what Laura said. VERY FRUSTRATING that us XLRP females (later stages) are not allowed to participate in the gene therapy trials. This kind of discrimination would not be allowed in other fields**!**

Comment 4

RP/XLRP has been likened to PTSD. You go through your day banging into things, each time you do, it's a reminder/trigger "I am going blind". Blindness is one of the top three fears along with death and divorce.

Beth – One comment submitted online

I am a 65yo female with significant symptoms and I am also very frustrated with the lack of access of clinical trials for me!!!

Laura – Four comments submitted online

Comment 1

I am a female with the *RPGR* gene version of RP. Although I was told I was a carrier, I started losing night vision in my teens, and have been legally blind since my late 40's. My niece (whose dad has RP) is following my pattern. Yet we are not considered eligible for the gene therapy trials due to our sex, which is maddening!

Comment 2

Hardest parts:

After 20 years as a PA Master Gardener, I am now giving up gardening because (1) sunlight is too bright, and (2) I can no longer distinguish between plants and weeds.

As a grandmother, I cannot read to my grandchildren, admire what they want to show me, or even babysit without assistance. This is heart-breaking.

My visual acuity is still very good, but my central vision has shrunk so much that I will soon no longer be able to read. This will truly be life altering, and cut me off from so much of the world.

Comment 3

With all the aspects of vision loss that my brother and I cope with, by far the most heartbreaking aspect is watching my son go blind. I will never forget the pain I felt, the first time I saw him walk down the street with a white cane. He was a professional private investigator working in NYC, and had to go on disability at the age of 33. He is now learning to be a full-time parent to his infant son. I admire his courage and ambition so much, even as I hurt for him.

Comment 4

I am about to move into a retirement community sooner than I would have liked, because of a need to be in a more "protected" environment. Although my husband is my helper, I feel very isolated at home, and worry about how I would cope if something happened to him. In the community we will give up some independence, but I will have access to classes, social activities, and a gym as well as support staff if needed.

Paige – Four comments submitted online

Comment 1

Q1) Of all the symptoms of X-Linked Retinitis Pigmentosa (XLRP) which 1-3 symptoms have the most significant impact on you or your loved one's life?

A1) Unable to see detail or faces. Loss of night vision and needing contrast to see words on a screen or outline of a person's figure.

Q2) How does XLRP affect you or your loved one on best and on worst days? Describe your best days and your worst days.

A2) Best days are us both working remotely and the two of us going out, walking arm in arm, and things working in our favor (no travel/commute issues). Worst days are when we're apart and trying to use Zoom or FaceTime when I offer to help. Also, when traveling to new places and I'm overwhelmed with directions or the Uber/Lyft doesn't show or when we're with groups and we're often slower.

Q3) Are there specific activities that are important that you or your loved one cannot do at all or as fully as you would like because of XLRP?

A3) Driving – He relies on me or family/friends or Uber/Lyft services

Watching TV or games – I try to narrate and describe but know it's so delayed and I get tongue-tied.

Horseback riding – We have tried this once with another handler leading his horse.

Biking, hiking, snowboarding/skiing – We haven't tried these yet but I'm optimistic we can figure out a way!

Q4) How has your loved one's ability to cope with the symptoms changed over time?

A4) I've only known him about 16 months, many years after his biggest struggles and difficulties during college, med school, and residency. Situations that I just can't imagine – the educational demands and competitiveness while facing biases and stereotypes among medical colleagues and superiors in a field which you'd think would be the most understanding. I rarely think about his vision when we're together. We just naturally get along and function well together. I think we do a

very good job of being creative and figuring out alternatives or better options to help us in situations. I am amazed how technology has helped him, but my eyes have been opened as to how inaccessible and challenging so much in this world is to those with vision impairments (websites, restrooms, sporting events, etc.). I'm excited for positive changes and medical advancements in the future to help those living with XLRP!

Comment 2

I am responding on behalf of my fiancée, Jeffrey, who's living with XLRP.

For some of the poll questions in Session 2 where I answered "other":

- Medications - In addition to Vitamin A, my fiancée also takes Fish Oil and Lutein supplements

- Management - use of a cane and Uber/Lyft ride services

Comment 3

I'm answering on behalf of my fiancée, Jeffrey, who has XLRP

How well do these treatments address effects.... I answered "somewhat" because use of a cane, inverting colors on computer, ZoomText software, iPhone/Siri, CCTV, and Uber/Lyft services are not always a guarantee every day. Software updates often change the layout. Siri can misspeak or miss text or notifications. Uber/Lyft are not always reliable or helpful. All of these have limitations. They do not replace fully one having eyesight.

What are the significant downsides...My fiancée gets fatigued quickly. He works on a computer for 10-11 hours during the week. On really tough days, his right eye seems more affected. (His left eye is stronger.) The stress of work and trying to always prove himself to his peers and superiors greatly affects his mental state and anxiety. He is very worried about not being able to see his computer one day.

Comment 4

My fiancée has expressed concern for trying a new treatment that would possibly make his current vision worse. Side effects would be a major factor in his decision to try a new treatment.

Ava – One comment submitted online

Hello, I am a 19-year-old female with XLRP. I am nightblind and have lost a good portion of my horizontal peripheral vision. The biggest issue this causes is my inability to drive. I don't have as much independence as I would like to have. I also can't navigate a new place by myself if the lighting is poor. I do not have training with a white cane, so I am currently holding onto a person I know while walking around.

Dawn – One comment submitted online

My 14-year-old son has some night blindness and emotional effects.

My 28-year-old daughter has night blindness and emotional effects.

They both are affected by sudden change in light.

They both would like to participate in gene trial.

Both have confirmed case with genetic testing through MyRetinaTracker.

SW – One comment submitted online

RP's biggest impact on my son's life so far has been in physical education class in his elementary school. Whenever they play ball sports, he struggles significantly and his classmates are too young to understand his difficulty seeing balls thrown at him.

Bernie – One comment submitted online

Hello. I am writing from Nova Scotia Canada. I am a music teacher, multi-instrumentalist, band leader and music producer. In 2020 I produced a video for Fighting Blindness Canada. I made the video to tell my vision story, and to also help educate others about vision research and my hopes for the future of vision research. Here is the link. Thanks so much. https://youtu.be/sJFOw42VVdQ

Joseh – One comment submitted online

Light sensitivity is a common symptom of RP. I noticed that some of the panel members use "inverted" or "white-on-black" high contrast themes on their computers. This relatively simple setting has extended my ability to use computer displays instead of just text-to-speech. If I use typical, black-on-white contrast, it's

almost as intense as looking into the sun. I took part in a clinical trial, and I often felt I could perform better on visual acuity testing if the letter chart were to have white text on a black background. I know this is non-standard, but I think the traditional eye chart artificially diminished my performance by causing white out or glare effects due to my condition.

Paul 3 – Two comments submitted online

Comment 1

I face anxiety, depression, anger, and frustration constantly. This interferes with every social interaction and relationships with my family. I continually struggle to suppress these feelings in order to be a normally functioning human being. Those feelings are not me, and it's a constant fight to be the positive upbeat person that I truly am inside.

Comment 2

No matter how I adjust and adapt and train, whether its cane training or OT at a blind rehab center or prescription drugs for anxiety or training to use computers and smartphones, the bottom line is that I'm still blind.

Jonathan – One comment submitted online

I have a question for the audience more so than a question. Has anyone used IVF or any other means of intervention in family planning to select for gender to prevent a next child with RP?

Mike 1 – One comment submitted online

My biggest fear is having to use a public restroom. They can be very dark and the different layouts can cause me big issues. I feel like a freak using a bright flashlight to navigate them. I would rather stay home.

Kim – Two comments submitted online

Comment 1

My son was diagnosed at age 5. He is now 19 and although he tries to remain positive, the peripheral and night vision loss has certainly impacted both him and our family over the years. Things we take for granted on a daily basis: inability for your child to participate in his 5th grade dance because the lights were dimmed

and he became frightened, embarrassed, and frozen in a corner because he could no longer see. Not being able to experience driving a car and get a drivers license while watching his younger brother accomplish those tasks. Limiting his social participation, especially at night, because he doesn't want people to know about his condition and see his challenges with maneuvering in various environments. The examples are endless, and numerous and extremely challenging.

Comment 2

My 19 y/o son was an early Phase I-II participant in a *RPGR* gene therapy trial and received gene therapy to one of his eyes approximately 2 years ago. Although he has already lost a significant portion of his peripheral vision, he has had great results so far with no further deterioration in his treated eye. His untreated eye however, continues to decline. Just wanted to provide some perspective from a family that has participated.

He also has been taking daily Vitamin A Palmitate, Lutein, a DHEA since he has been 5 years old.

Tiffany – One comment submitted online

Struggle to read and everyday chores such as shopping, cooking

Christine – One comment submitted online

My son is 8.5. He was "accidentally" diagnosed with XLRP through genetic testing when he was 3. Genetic testing confirmed that he had a suspected respiratory condition (primary ciliary dyskinesia, PCD) and XLRP. He has trouble transitioning from light to dark spaces and seeing at night. Fortunately, to date, his condition has not significantly impacted his life. He does well in school and plays baseball. He wears glasses with transition lenses but does not use any other devices or treatments. We see a retina specialist yearly to track progression XLRP.

Jeff – One comment submitted online

We are really hoping that the two companies conducting phase 2/3 trials will consider enrolling their qualified phase 1/2 patients in a crossover cohort so those patients can have their other eye treated (similar to what Spark did with their RPE65 Luxturna treatment). Or alternatively establish a compassionate use program for those phase 1/2 patients to give them the opportunity to have their

untreated eye treated. These phase 1/2 patients took on a lot of risk and spent huge amounts of time and endured big disruptions to their lives to advance these treatments to the next stage and should be offered the opportunity to have their other eye treated as soon as possible.

Mike 2 – One comment submitted online

I had gene therapy in one eye in 2017, but since then the treated eye has deteriorated at the same rate as the untreated eye. The treated eye also took a one-off hit from the invasive nature of the surgery itself.

However, I only got a low dose, and I am confident that once optimal doses have been found gene therapy will be effective, especially for younger patients (at 46 at the time I was probably too old to benefit for gene therapy).

For a massive boost to night vision I am using Augmented Reality smart glasses.

Other patients should test out various VR/AR glasses.

Nancy – One comment submitted online

My sons (16 and 20) both are affected with XLRP. Their limited peripheral and night vision affects all the other choices in the poll. We are hopeful that both will qualify and participate in clinical trials in the next few years. Thank you for the webinar

Michael – One comment submitted online

The Problem: I'd like to express our family's frustrations with the eligibility criteria for the various X-linked *RPGR* clinical studies. Exclusion criteria include no one over 65 y/o, no women (lyonization), no one below the Mean Retinal Sensitization score of 2.0 dB, and no one with an anomaly in just one eye (e.g., calcium deposit, nevous). These exclusion criteria eliminated nine of our family members and allowed only one family member to participate. That one family member is now seeing better than his pre-treatment levels.

The Solution: The clinical trials already have enough safety and efficacy data to broaden their inclusion criteria to include persons older than 65 y/o, women, any one eye that is free of calcium deposits or nevous, and MRS scores below 2.0 dB.

The clinical studies should also hasten FDA approval. Too many people are running out of time for rescue.