Executive Summary

Voice of the Patient Report

EL-PFDD Held October 8, 2021

This document contains excerpts from the Gorlin Syndrome Alliance's "Voice of the Patient Report". The Report Overview and Key Meeting Messages was copied from page 5-6. Direct quotes from community members were taken from other areas in the report and inserted below the key statements to assist in understanding the impact of how affected individuals and their personal caregivers feel, function and survive. These are highlighted in gray.

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"*In my mind's eye, I see my daughter's joyful face transformed into one with shining scars spread like leopard spots that torque and pull her features and eat away at her nose and her eyelids and her ears. The ache of knowing a future I cannot protect her from is deep and penetrating. There is a morbid assurance of constancy that comes with this disease. There will never be a time when she can pause the march of cuts across her body. How do I prepare a child for that?*" - Meredith, mother of a teen-aged daughter with Gorlin syndrome.

Report Overview and Key Meeting Messages

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"*We are not cancer survivors. We are cancer livers, and I'm not talking about the organ, the liver. We live with cancer every day.*" – Julie, an individual with Gorlin Syndrome

1. **Individuals with Gorlin syndrome experience a lifelong cancer burden**. The unremitting and recurrent nature of this rare genetic disorder means that more BCCs, jaw cysts and manifestations will always appear and/or recur. People living with Gorlin syndrome experience no relief, break or remission, and they know that undergoing painful, invasive, and disfiguring treatments will always be necessary. They also live with an underlying fear that the BCCs could metastasize and kill them or that some other manifestation could lead to a premature death.

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"*Even though he was proactive in his own care, the skin cancer went from his lymph nodes to his lungs, and he had an agonizing and breathless death.*"

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Trudy has between 11 to 14 BCCs removed every second month, "*because if I don't, this disease will become unmanageable really quick. … I use my vacation days solely for Gorlin syndrome appointments, so I can maintain employment to finance this relentless disease.*"

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Stacy, the mother of a daughter with Gorlin syndrome, says- "*We know more surgery, more needles, more permanent scarring are in her future. Some days it is incredibly overwhelming that I start crying just getting her ready for school or swim class. BCCs grow everywhere, even on her labia. They're relentless. I wish more than anything it was easier to manage*

2. **There is no cure and there are no FDA-approved treatments for the multitude of Gorlin syndrome manifestations**. Existing treatment approaches and lifestyle modifications do not stop the appearance of new BCCs, nor do they prevent jaw cysts and other from growing or recurring. Surgeries are often brutal, painful, and disfiguring, and treatment outcomes may be uncertain.

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"*The surgeries, the cutting, the burning and all of the things that are necessary to remove these BCCs are nothing short of barbaric.*" Duane described that his 13-year-old grandson, "*At the age of 9 he had 139 of them removed under anesthesia at one time.*"

3. **Most individuals with Gorlin syndrome have a tremendous number of basal cell carcinomas during their lifetime, many over 1000**. Removal of these cancers is always painful, negatively impacts quality of life, and require time for recovery. These procedures cause increasing disfiguration over one's lifetime, as more skin is cut away.

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Bob described how his BCCs escalated in childhood and as he got older, their treatment became invasive and required "*repeated removal of 10 – 15 at a time, five to six times a year. …The scarring from the continued removal of some cancers became a challenge both physically and mentally.*"
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Meredith described her daughter's first experience with Mohs surgery at the age of 13 years. "*The average age for first time Mohs patient is 68. She had three lesions on her lash line. For four hours, they repeatedly anesthetized her lid and scooped out diseased tissue while she watched. The next day, she returned for plastic surgery to repair the lid. She repeated Mohs again this summer to remove a piece of flesh from her scalp.*"

4. **Gorlin syndrome can manifest in any organ system in the human body.** Most people living with Gorlin syndrome have multiple manifestations of the disease, which vary from one person to the next even within the same family. Manifestations can include basal cell carcinomas, jawbone tumors, hydrocephalus, ventricular asymmetry, brain tumors (malignant and benign), ovarian cysts, large skulls, improperly formed bones, palmar pitting, as well as many other symptoms.

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From statement of Medical Expert, Dr. Joyce Teng, Dermatologist at Stanford University.

Gorlin syndrome is a multi-system disorder and can affect all parts of the body. Basal cell carcinomas (BCCs), the most common manifestation, are a type of skin cancer that appear on the entire body, even in some children. Benign but aggressive and frequently

recurrent jaw cysts called odontogenic keratocysts (OKCs) or keratocystic odontogenic tumors (KCOTS) are another major manifestation. Gorlin syndrome has myriad of other manifestations including palmer/plantar pits (small depressions or pits in the palm of the hand and soles of the feet), calcification of the falx cerebri (in the brain), improperly formed bones of the spine, ribs, and a large skull (macrocephaly), as well as ocular anomalies. Gorlin syndrome includes many other types of cancers such as medulloblastoma (in the brain), as well as ovarian or cardiac fibromas.

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"*My 29-year-old daughter has had dozens of BCCs surgically removed thus far as well as 15 surgeries related to her other Gorlin syndrome manifestations. Prior to the age of 30, she's had over 40 invasive surgeries because of this disease.*"

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Leslie's son with Gorlin syndrome is only five years old and, "*he has been under anesthesia 20 times for MRIs and eight surgeries, all related to various manifestations of Gorlin Syndrome*."

5. **Gorlin syndrome imposes a heavy psychological burden. This point was emphasized throughout the meeting.** People living with Gorlin syndrome spend their entire lives on high alert, waiting for "what's next", especially cancer and tumor occurrence and recurrence. They have endless worries and uncertainty about the future. Despite displaying unbelievable resilience, many people living with Gorlin syndrome described being worn down by the unrelenting nature of the disease and the long-term treatment impacts; these may include but are not limited to disfigurement, pain, and the erosion and loss of self-esteem. For this reason, some stop or burn out on being treated. This has led to pre-mature death.

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   "Sometimes I wish that he had leukemia or a brain tumor or something that was treatable. And we could say, 'Now you're in remission, and we can move on from this.' There will never be a day that I will wake up when I will know my son is cancer-free, and there will never be a day for him that he will wake up and say, "I am cancer free." That is a heavy burden for a child.

6. **All activities of daily life are impacted.** Extreme lifestyle modifications are necessary to prevent sun and UV light exposure in this sensitive population. Monitoring and treatment by a variety of medical specialists is a way of life. It significantly impacts quality of life and the ability to live as the typical population does. Symptoms and treatments create barriers to regularly attending school, working, participating in sports and social activities, and developing relationships. To avoid passing the gene to the next generation, many described the excruciatingly difficult decision of not having children. Significant time and resources (financial and personal) are required to navigate the healthcare system to maintain high level of vigilance and appropriately manage the multitude of appointments and treatments (surgical and others) needed to care for oneself or a loved one. A global survey concluding in 2020 by the Gorlin Syndrome Alliance revealed that affected individuals and loved ones missed, on average, 25 days of work/school/activities in the prior year for treatments, appointments, and recovery.

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"The biggest challenge in his life currently is the sun. He's 13, he wants to go outside, he wants to play with his friends. He has to wear a bucket hat. He has to wear sun protective clothing. It's hard to tell your child, your son, when they want to go outside and play that they should probably stay inside because the UV rays are high that day. …Everything outside is a struggle. Water sports, any outdoor sport really. Every time we're outside, it's harmful for my son."

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With Gorlin syndrome, Sasha says that "*Limiting the outdoor errands and activities I do per week are necessary because of the risks of this syndrome, even at the cost of seeing friends and family.*"

7. **Diagnosis is often delayed by years or decades.** While the first signs and symptoms of Gorlin syndrome can occur in utero or infancy, a formal Gorlin syndrome diagnosis is often delayed for many years. The time before a diagnosis is characterized by uncertainty, bewilderment and fear, as new symptoms keep appearing. This time is also potentially catastrophic for those who receive x-rays and other ionizing radiation that will cause more BCCs later in life.

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   Connie's daughter with Gorlin syndrome had a malignant medulloblastoma and benign meningiomas. These are brain tumors that are Gorlin syndrome manifestations. "*My daughter was diagnosed with a medulloblastoma when she was 15 months old. She had two years of chemo followed by radiation to the brain and spine at the age of three. She's had multiple meningiomas in her brain, ovarian fibromas, as well as multiple basal cell carcinomas.*" It should also be noted that despite a lifetime of manifestations, Connie's daughter was not diagnosed with Gorlin syndrome until the age of 32.

8. **Safe and effective treatments are needed**. People with Gorlin syndrome need a better way to prevent and manage the endless flood of basal cell carcinomas; a clinically meaningful outcome for the Gorlin syndrome community is a 30% reduction in BCCs. Preventing transmission to the next generation and treating the root cause of the disease were also priorities. People living with Gorlin syndrome need a better way to treat and reduce the recurrence of jaw cysts that can result in the loss of permanent teeth, disfigurement, and facial numbness.

   More humane treatments will not only lessen the physical damage and scarring but tremendously improve the psychological impact and quality of the lives of all those affected with and by Gorlin syndrome.

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   My hope is future prophylactic medicines will be 100% effective without debilitating side-effects.

Until there is a cure, I wish there were topical treatments that would shrink and prevent my skin cancers without an ugly irritated reaction.