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SYNDROME ALLIANCE

Gorlin Syndrome Alliance
2026 Research Roadmap

Meaningful Progress Toward a Cure for Gorlin Syndrome

About the Gorlin Syndrome Alliance

The Gorlin Syndrome Alliance was founded by patients, for patients. Every aspect of our work is guided by the experiences and priorities of people living with Gorlin syndrome and the shared belief that a different future is possible.

We believe lasting change is achieved through focused collaboration. By bringing together patients, families, clinicians, researchers, industry partners, and advocates, we build coalitions that span institutions, disciplines, and geographic boundaries while uniting diverse stakeholders around a common purpose: improving the lives of people affected by Gorlin syndrome.

Our role is to transform lived experience into research priorities, scientific opportunity into patient impact, and individual efforts into collective progress. Together, we are building the ecosystem needed to accelerate discovery, advance therapeutic development, expand access to expert care, and move the Gorlin syndrome community toward prevention, disease-burden reduction, and ultimately a cure.

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Defining a Cure

The Gorlin Syndrome Alliance Research Roadmap is grounded in a patient-centered vision of what it means to advance toward a cure for Gorlin syndrome.

For the purposes of this roadmap, a cure is defined as the prevention, interception, or substantial reduction of new basal cell carcinomas (BCCs) and odontogenic keratocysts (OKCs) and their impact on the lives of people with Gorlin syndrome.

While complete and permanent prevention of disease manifestations remains the ultimate goal, meaningful reductions in disease burden, surgical procedures, surveillance requirements, and quality-of-life impacts represent important progress along the path to a cure. The GSA recognizes that success should not be viewed as a binary outcome. Every step that reduces the burden of disease for individuals and families living with Gorlin syndrome represents meaningful advancement.

This definition reflects the priorities identified through patient interviews, community engagement, survey initiatives, and discussions with clinicians and researchers. Although Gorlin syndrome affects multiple organ systems and can cause a wide range of manifestations that significantly impact patients and families, BCCs and OKCs were consistently identified as major contributors to lifelong disease burden due to their frequency, cumulative treatment burden, and impact on quality of life.

These manifestations often drive repeated surgeries, chronic surveillance, pain, scarring, functional impairment, financial burden, and psychosocial stress throughout the patient journey. As a result, reducing the formation and impact of BCCs and OKCs represents one of the most meaningful opportunities to improve quality of life for the greatest proportion of the Gorlin syndrome community.

This definition serves as the foundation for the roadmap and guides the strategic priorities that follow. The focus areas were identified based on a central question:

What knowledge, infrastructure, partnerships, and therapeutic advances are needed to prevent, intercept, or substantially reduce the burden of BCCs and OKCs and improve the lives of people with Gorlin syndrome?

Defining a Cure (continued)

Progress Toward a Cure Includes

- Delaying onset of BCCs and OKCs
- Preventing lesion development
- Intercepting lesions before they become clinically significant
- Reducing the frequency of new lesions
- **Improving quality of life**
- Reducing surveillance burden
- Reducing anxiety and uncertainty
- Reducing surgeries and procedures
- Achieving durable prevention

The GSA recognizes that Gorlin syndrome can cause a broad range of additional manifestations that significantly affect patients and families, including skeletal, developmental, neurological, and other disease-related complications.

The decision to focus this roadmap on BCCs and OKCs reflects the priorities identified through patient engagement and the substantial burden these manifestations impose across the largest proportion of the Gorlin syndrome community.

This focus is intended to guide strategic prioritization and does not diminish the importance of improving outcomes across the full spectrum of disease manifestations.

How the Roadmap Was Developed

The GSA Research Roadmap was developed through a patient-centered and evidence-informed process incorporating input from patients, caregivers, clinicians, researchers, industry representatives, and rare disease experts.

Patient interviews, survey initiatives, community discussions, scientific stakeholder engagement, and review of the current research landscape consistently emphasized the importance of reducing disease burden while advancing toward a cure. Patients repeatedly described the cumulative impact of repeated surgeries, chronic surveillance, pain, scarring, uncertainty, and disruption to daily life. Clinicians and researchers highlighted opportunities to improve care delivery, accelerate therapeutic development, strengthen research infrastructure, and better understand the factors that influence disease severity and progression.

The roadmap therefore prioritizes activities that have the greatest potential to improve patient outcomes while creating a foundation for future therapeutic advances. The focus areas were identified through a refinement process that asked:

> **What actions can most effectively reduce the burden of Gorlin syndrome today while advancing prevention, interception, and future curative strategies?**

Although presented as separate focus areas, the roadmap is intentionally designed as an interconnected strategy. Improvements in care delivery support research participation and long-term patient engagement. Research infrastructure enables therapeutic development and clinical trial readiness. Therapeutic studies generate new insights that improve clinical care and inform future discovery. Together, these activities create a cycle of learning and innovation that accelerates progress across the patient journey.

The roadmap reflects the GSA's commitment to balancing near-term impact with long-term ambition—improving the lives of individuals and families living with Gorlin syndrome today while building the foundation for the breakthroughs of tomorrow.

A Vision for the Future

Gorlin syndrome is a rare genetic disorder characterized by lifelong predisposition to basal cell carcinomas (BCCs), odontogenic keratocysts (OKCs), and multisystem manifestations affecting the skin, jaw, skeleton, and other organ systems. Although substantial progress has been made in understanding the biology of the disease and improving clinical management, individuals and families affected by Gorlin syndrome continue to experience significant lifelong disease burden.

For many patients, disease management involves repeated surgeries, chronic surveillance, cumulative scarring, pain, uncertainty, and emotional stress that may begin in childhood and continue throughout adulthood. Current treatment approaches remain largely reactive, focusing on management of disease manifestations after they occur rather than preventing them before they become clinically significant.

The Gorlin Syndrome Alliance believes that a different future is possible.

Advances in therapeutic development, precision medicine, data science, rare disease collaboration, and clinical research have created new opportunities to improve outcomes for individuals living with Gorlin syndrome.

This roadmap is grounded in a shared vision: to accelerate progress toward prevention, interception, disease-burden reduction, and ultimately a cure for Gorlin syndrome.

Achieving this vision will require coordinated investment in patient care, research infrastructure, therapeutic development, and strategic collaboration across academia, industry, advocacy organizations, regulatory stakeholders, and the patient community. Success will depend not only on scientific discovery, but also on our ability to translate knowledge into meaningful improvements in the lives of patients and families.

Importantly, the pursuit of a cure does not diminish the urgency of improving patients' lives today. The roadmap therefore embraces both near-term and long-term goals: reducing disease burden now while building the foundation for future therapeutic advances. Every step that delays disease onset, prevents lesion formation, reduces procedures, improves quality of life, or decreases lifelong disease burden represents meaningful progress toward a future in which Gorlin syndrome has a far smaller impact on the lives of those it affects.

A Moment of Opportunity

The Gorlin syndrome community is experiencing a uniquely important moment.

Over the past decade, significant advances in genetics, cancer biology, and rare disease research have expanded understanding of the pathways that drive disease manifestations in Gorlin syndrome. At the same time, growing collaboration among patients, clinicians, researchers, advocacy organizations, and industry partners has created new opportunities to translate scientific knowledge into meaningful improvements in patient care.

Importantly, there is increasing recognition that the burden of Gorlin syndrome extends beyond management of individual basal cell carcinomas alone. Odontogenic keratocysts, disease heterogeneity, lifelong surveillance requirements, repeated procedures, psychosocial impacts, and variability in disease severity all represent important unmet needs requiring additional attention.

The rare disease landscape has also evolved considerably. Patient registries, natural history studies, collaborative research networks, Centers of Excellence, and advocacy-driven initiatives now provide opportunities to better understand disease progression, identify meaningful clinical endpoints, support clinical trial readiness, and accelerate therapeutic development.

At the same time, advances in therapeutic development, precision medicine, computational biology, and emerging technologies are creating new opportunities to develop prevention-focused strategies, improve existing treatments, and explore novel approaches that may ultimately reduce disease burden and improve long-term outcomes.

The Gorlin syndrome community is increasingly aligned around a shared goal: reducing the lifelong burden of disease while advancing toward a cure.

Patients, families, clinicians, researchers, and advocacy organizations all have critical roles to play in achieving this vision.

This convergence of scientific progress, patient engagement, clinical expertise, and therapeutic innovation creates an unprecedented opportunity to accelerate progress. The GSA believes that by strategically investing in patient-centered care, research infrastructure, therapeutic development, and collaborative partnerships, the field can move beyond incremental improvements toward transformative change.

Patient-Centered Priorities

The GSA Research Roadmap is grounded in the experiences and priorities of individuals and families living with Gorlin syndrome.

Through patient interviews, community discussions, survey initiatives, and engagement with clinicians and researchers, several recurring themes consistently emerged. Patients repeatedly emphasized the cumulative burden associated with repeated procedures, chronic surveillance, scarring, pain, uncertainty surrounding disease progression, and the ongoing impact of disease management on daily life. Many individuals described the psychological effects of living with a lifelong condition, including anxiety related to recurrence, future disease burden, cosmetic outcomes, and uncertainty about what lies ahead.

Importantly, patients consistently expressed that success should not be defined solely by the number of tumors or cysts prevented, but also by meaningful improvements in quality of life, reduction in treatment burden, increased access to expert care, and the ability to live with less disruption from disease. Several key patient-centered priorities therefore guide this roadmap:

KEY PATIENT PRIORITIES

- **Prevent & intercept lesions:** Preventing, intercepting, or reducing the formation of new BCCs and OKCs
- **Reduce procedural burden:** Reducing pain, scarring, and cumulative procedural burden
- **Quality of life:** Improving quality of life and psychosocial well-being
- **Expert care access:** Expanding access to multidisciplinary expert care
- **Coordinated care:** Improving care coordination throughout the patient journey
- **Safer treatments:** Advancing safer, more effective, and less invasive treatments
- **Reduce surveillance burden:** Reducing surveillance burden and disease-related uncertainty
- **Earlier intervention:** Supporting earlier intervention and prevention-focused approaches
- **Beyond reactive care:** Building a future beyond lifelong reactive disease management

The roadmap recognizes patients and families not simply as participants in research, but as active partners in shaping care priorities, research initiatives, therapeutic development, and the long-term vision for the Gorlin syndrome community. Their experiences and perspectives serve as the foundation for the goals and priorities outlined throughout this roadmap.

How the Focus Areas Work Together

The three focus areas—Building a Research and Care Ecosystem, Accelerating Therapeutic Development, and Understanding Disease Variability and Therapeutic Opportunity—are presented separately for clarity, but they are intentionally designed as an interconnected strategy that advances both patient care and progress toward a cure.

Building the Research & Care Ecosystem

The Research and Care Ecosystem serves as the foundation of the roadmap. Centers of Excellence, clinical practice guidelines, the Natural History Study, and collaborative networks help improve patient care while generating the data, expertise, and infrastructure needed to support research and therapeutic development.

Accelerating Therapeutic Development

Therapeutic Development builds upon this foundation by supporting studies, partnerships, and clinical trials aimed at preventing disease manifestations, reducing disease burden, and improving patient outcomes. Insights gained through therapeutic research help identify meaningful clinical endpoints, refine treatment strategies, and guide future investment priorities.

Advancing Precision Medicine

Understanding the Genetic Landscape provides an additional layer of knowledge by linking genomic information with longitudinal clinical data. These integrated resources help researchers better understand disease variability, identify factors that influence disease severity, support therapeutic development, and prepare the community for future precision medicine and emerging curative technologies.

Together, these focus areas create a continuous cycle of learning and improvement. Better care supports research participation. Research generates new knowledge. New knowledge informs therapeutic development. Therapeutic advances improve patient outcomes.

Focus Area 1

Building the Research & Care Ecosystem

GOAL: Develop the clinical, organizational, and research infrastructure necessary to improve care for individuals with Gorlin syndrome while generating the knowledge, expertise, and resources needed to support future therapeutic development.

The GSA believes that improving patient outcomes begins with improving access to coordinated, expert care. Individuals with Gorlin syndrome often require management across multiple specialties, including dermatology, oral and maxillofacial surgery, genetics, genetic counseling, and other disciplines. Variability in access to expertise can lead to differences in care, treatment approaches, and patient outcomes.

To address these challenges, the roadmap prioritizes development of multidisciplinary Centers of Excellence capable of providing coordinated, evidence-informed care throughout the patient journey. These centers will serve as hubs for clinical expertise, care coordination, patient education, and implementation of standardized care pathways. They will also create opportunities for longitudinal follow-up, research participation, and future clinical trial engagement.

The roadmap also supports continued growth of the GSA Natural History Study as a longitudinal research platform that includes patient-reported information and clinical data. Increased participation in the study will strengthen understanding of disease progression, treatment outcomes, quality-of-life impacts, and variability in disease burden, while helping define meaningful clinical endpoints for future therapeutic studies.

Importantly, the GSA recognizes that patient care and research are mutually reinforcing. Improved care creates opportunities for long-term follow-up, patient engagement, and research participation, while research generates new knowledge that can be translated into better care. Through coordinated networks, standardized practices, and collaborative partnerships, the GSA seeks to build an ecosystem that advances both patient outcomes and scientific progress.

Building a Research and Care Ecosystem (continued)

Short-Term Goal

Establish a coordinated network of Centers of Excellence that improves patient care, standardizes clinical management, supports research participation, and creates a foundation for future therapeutic development.

Long-Term Goal

Create a sustainable global Gorlin syndrome ecosystem that improves patient outcomes, accelerates therapeutic development, and supports progress toward a cure.

Key Priorities

- **Develop multidisciplinary Centers of Excellence** that provide coordinated care, support longitudinal follow-up, facilitate research participation, and serve as hubs for expertise sharing across the Gorlin syndrome community.

- **Establish standardized outcome measures, disease severity classifications, and clinical trial readiness infrastructure** to support therapeutic development, multicenter studies, and future clinical trials.

- **Strengthen global collaboration and knowledge sharing** among clinicians, researchers, patient organizations, and other stakeholders to accelerate improvements in care, research, and therapeutic development.

- **Expand the GSA Natural History Study** through increased patient participation and continued collection of clinician-validated clinical data and patient-reported outcomes to better understand disease progression, treatment outcomes, and quality-of-life burden.

- **Advance evidence-based clinical practice guidelines** by building upon the recently published recommendations for basal cell carcinomas (BCCs) and prioritizing development of guidance for odontogenic keratocysts (OKCs) to promote consistent, high-quality care, reduce treatment variation, and identify future research priorities.

Long-Term Vision

Create a coordinated global ecosystem that delivers expert care, supports research participation, generates meaningful clinical evidence, and provides the foundation necessary to accelerate therapeutic development and advance toward a cure for Gorlin syndrome.

Focus Area 2

Accelerating Therapeutic Development

GOAL: Advance therapeutic development by supporting innovative research, strategic partnerships, and clinical translation efforts that improve patient outcomes and reduce the lifelong burden of Gorlin syndrome.

Current management of Gorlin syndrome remains heavily dependent upon repeated surgical treatment of basal cell carcinomas (BCCs) and odontogenic keratocysts (OKCs). Although these interventions are often effective for individual lesions, repeated procedures over a lifetime contribute substantially to physical, emotional, cosmetic, and financial burden.

The GSA therefore prioritizes therapeutic strategies aimed not only at treating existing disease manifestations, but also preventing lesion development, intercepting disease before it becomes clinically significant, and reducing the cumulative burden associated with lifelong disease management.

A central component of this effort is strategic investment in research. Through initiatives such as the GSA Cure Accelerator Grant Program, sponsored fellowships, and partnerships with organizations including the Pediatric Dermatology Research Alliance (PeDRA), the GSA seeks to accelerate studies that have the greatest potential to improve patient outcomes and advance the field.

The roadmap supports investigation of prevention-focused therapies, novel approaches for BCC and OKC management, next-generation Hedgehog pathway inhibitors, drug repurposing opportunities, innovative drug delivery systems, and emerging therapeutic technologies. Particular emphasis is placed on identifying interventions capable of reducing disease burden, delaying disease progression, and improving quality of life.

The GSA is also encouraged by advances in gene therapy, RNA therapeutics, and other emerging curative technologies. While these approaches remain subject to important scientific, safety, feasibility, and cost considerations, the roadmap seeks to position the Gorlin syndrome community to evaluate and support such opportunities as the field continues to evolve.

Accelerating Therapeutic Development (continued)

Short-Term Goal

Support and fund research that reduces disease burden, prevents formation of new BCCs and OKCs, and advances promising therapeutic approaches for individuals living with Gorlin syndrome.

Long-Term Goal

Accelerate development of disease-modifying therapies capable of preventing, intercepting, or substantially reducing the burden of BCCs and OKCs while advancing toward a cure.

Key Priorities

- **Fund high-impact therapeutic research** through grants, fellowships, and strategic partnerships that accelerate therapeutic development and address critical unmet needs in Gorlin syndrome.

- **Advance prevention-focused therapeutic strategies** aimed at reducing or preventing formation of new BCCs and OKCs and decreasing lifelong disease burden.

- **Develop improved therapies for BCCs and OKCs** including non-surgical approaches, novel therapeutic modalities, and strategies designed to reduce recurrence and cumulative procedures.

- **Support innovative therapeutic discovery and development** through drug repurposing, computational biology, artificial intelligence, and emerging technologies that may accelerate identification of promising treatment opportunities.

- **Strengthen clinical trial readiness and patient-centered outcome measures** to support therapeutic evaluation and focus on meaningful reductions in disease burden, treatment burden, and quality-of-life impacts.

Long-Term Vision

Create a robust therapeutic development pipeline that advances prevention, interception, and disease-burden reduction strategies while positioning the Gorlin syndrome community to benefit from future scientific and therapeutic breakthroughs on the path toward a cure.

Focus Area 3

Advancing Precision Medicine

GOAL: Improve understanding of why disease severity varies among individuals with Gorlin syndrome in order to support therapeutic development, enhance clinical trial readiness, and identify opportunities to reduce disease burden.

Although pathogenic variants in PTCH1 and other Hedgehog pathway genes are well-established drivers of Gorlin syndrome, substantial variability exists among patients with respect to BCC burden, OKC development, age of onset, recurrence patterns, treatment outcomes, and overall disease severity. Some individuals experience relatively mild disease throughout their lives, while others face significant cumulative disease burden, repeated procedures, and intensive surveillance.

Understanding the factors that contribute to this variability remains one of the most important unanswered questions in Gorlin syndrome. Identifying the genetic and clinical factors associated with disease severity may reveal opportunities to improve prevention strategies, guide therapeutic development, identify patients most likely to benefit from specific interventions, and support more personalized approaches to care.

To address these questions, the GSA seeks to integrate genetic information with longitudinal clinical data collected through the Natural History Study. By linking genetic findings with real-world patient outcomes, researchers can better understand disease progression, treatment response, and factors associated with BCC burden, OKC development, and overall quality of life.

Importantly, an integrated clinical-genetic resource can also serve as a powerful tool for therapeutic development. Linking genetic and longitudinal clinical data may help identify patient populations most likely to respond to specific therapies, support biomarker discovery, improve patient stratification, and define meaningful clinical endpoints for future studies.

Advancing Precision Medicine (continued)

Short-Term Goal

Establish an integrated clinical-genetic resource that links genetic information from individuals and families affected by Gorlin syndrome with longitudinal clinical data collected through the GSA Natural History Study.

Long-Term Goal

Leverage integrated clinical and genetic data to better understand disease variability, support therapeutic development, improve clinical trial readiness, and position the Gorlin syndrome community to benefit from future advances in precision medicine and emerging therapeutic technologies.

For rare diseases such as Gorlin syndrome, robust longitudinal datasets may also help establish natural history comparators and external control cohorts that can reduce barriers to clinical trial execution. These resources can make therapeutic development more efficient and help position the Gorlin syndrome community as an attractive partner for academic investigators, biotechnology companies, and pharmaceutical organizations seeking to develop new treatments.

Through these efforts, the GSA aims to create a resource that not only advances scientific understanding of Gorlin syndrome, but also accelerates translation of that knowledge into therapies that meaningfully improve patient outcomes.

Key Priorities

- **Integrate clinical and genetic data** from the GSA Natural History Study to better understand disease progression, treatment outcomes, quality-of-life impacts, and variability in disease burden.

- **Identify drivers of disease severity** by studying genetic, molecular, and clinical factors associated with differences in BCC burden, OKC development, recurrence risk, and overall disease impact.

- **Develop a clinical-genetic research resource** that supports collaborative research, therapeutic development, industry partnerships, and future precision medicine initiatives.

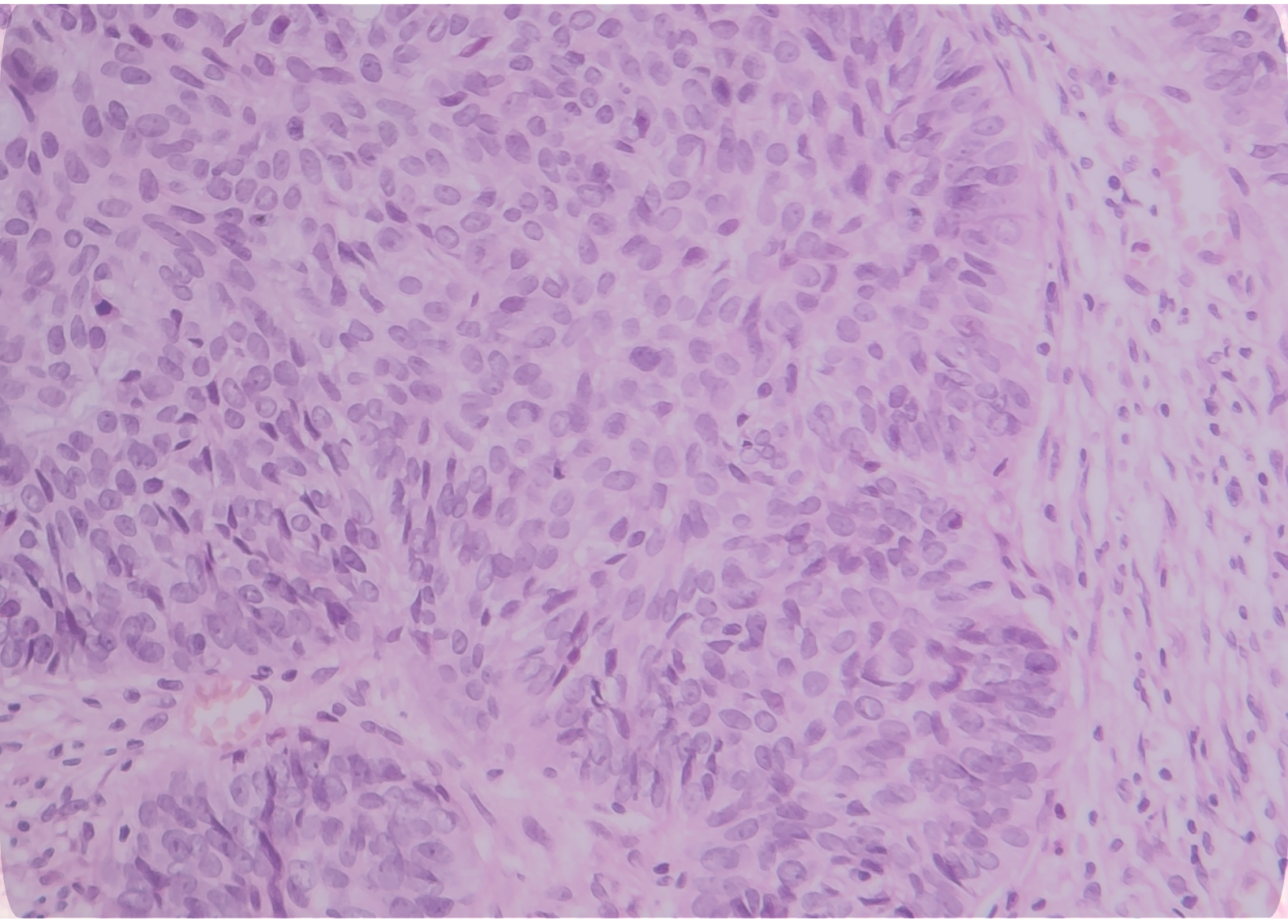
- **Establish disease severity classifications and patient stratification approaches** by integrating genetic, clinical, and longitudinal outcomes data to identify factors associated with differences in disease burden, treatment outcomes, and progression.

- **Support clinical trial design and therapeutic development** through development of meaningful clinical endpoints, identification of target patient populations, and generation of longitudinal datasets that may serve as natural history comparators or external control cohorts.

Advancing Precision Medicine (continued)

Long-Term Vision

Establish a sustainable clinical-genetic resource that improves understanding of disease variability, supports therapeutic development, enables more efficient clinical trial design, facilitates industry partnerships, and helps accelerate the development of therapies that reduce the burden of Gorlin syndrome.



Looking Ahead

Advancing toward a cure for Gorlin syndrome will require visionary thinking, sustained investment, scientific collaboration, and meaningful partnership with patients and families.

While significant challenges remain, there has never been a more promising time to accelerate progress. Growing collaboration among patients, clinicians, researchers, advocacy organizations, industry partners, and other stakeholders has created new opportunities to improve care, advance therapeutic development, and deepen understanding of the factors that drive disease burden.

The GSA believes that meaningful progress can be achieved through a coordinated strategy that strengthens the research and care ecosystem, accelerates development of new therapies, and builds the clinical-genomic resources needed to support future discovery and innovation. Together, these efforts have the potential to improve patient outcomes today while creating the foundation for tomorrow's breakthroughs.

Importantly, progress toward a cure should not be measured solely by a single future milestone.

> ***Every advancement that delays disease onset, prevents lesion formation, reduces procedures, improves quality of life, expands access to expert care, or lessens the burden of lifelong disease management represents meaningful success for individuals and families living with Gorlin syndrome.***

By strategically investing in patient-centered care, therapeutic development, collaborative partnerships, and research infrastructure, the Gorlin Syndrome Alliance seeks to help build a future in which Gorlin syndrome can be managed more effectively and ultimately have a far smaller impact on the lives of those it affects.

The path to a cure will not be defined by a single breakthrough, but by the collective progress we make together. Every patient enrolled, every partnership formed, every discovery advanced, and every burden reduced brings the Gorlin syndrome community closer to a future where this disease no longer defines the lives of those it touches.

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