CTNNB1 FOUNDATION
Bringing hope to children

2021 - 2024 FINANCIAL REPORT

March 2025

CTNNB1 Foundation, The Gene Therapy Research Institute
www.ctnnb1-foundation.org

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FOUNDER'S STATEMENT

Driven by a deeply personal mission, the CTNNB1 Foundation was founded on February 5, 2021, shortly after the Foundation's President received confirmation that her son, Urban, had been diagnosed with CTNNB1 Syndrome. What began as a mother's determination to help her child quickly transformed into a global movement to support all children affected by this rare genetic disorder.

The Foundation was officially registered on March 7, 2021, and received official recognition March 10, 2021, from the Ministry of Health of the Republic of Slovenia. Since its inception, the Foundation has been dedicated to advancing research, developing treatments, and improving the quality of life for individuals diagnosed with CTNNB1 Syndrome.

As a non-profit organization, we are committed to addressing the urgent need for therapeutic solutions in the rare disease community. Many rare conditions, often referred to as "orphan diseases," lack commercial incentives for pharmaceutical companies to pursue research and treatment development. As a result, families and advocacy groups - rather than large medical institutions - often lead the search for solutions.

The Foundation's core mission is to develop an effective and safe treatments for CTNNB1 Syndrome. Beyond this, our research holds the potential to provide valuable insights into other genetic disorders, contributing to the broader field of rare disease research. By advancing scientific understanding and fostering innovation, we aim to create lasting impact - not only for children diagnosed with CTNNB1 Syndrome, but also for future generations affected by rare diseases worldwide.

ŠPELA MIROŠEVIČ
CTNNB1 Foundation Founding President

ORGANIZATION OVERVIEW

BASIC INFORMATION

Name: CTNNB1 Foundation, The Gene Therapy Research Institute

Address: Dalmatinova ulica 5, 1000 Ljubljana
Registration number: 4125878000
Tax number: SI62919571
Bank account: SI56 6100-00025350715

Founders: Špela Miroševič, Samo Miroševič
Board members: Damjan Osredkar, MD, PhD
Duško Lainšček, PhD
Špela Miroševič, PhD

President: Špela Miroševič, PhD
Vice-president: Ana Gonzalez Hernandez, PhD

Contact: +386 31 731 269
Email: spela@ctnnb1-foundation.org

OUR TEAM

LEADING TEAM

- Špela Miroševič, PhD, Founding President
- Ana Gonzalez Hernandez, PhD, Vice-President
- Bruno Ramalho, Technical Director
- Lavra Debeljak, Research and Patient Relations Associate
- Effie Parks, Family Network Liason
- Sneha Kranthi, Regulatory Expert
- Estibaliz Martin Medina, Spanish Network
- Mirela Ferraro, Italian Network
- Katharin Wisniewski, German Network
- Lucy Mort, Australian Network
- Emilie Francisci, French Network

MEDICAL & SCIENTIFIC ADVISORY TEAM

CLINICAL TEAM

- Damjan Osredkar, MD, PhD, University Medical Centre Ljubljana
- Nina Žakelj, MD, University Medical Centre Ljubljana
- David Gosar, PhD, University Medical Centre Ljubljana
- Laurent Servais, MD, PhD, University of Oxford
- Fiona Moultrie, MD, PhD, University of Oxford
- Charlotte Lilien, University of Oxford
- Michelle Ferrar, Sydney Children's Hospital

RNA DEVELOPMENT & PRECLINICAL TESTING

- Roman Jerala, PhD, National Institute of Chemistry
- Duško Lainšček, PhD, National Institute of Chemistry
- Petra Sušjan, PhD, National Institute of Chemistry
- Vida Forstnerič, PhD, National Institute of Chemistry
- Matea Maruna, PhD, National Institute of Chemistry

VECTOR DEVELOPMENT & PRECLINICAL TESTING

- Leszek Lisowski, PhD, Children's Medical Research Institute
- Andrea Perez-Iturralde, PhD, Children's Medical Research Institute

VECTOR MANUFACTURING

- Cristina Martin Quintin, Viralgen Vector Core
- Sonya Banks, Viralgen, Vector Core

INDEPENDENT CONSULTANTS

- Ruud Bueters,Toxicology Expert
- Elise Destree, Regulatory Expert

PATIENT-DRIVEN ORGANISATION SUPPORT

- Terry Pirovalski, Elpida & SPG50
- Julia Taravella, Rare Trait Hope Fund & AGU
- Pat Furlong, Parent Project Muscular Dystrophy (PPMD)
- Amber Freed, SLC6A1 Connect

EXECUTIVE SUMMARY

OUR MISSION, PROJECTS AND PROGRAMS

The CTNNB1 Foundation is dedicated to advancing research, developing treatments, and improving the quality of life for individuals diagnosed with CTNNB1 Syndrome. Since our establishment in 2021, we have worked relentlessly to bridge the gap between scientific discovery and real-world solutions for affected families.

Our core initiatives focus on three key areas:

1. CTNNB1 conference – An annual event that brings together leading researchers, medical professionals, and families from around the world to discuss the latest advancements in CTNNB1 research, clinical care, and therapeutic developments. This conference fosters collaboration and accelerates progress in the rare disease space.

2. Natural History Study (NHS) – A crucial research effort aimed at documenting the natural progression of CTNNB1 Syndrome. This study allows us to collect long-term clinical data, providing a deeper understanding of the syndrome and establishing essential baseline data for our upcoming clinical trial. We are committed to making this study international, ensuring that patients are included regardless of their location or language.

3. Advancing gene therapy – Our most ambitious project focuses on developing a gene therapy treatment for CTNNB1 Syndrome. This groundbreaking effort aims to correct the underlying genetic mutation, offering hope for improved motor function, cognitive abilities, and overall quality of life for affected individuals.

NOTABLE MILESTONES 2021 - 2024

Over the past four years, the CTNNB1 Foundation has made significant progress in advocacy, research, and treatment development. Some of our most impactful milestones include:

- **Amendment of Slovenian law** – We successfully advocated for a legislative change that enhances support for early-stage advanced therapy programs.
- **Manufacturing of GMP clinical batch** – After years of dedicated research, collaboration with leading scientists, and extensive preclinical testing in cell and animal models, we obtained an exclusive license from CMRI and initiated the GMP manufacturing process for AAV9 Gene Replacement Therapy (Urbagen) with Viralgen. This marks a critical step toward clinical application.
- **Advancing research & knowledge sharing** – We have organized multiple international CTNNB1 Conferences, published three scientific articles, and launched an ongoing Natural History Study, all of which contribute to a deeper understanding of CTNNB1 Syndrome and its potential treatments.
- **Expanding global awareness and research efforts** – Through dedicated fundraising efforts, the Foundation has raised over €4 million between 2021 and 2024, an extraordinary achievement that has accelerated our research and brought us closer to clinical trials.

These milestones reflect our commitment to collaboration, patient advocacy, and driving meaningful change for families affected by CTNNB1 Syndrome.

KEY PARTNERSHIPS AND COLLABORATIONS

Collaboration is the foundation of our success. By partnering with leading research institutions and advocacy organizations, we have significantly strengthened our ability to drive meaningful change in CTNNB1 Syndrome research and treatment. Some of our most impactful collaborations include:

- **Children's Medical Research Institute, National Institute of Chemistry, Faculty of Medicine, Czech Centre for Phenogenomics, Labena Slovenija, and CIMA** – where proof-of-concept data was generated and our key toxicology studies were conducted.
- **Viralgen** – where our GMP clinical batch was successfully manufactured.
- **University Medical Centre Ljubljana (UMC) & Oxford University** – where our Natural History Study was designed and where clinical trial development is underway. UMC Ljubljana will also serve as the site for our Phase I/II clinical trial.
- **Palčica Pomagalčica in Dobrodelni Škratki & Asociación CTNNB1**– our major donor contributors, who have supported us unwaveringly since the very beginning.

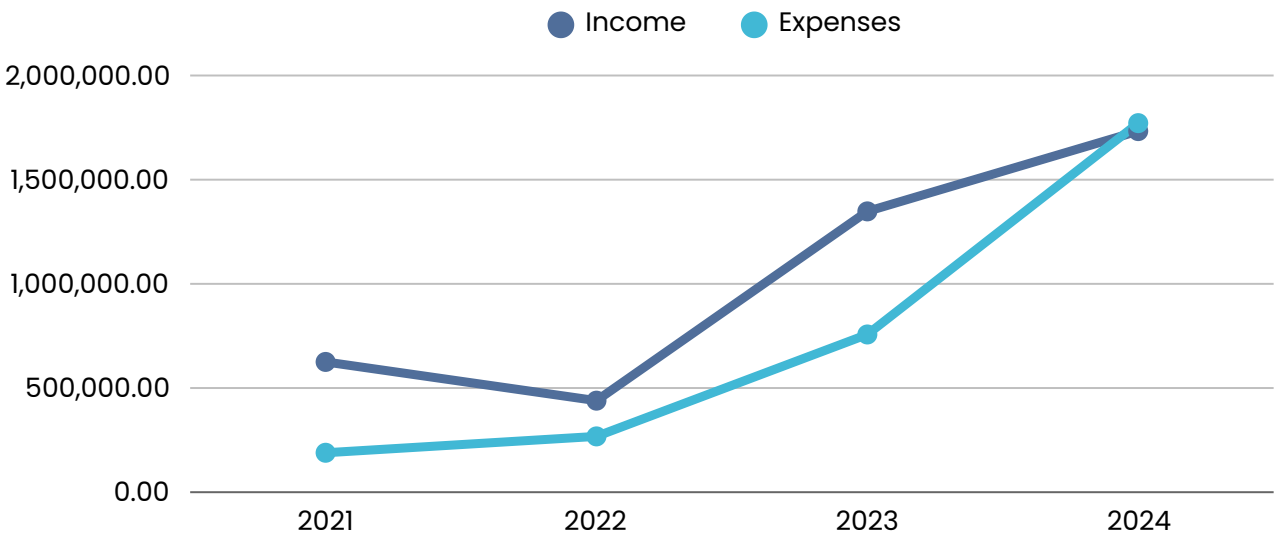
These collaborations highlight our commitment to international cooperation, reinforcing our belief that breakthroughs in rare disease treatment can only be achieved through collective effort, shared expertise, and a united vision.

A sincere thank you to everyone who has dedicated their time, effort and resources for our cause.

FINANCIAL OVERVIEW

GENERAL FINANCIAL TRENDS (2021 - 2024)

Over the years, the CTNNB1 Foundation significantly increased in income, particularly in 2023 and 2024, coinciding with large donations/funding opportunities. However, expenses have also risen dramatically, particularly in 2024, due to manufacturing and preclinical testing costs.



Yearly summary of incoming funds and expenses

Year	Income (€)	Expenses (€)
2021	625,270.05	189,294.49
2022	439,361.08	267,846.88
2023	1,347,848.02	757,052.58
2024	1,733,205.12	1,771,408.81

Note: In 2025, total income amounts to €61,198.42, while expenses have risen to €486,823.80, reflecting a significant increase in costs as we advance toward the clinical trial phase.

OUR TOP 5 DONORS

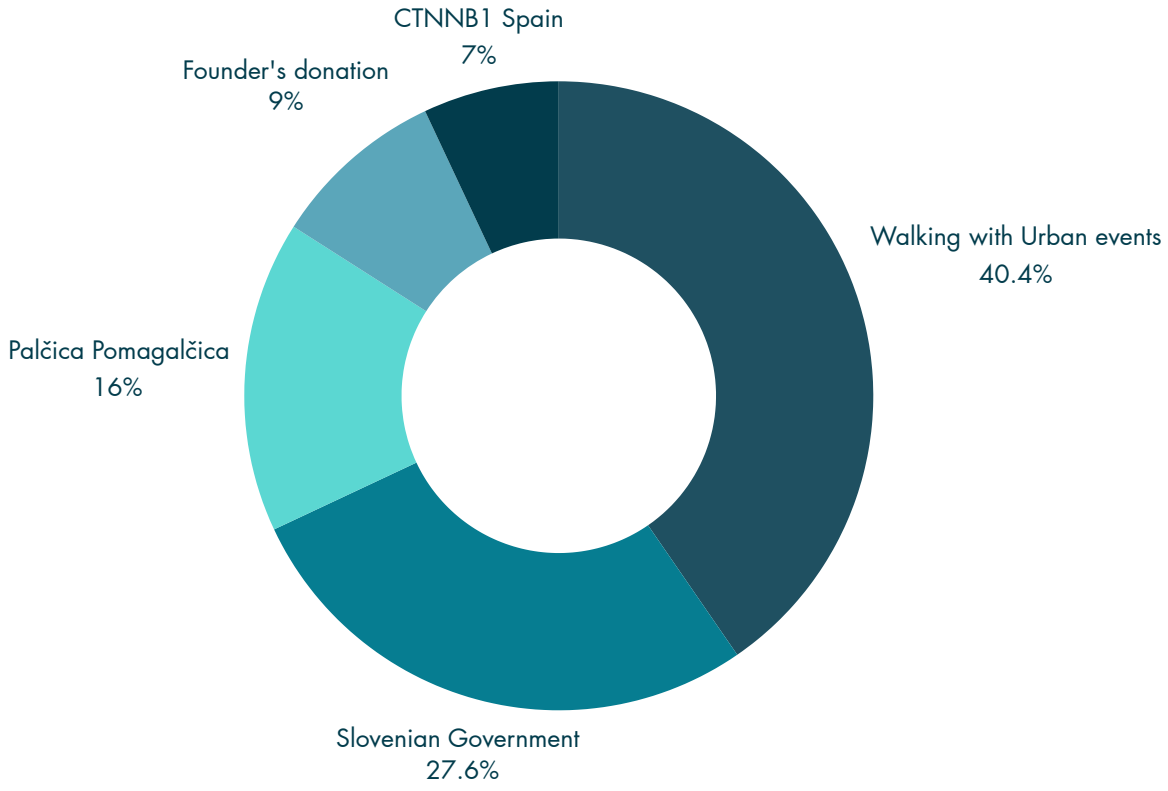
Our top five contributors from 2021 to 2024 have provided **86% of our total funding**, playing a key role in advancing our research and development efforts. Their support has been essential in moving our gene therapy program forward and ensuring continued progress toward clinical trials.

The "Walking with Urban" fundraising campaigns have raised €1,462,531 through numerous events held between 2021 and 2024. These campaigns have brought together communities and supporters to fund vital research, preclinical studies, and clinical trial preparations. The Slovenian government has contributed €1,000,000 to support our early-stage gene therapy program, recognizing the importance of developing treatments for CTNNB1 Syndrome.

The Slovenian Association “Palčica Pomagalčica” has raised €580,000, providing continuous support for our mission. A personal donation from founders, amounting to approximately €325,000, reflects a deep commitment to the cause and a strong belief in the urgency of developing an effective therapy.

Lastly, CTNNB1 Spain has contributed €253,000 over several years through intensive fundraising efforts. Their dedication has helped expand awareness and resources, making a significant impact on our progress.

These contributions have been essential in driving our research forward, demonstrating the power of collective support in the fight against CTNNB1 Syndrome.



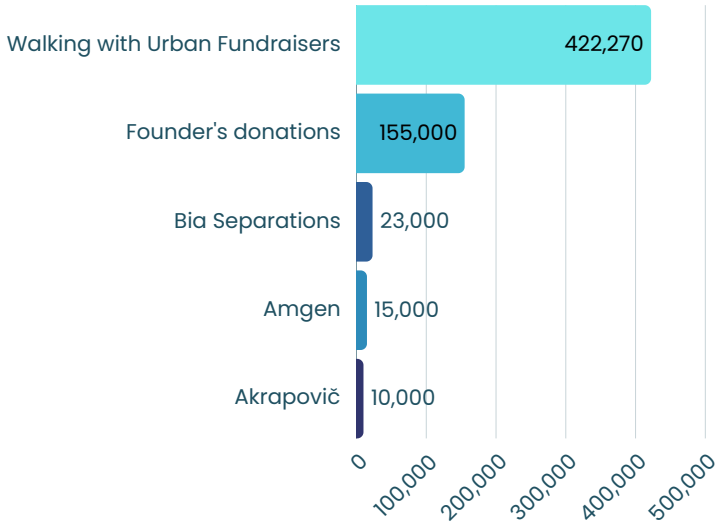
ANNUAL BREAKDOWN FOR 2021

MAIN CONTRIBUTORS IN 2021

2021 marked the official founding of the CTNNB1 Foundation and the beginning of our mission to develop the first gene therapy for CTNNB1 Syndrome. The groundwork had been laid the year before, as we assembled a multidisciplinary team of experts and launched fundraising efforts to support research.

One of the first stepping stones was securing a research agreement with CMRI Sydney, establishing key partnerships with leading scientists. We also launched our first clinical research project, the Genotype-Phenotype Study, enrolling the first CTNNB1 patients in clinical interviews. Collaboration with Columbus Foundation and Viralgen began, supporting our therapeutic development. Additionally, patient cells were sent to international partners to create iPS cells and brain organoids, crucial for preclinical testing. Meanwhile, in vitro studies were initiated, testing six engineered variants to assess the feasibility, safety, and efficacy of gene therapy.

None of this would be possible without the help of generous donors, such as the Founder's donations (€155,000.00, 24.8%), Bia Separations (€23,000.00, 3.7%), Amgen (€15,000.00, 2.4%), and Akrapovič (€10,000.00, 1.6%), whose contributions are reflected in the accompanying graph. "Walking with Urban" Fundraisers proved to be very successful, bringing in 67.5% of all contributions. By the end of the year, we had secured a total revenue of €625,270.05.



MAIN EXPENSES AND ALLOCATIONS IN 2021

The year 2021 was mainly financed by the founder's personal initiatives and by fundraising campaigns and events organized in the name of the founder's child. The majority of our resources for that year were allocated to the University of Sydney (€167,718.95, 88.7%) for the development of AAV gene therapy program.

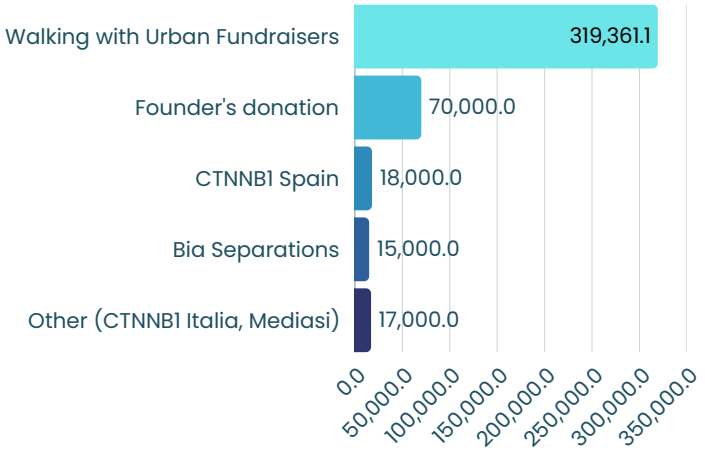
ANNUAL BREAKDOWN FOR 2022

MAIN CONTRIBUTORS IN 2022

Fundraising efforts had progressed, surpassing the €1 million milestone in March 2022. Once again, the "Walking with Urban" events played a key role, raising 72.7% of all contributions, and demonstrating the remarkable dedication of the Slovenian community to supporting children in need. This year also marked a significant international collaboration, as CTNNB1 Foundation and Asociación CTNNB1 joined forces, with the Spanish association contributing 4.1% of all funds raised.

ERN Ithaca expanded our advocacy work and strengthened our voice in the rare disease community. In addition, at the Innovation Task Force meeting with the EMA, we received valuable regulatory guidance that further refined our gene therapy program and we were selected as one of the best advanced therapy programs.

We closed the year with strong financial support, and total revenue of €439,361.08. Additional key contributions came from our founder (€70,000, 15.9%), CTNNB1 Spain (€18,000, 4.1%), Bia Separations (€15,000, 3.4%), and Mediasi & CTNNB1 Italia (€17,000, 3.8%), as shown in the accompanying graph.



MAIN EXPENSES AND ALLOCATIONS IN 2022

In 2022, the majority of our funding was directed toward critical research initiatives, including the development of the CTNNB1 mouse model at The Jackson Laboratory (€114,638.46, 42.8%), a key step in understanding disease mechanisms.

At the same time, we continued to support studies at the University of Sydney/CMRI (€124,902.65, 46.6%), driving progress in gene therapy research.

Additional notable expenses (€28,305.77, 10.6%) covered collaborations with Washington University in St. Louis, Gene Tools, and essential operational costs, such as accounting.

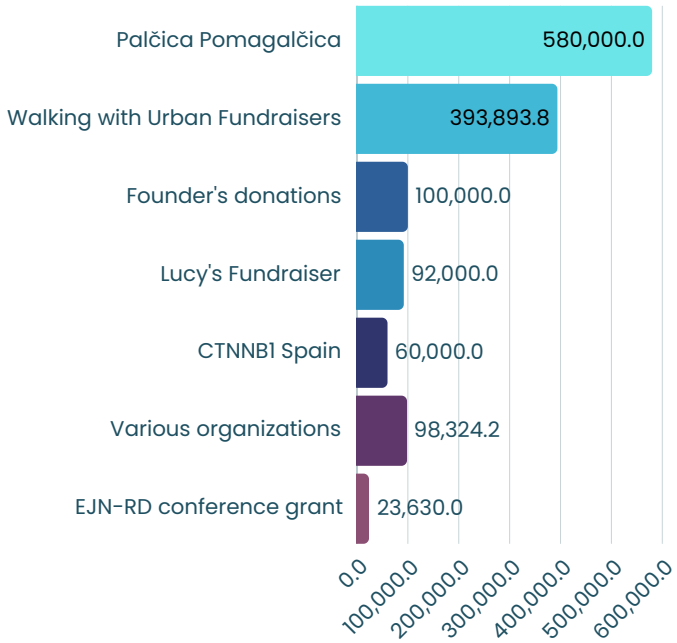
ANNUAL BREAKDOWN FOR 2023

MAIN CONTRIBUTORS IN 2023

In 2023, we made significant progress in advancing AAV9 gene replacement therapy, with efficacy and long-term studies continuing at CMRI and Charles River Laboratory. Additionally, we expanded our research efforts by supporting RNA-based therapies at the National Institute of Chemistry, further diversifying our approach to potential treatments.

This year also marked a major milestone in community engagement and advocacy, as we successfully organized the 1st International CTNNB1 Syndrome Conference in Madrid, Spain, in collaboration with Asociación CTNNB1. The event brought together leading researchers, medical professionals, and families, strengthening global collaboration and awareness.

Fundraising efforts saw a significant increase, with major contributions from Slovenian and international donors. The largest support came from Palčica Pomagalčica (€580,000, 43.0%), followed by "Walking with Urban" events (€393,893.83, 29.2%), Founder's donations (€100,000, 7.4%), and Lucy's fundraiser (€92,000, 6.8%). Additional contributions were made by CTNNB1 Spain (€60,000, 4.5%), as well as organizations such as Sparkasse, Lions Club, Rotary Club, Mediasi, Andersen family, Jacqueline Marie Fund, and Rare Village (€98,324.19, 7.3%). We also secured an EJN-RD conference grant (€23,630, 1.8%), further supporting our efforts.



MAIN EXPENSES AND ALLOCATIONS IN 2023

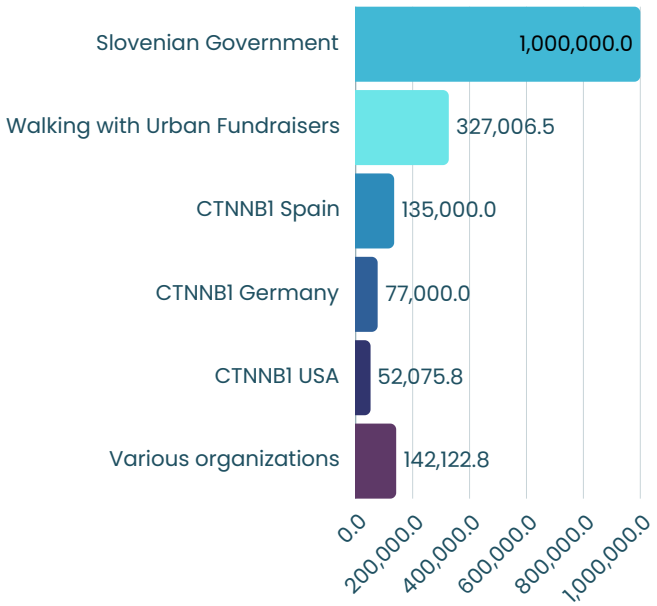
The majority of our expenses were dedicated to research, with Charles River Laboratory (€569,028.68, 75.1%) receiving the largest allocation for efficacy studies. Additional funding was directed toward RNA-based therapy development at the National Institute of Chemistry (€100,000, 13.2%), as well as the CTNNB1 Conference (€55,609.43, 7.9%). Other expenses included a donation to RKS Škofja Loka (€10,000, 1.3%), alongside costs for accounting, fundraising events, and travel for key meetings (€22,414.47, 2.5%).

ANNUAL BREAKDOWN FOR 2024

MAIN CONTRIBUTORS IN 2024

In 2024, the Slovenian government became the largest contributor, enabling the Foundation to begin manufacturing AAV9 gene therapies and support pre-approval toxicology and biodistribution studies. The CTNNB1 community also played a crucial role, with significant contributions from fundraising efforts across multiple countries.

The largest funding sources included the Slovenian Government (€1,000,000, 57.7%), followed by "Walking with Urban" events (€327,006.50, 18.9%), CTNNB1 Spain (€135,000, 7.8%), CTNNB1 Germany (€77,000, 4.4%), and CTNNB1 USA (€52,075.80, 3.0%). Additional support came from fundraisers and donations from families and organizations worldwide, including Sneha's GoFundMe, Rose's GoFundMe, Julien's fundraiser, Akhilesh's fundraiser, CTNNB1 Portugal, CTNNB1 France, Hoyrup, Verwest family, Leschner family, and the Founder's donations (€142,122.82, 8.2%).



MAIN EXPENSES AND ALLOCATIONS IN 2024

The majority of expenses were allocated to Viralgen (€1,222,235, 69.0%) for AAV9 manufacturing. Other key expenses included research at CIMA Spain for non-human primates studies (€244,692, 13.8%), organization of the 2nd CTNNB1 Conference (€70,698.91, 4.0%), biodistribution study with Niba Labs (€52,075.80, 2.9%), Oxford University (€38,549.47, 2.2%), and the Institute of Molecular Genetics for initiation of the GLP study in mice (€44,531.50, 2.5%).

Additional costs covered sample transport, patent applications, regulatory consultancy, accounting, and travel for key meetings (€98,626.13, 5.6%.

CURRENT FINANCIAL STATE & 2025 OUTLOOK

Balance of funds on the CTNNB1 Foundation's bank account (as of February 22, 2025)

Category	**Amount**
Account Balance (EUR)	625,193.23 EUR
Account Balance (USD)	114,223.76 USD
Account Balance (CHF)	75.00 CHF
Total (converted to EUR)	**734,456.13 EUR**

The table above outlines our financial position as of February 2025. Although the year has just begun, we have already received generous contributions from the international CTNNB1 community, with CTNNB1 Spain (€40,000, 65.4%) as the largest donor, followed by donations from Akhilesh, the Hoyrup family, and others (€21,198.42, 34.6%).

So far, the majority of funds have been allocated to Viralgen (€470,250.00, 96.6%) to advance gene therapy production, while the remaining sum (€16,573.80, <4%) covered essential expenses such as sample transport, consulting, accounting, and travel for key meetings.

Looking ahead, 2025 marks a pivotal year for the CTNNB1 Foundation, as we move closer to developing a gene therapy treatment. Our key objectives include:

- Completing regulatory-enabling studies to ensure the safety of our therapy and submitting the necessary documentation to the European Medicines Agency.
- Initiating the first CTNNB1 community clinical trial (Phase I/II) in collaboration with the University Medical Centre Ljubljana, marking a major milestone for CTNNB1 community.
- Expanding our Natural History Study, which will serve as a pre-interventional study for our upcoming clinical trial. We aim to strengthen collaborations in Australia, Brazil, the USA, and Canada to ensure broader participation and data collection.
- Successfully organizing the 3rd International CTNNB1 Syndrome Conference in Bilbao, Spain, bringing together researchers, clinicians, and patient advocates to share knowledge and advance global efforts in treating CTNNB1 Syndrome.

With the support of our donors, partners, and scientific community, we are closer than ever to achieving life-changing breakthroughs for individuals affected by CTNNB1 Syndrome.

FIXED AND ESTIMATED OUTSTANDING COSTS FOR GENE THERAPY DEVELOPMENT PROGRAM (2025)

Outstanding costs of gene therapy development for 2025

Category	Amount (€)	Payment deadline (all 2025)
Clinical grade vector manufacturing	382,750.00	May
In life GLP study in mice and toxicity analysis	85,000.00	May
In life non-GLP study in NHP and toxicity analysis	104,868.00	May
Biodistribution analysis in mice and NHP (estimate)	200,000.00	February to May
Expert support for JAZMP documentation (estimate)	25,000.00	January to May
Potency testing, additional cell testing (estimate)	120,000.00	March
NHS & Conference (estimate)	40,000.00	May-June
Clinical trial protocol development (estimate)	50,000.00	February to June
Clinical trial activities (secondary packaging, transport, storage) (estimate)	50,000.00	April to December
Insurance of the product	50,000.00	Before the start of clinical trial
Total	**€1,107,618.00**	

Based on our current financial position and the confirmed and estimated costs for 2025, we face a **funding gap of €373,161.87** to fully support the next phases of our gene therapy development program.

Outstanding payments required in 2025:

- **Clinical-grade vector manufacturing**
- **GLP and non-GLP studies in mice and NHP**
- **Biodistribution analysis**
- **Clinical trial activities**

Notably, **clinical trial costs are not yet included in this financial projection**. Discussions with University Medical Centre Ljubljana regarding the execution of clinical trials are ongoing. Additionally, the cost of clinical trials remain uncertain at this stage and will very likely be included as a separate cost per patient.

Securing additional funding will be crucial in ensuring the successful transition to clinical trials and bringing us closer to a life-changing treatment for CTNNB1 Syndrome.

TIMELINE FOR PRECLINICAL AND CLINICAL DEVELOPMENT OF THE GENE THERAPY PROGRAM FOR CTNNB1 SYNDROME

Based on the development timeline, 2025 is a pivotal year with major milestones in both preclinical and clinical phases. This chapter outlines our key objectives and planned activities for each quarter as we move closer to bringing gene therapy for CTNNB1 Syndrome to clinical trials.

Timeline for preclinical and clinical development

Activity	2021	2022	2023	2024	2025
Preclinical Development	Q1-Q4	Q1			
Construct development		Q2-Q3			
iPS cell development		Q1-Q4	Q1-Q4		
In vitro efficacy testing in cell models		Q1-Q3			
In vivo efficacy testing in mice		Q3-Q4	Q1		
8-month safety monitoring in WT mice			Q3-Q4	Q1	
RNA-seq/overexpression study				Q2-Q3	
Development of toxicological plasmid				Q2-Q3	
Development of toxicological vector				Q3-Q4	
GLP toxicology and biodistribution study in mice				Q3-Q4	**Q1 -Q2**
Toxicology and biodistribution study in primates				Q4	**Q1-Q2**
Product comparability testing				Q3-Q4	**Q1 -Q2**
Potency assay development and testing					**Q1-Q2**
Clinical Development					
Genotype-phenotype Study	Q1-Q4				
Natural history study				Q2-Q4	**Q1-Q4**
Clinical plasmid				Q3	
Clinical vector				Q4	**Q1**
Scientific advice (JAZMP, EMA, FDA)				Q3-Q4	**Q1 -Q2**
Phase I/II clinical trial					**Q3-Q4**

PRECLINICAL DEVELOPMENT PLANS IN 2025

GLP toxicology and biodistribution study in mice (Q1-Q2)

- This study evaluates the safety and biodistribution of the gene therapy in mice. The results will provide crucial insights for optimizing the clinical trial design, identifying potential side effects, and determining how the treatment is distributed throughout the body.
- Conducted under Good Laboratory Practice (GLP) standards, it is a key regulatory step before human trials can begin.

Toxicology and biodistribution study in primates (Q1-Q2)

- Following mouse studies, this research extends to non-human primates (NHPs) to provide a more detailed understanding of the therapy's safety profile and how it spreads in the body.
- Since primates share closer biological similarities with humans, this study will provide critical insights into potential risks, dosing strategies, and treatment distribution, helping us better predict outcomes for the first human clinical trial.

Product comparability testing (Q1-Q2)

- Ensures that the gene therapy batches produced at a large scale for human trials are chemically and biologically consistent with the ones tested in preclinical research.
- Any variation in production can affect safety and effectiveness.

Potency assay development and testing (Q1-Q2)

- A test to measure the biological activity and strength of the gene therapy.
- Helps determine if the therapy is effective at the intended dose and meets quality control standards before clinical trials begin.

CLINICAL DEVELOPMENT PLANS IN 2025

Natural history study (Q1-Q4)

- Continues collecting long-term clinical data on individuals with CTNNB1 Syndrome to better understand the disease's progression.
- This data will help establish baseline measures for evaluating gene therapy effectiveness in planned clinical trial.

Clinical vector development (Q1)

- The final production of the AAV9 gene therapy vector intended for use in human clinical trials will be completed.
- Comprehensive quality control assays will be conducted to ensure the therapy meets regulatory and safety standards.

Scientific Advice (JAZMP, EMA, FDA) (Q1-Q2)

- Consultation with regulatory bodies to review preclinical data and discuss requirements for clinical trial approval.

Phase I/II Clinical Trial (Q3-Q4)

- The first-in-human study of the gene therapy.
- Phase I/II focuses on safety, dosage and establishes preliminary efficacy (how well the therapy works).
- This marks the official start of human testing for the CTNNB1 gene therapy.

ACHIEVED AND EXPECTED GOALS OF THE AAV9 CTNNB1 GENE THERAPY PROGRAM

Preclinical goals

Development of constructs, including optimizing the therapeutic gene, promoter, and regulatory elements for safe and effective expression.	**Achieved/Completed**
Creation of iPS cells from CTNNB1 syndrome patients and animal model.	**Achieved/Completed**
In vitro and in vivo efficacy testing on iPSCs, organoids, and CTNNB1 mutant animal model to evaluate the therapeutic gene's function and improvements.	**Achieved/Completed**
Safety studies to monitor long-term toxicity in WT mice and perform RNA-sequencing to assess transgene overexpression effects.	**Achieved/Completed**
Development of standardized toxicological plasmids and vectors for GLP-compliant studies.	**Achieved/Completed**
Toxicology and biodistribution studies in mice and primates to evaluate the drug's safety and vector distribution for clinical use.	In Progress

Clinical goals

Genotype-phenotype study to explore the correlation between genetic mutations and clinical symptoms in CTNNB1 syndrome patients.	**Achieved/Completed**
Natural history study to collect data on disease progression without intervention, defining clinical baselines and endpoints.	In Progress
Development of clinical plasmids and vector to prepare GMP materials for clinical studies.	**Achieved/Completed**
Regulatory advice (JAZMP, EMA, FDA) to obtain guidance and approval for the clinical trial.	In Progress
Phase I/II clinical trial to evaluate the safety and preliminary efficacy of Urbagen in a controlled clinical setting.	In Progress

FINANCIAL CHALLENGES

Funding research and treatments for ultra-rare diseases like CTNNB1 Syndrome presents significant financial challenges. Unlike more common conditions that attract substantial public and private investment, rare disorders often face limited funding opportunities, high research costs, and accessibility barriers. The CTNNB1 Foundation is committed to overcoming these obstacles.

FUNDING GAPS AND FINANCIAL RISKS

One of the biggest challenges in researching rare diseases is the high cost of developing treatments. Gene therapy, in particular, requires **years of investment, expensive technology, and extensive clinical trials** before becoming available to patients. We have made tremendous progress in the last few years, but sustainable funding is crucial to maintain our progress and avoid delays in the next development phases.

Additionally, the lack of commercial incentives for pharmaceutical companies to invest in ultra-rare diseases means that much of the financial burden falls on nonprofits, advocacy groups, and families themselves. This creates funding gaps, making it difficult to sustain long-term research efforts. We are thankful for companies like **Viralgen** and **Fundación Columbus** who have shown real interest in creating and supporting the development of a cure.

COST BARRIERS IN MEDICAL ACCESS

Most of our clinical activities and research collaborations are currently based in Europe, but we are actively working to **expand our network** to include hospitals in Australia, Canada, the USA, and Brazil as **potential clinical sites**. While we have successfully secured partnerships in Australia and Canada, establishing similar agreements in the United States has proven more challenging.

Accessing clinical evaluations in the U.S. presents a significant financial hurdle, as healthcare costs there are among the highest in the world. Our goal is to ensure that families outside of Europe, particularly in the U.S. and South America, can participate in our study and future clinical trials without facing excessive financial burdens.

Currently, families must travel to Europe annually for clinical assessments, incurring substantial expenses for flights and accommodation. This is neither a sustainable nor long-term solution for families or the Foundation. **We remain deeply committed to breaking down these barriers and ensuring equal medical access for all CTNNB1 families.** By expanding partnerships, gathering critical data, and advancing our research, we aim to bring life-changing gene therapy within reach of every child affected by CTNNB1 Syndrome.

LET'S MAKE IT HAPPEN!

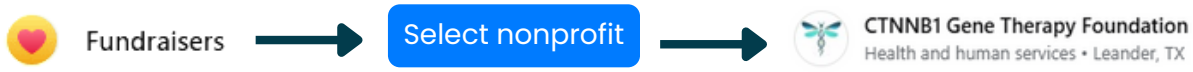
While we are in the process of collecting clinical data, we will remain largely dependent on donations or fundraising. **That is why every contribution counts.** Below are the various ways you can help support our Foundation to achieve our goals:

Direct Bank Transfer
Name: CTNNB1 Foundation, The Gene Therapy Research Institute
Address: Dalmatinova ulica 5, Ljubljana
Registration Number: 4125878000
Tax Number: 62919571
Bank Account: SI56 6100-00025350715
Bank Name: HDELSI22 / Delavska hranilnica d.d., Ljubljana

PayPal
Use our PayPal platform to make your donation quickly and securely.

Website
Donate directly through our website.

Fundraise via Facebook
On Facebook's Fundraisers page, you can specifically select our non-profit **CTNNB1 Gene Therapy Foundation:**



For German Donors
Families and supporters coming from German-speaking countries have organized themselves and are currently fundraising via GoFundMe platform: https://gofund.me/e6b03974

For Spanish Donors
The Spanish Asociación CTNNB1 is a dedicated advocate for families, uniting 30 families to organize impactful events across the country. Click HERE to learn more about their mission and how you can support our program.

For US Donors (Tax-Deductible Receipt)
Donate through our sister organization, a registered 501(c)(3) entity in the US: https://givebutter.com/ctnnb1genetherapy

CONTACT US

CONTACTS

Email

- spela@ctnnb1-foundation.org – Urgent matters related to fundraising and clinical trials
- lavra@ctnnb1-foundation.org – General, non-urgent questions about the foundation's work
- bruno@ctnnb1-foundation.org – Technical support, including website issues and conference registration
- ana@ctnnb1-foundation.org – Scientific inquiries and participation in CTNNB1 Spain

Telephone

+386 31 731 269 (urgent matters only)

Website

www.ctnnb1-foundation.org

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CTNNB1 FOUNDATION
Bringing hope to children