2022 Corporate Responsibility Report

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About this Report

In our 2022 Corporate Responsibility Report, we aim to share our commitment to corporate responsibility and highlight progress on our environmental, social and governance (ESG) priorities that are important to the success of our company. Unless otherwise noted, all performance reporting covers January 1, 2021 to December 31, 2021. All financial information is reported in United States (U.S.) dollars. Information on documents filed with the Securities and Exchange Commission (SEC), such as our annual Form 10-K, can be found at www.ionispharma.com.

Brett P. Monia, Ph.D.
Chief Executive Officer

A Message From Our CEO

Ionis is committed to being a good corporate citizen. Our 2022 Corporate Responsibility Report reflects this commitment by highlighting how we work with integrity and purpose as we discover, develop and deliver medicines with the potential to transform the lives of patients in need and deliver value for all our stakeholders.

We continue to progress our corporate responsibility program and environmental, social and governance (ESG) framework to support our ongoing efforts to operate our business responsibly and sustainably. This year, we established a Corporate Responsibility Steering Committee to provide oversight and ensure we develop the right programs and policies to continue to integrate ESG principles across our organization. This Committee's leadership is key to driving our efforts to advance our corporate responsibility strategy.

The Committee is currently focused on these priorities:

Promoting health equity in clinical trials – Enhancing patient access and diversity in our clinical trials, including promoting initiatives to better match the demographics of trial participants with affected patient populations

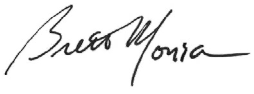
Empowering our employees – Fostering an inclusive culture to support the growth and success of our employees, including adding an objective to our 2022 corporate objectives to enhance and improve diversity, equity and inclusion (DEI) across our organization

Enhancing our environmental disclosures – Initiating our first Task Force on Climate-related Financial Disclosure (TCFD) and including 2021 environmental data in this report to transparently share this information with our stakeholders

Looking ahead, we plan to identify, measure and report on additional key aspects of our business that reinforce our commitment to be a responsible corporate citizen while we continue to deliver novel medicines to people who depend on us.

I am grateful to every one of our employees whose hard work and commitment make this journey possible. I am tremendously proud of the progress we have made together, and I am excited about our future as we continue to build on our success to help more patients in need.

Best regards,



Brett P. Monia, Ph.D.
Chief Executive Officer

About Ionis: A Passion for Innovation

For more than 30 years, Ionis has been the leader in RNA-targeted therapies. Our scientific innovation began and continues with the knowledge that sick people depend on us.

Building on Our Legacy to Become the Leader in Genetic Medicines

Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry-leading cardiovascular and neurological franchises. We're making advancements in our pioneering technology, moving us closer to achieving our vision of becoming the leader in genetic medicine, utilizing a multi-platform approach to discover, develop and deliver life-transforming therapies.

This past year, we advanced our strategic priorities, making significant progress toward becoming a fully integrated research, development and commercial organization. We continued go-to-market commercial preparations for our near-term product opportunities, eplontersen, olezarsen and donidalorsen. And, following nine positive data readouts in 2022, we look forward to potentially having two new medicines on the market in 2023 and our Phase 3 pipeline is poised to expand.

For more information, visit Ionis Innovation at www.ionispharma.com.

$810M 2021 Total Revenue

$644M 2021 R&D Investment

640+ Total Employees

52% Women in our workforce

42% People of Color represented in our workforce

13K+ Patients treated with SPINRAZA globally to date

Data as of December 31, 2021 unless otherwise noted

Our Approach to Corporate Responsibility

At Ionis, we work with a sense of urgency to discover, develop and deliver breakthrough medicines to create a better future for people with devastating diseases. We believe operating responsibly and sustainably creates value for our company and our stakeholders. We consider the long-term impact we can make across five key areas:

PATIENTS	At the core of everything we do is the belief in the potential of our medicines to transform lives.
INNOVATION	We are a science-centric organization dedicated to the perseverance and rigor that the scientific approach demands.
EMPLOYEES	We offer a rewarding and supportive environment that empowers our employees to thrive.
COMMUNITIES	We are proud of the work we do to support and uplift our communities.
ENVIRONMENT	We believe we have a responsibility to help create a better, more sustainable future.

We continue to build our corporate responsibility program and ESG framework to support our ongoing commitment to operate our business responsibly and sustainably. In 2022, we established a formal Corporate Responsibility Steering Committee to ensure we develop the right programs and policies to continue to integrate ESG across our organization. Our corporate responsibility initiatives, policies and programs are reviewed on a regular basis by the Committee and its recommendations are key to driving efforts to advance our corporate responsibility strategy to support our growth.

The Committee reports to our Chief Executive Officer and consists of senior leaders in key functions across the company, including legal, finance, human resources and corporate affairs. The Committee is now part of our governance framework, which defines responsibilities and ensures we have the right systems and controls to oversee ethical operations across our business. The Committee periodically updates our executive leadership and the appropriate committees of our Board of Directors on our ongoing ESG efforts.

We look to our stakeholders and third-party frameworks such as the Sustainability Accounting Standards Board (SASB) Health Care - Biotechnology and Pharmaceuticals Standard and the Task Force on Climate-Related Financial Disclosures (TCFD) to inform our approach and our disclosures. Our SASB Index and TCFD reporting are included in the appendix of this report.

Identifying Our ESG Priorities

In 2021 and 2022, we took steps to formalize our corporate responsibility program and capture and report on the impact of our ESG efforts. As part of this work, we completed an assessment of the corporate responsibility areas most important to our business.

These are:

- Safety of patients in clinical trials
- Product quality and safety and supply chain management
- Access to medicines and tackling untreatable diseases
- Environmental sustainability
- Human resources management
- Diversity, equity and inclusion
- Employee health and safety
- Governance and business ethics

Our Focus on Patients

At Ionis, we are committed to discovering, developing and delivering life-changing medicines for patients with severe unmet needs. From drug discovery to development and to the market, we are committed to pursuing the highest levels in quality, compliance, safety and performance to help deliver effective and safe transformational therapies to those who need them most. We also continue to pursue efforts to enhance patient access and diversity to ensure we are innovating for all patients, regardless of race or ethnicity.

Product Quality and Safety

We rigorously monitor the quality and safety of our products throughout their lifecycle. Our products are tested at every stage of the process against pre-defined acceptance criteria using validated or compendial methods.

Our senior management is focused on proactively managing risks associated with quality and safety. The Ionis Quality Steering Committee, which includes our SVP and Chief Compliance and Quality Assurance Officer, oversees our quality programs including our formal Quality Management System (QMS).

Quality Management System

The principles and structure of our integrated QMS are outlined in our Quality Manual, available to all our employees. Our QMS exists as part of a larger, overall management system that includes an established, documented Quality Policy and related processes for providing products that meet or exceed customer requirements. Our QMS complies with applicable global standards and regulations (GxP) and supports the development and commercialization of our manufactured products to ensure the quality and integrity of those used in nonclinical, preclinical and clinical studies, as well as commercial supply.

Quality risk management is embedded in our QMS, which outlines a systematic, proactive and objective approach to identify, assess, control, monitor and document risks. Risk management processes are managed collaboratively by functional area management and Quality Assurance and Quality Control (QA/QC) to ensure risk management procedures are defined, deployed and controlled for projects, processes and systems. Our quality risk management includes, but is not limited to, the following:

- Quality surveillance (monitoring and auditing of external vendors, investigator sites and internal systems)
- Safety monitoring
- Selection of qualified investigators and vendors
- Clearly defined roles and responsibilities for all GxP employees and vendors
- Clear and well-written protocols, procedures and master-batch records
- Well-designed studies and processes
- Qualified and trained personnel
- Mechanism and processes for issue escalation and reporting
- Quality metrics for corrective and preventative actions, investigations and change control
- Ongoing surveillance of new or revised regulatory requirements and processes for adopting these requirements, if applicable

Ionis actively monitors the performance of our QMS through the product lifecycle. Our senior management performs a comprehensive, cross-functional assessment of the performance, adequacy and suitability of the QMS during the semi-annual Quality Management Review (QMR).

Change Management Process

Our QMS includes a rigorous process to identify required changes to systems, procedures and processes arising from external sources, such as from regulatory agencies, and from internal sources, including continuous improvement initiatives and self-inspection programs. We apply a cross-functional approach, and the impact of any change is assessed in terms of risk to patient safety and product quality. Each change action is monitored throughout implementation and the impact of the change is assessed upon completion. The process is appropriately documented throughout. Processes are also in place to share learnings from projects and inspections during the twice-yearly QMR.

Quality Testing

We use recognized international standards to validate our testing methods, such as those published by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), to demonstrate consistent and accurate results. In the event of an out-of-specification test result, we investigate fully. No product is released for patient use without analytical results that comply with these standards, which are independently reviewed and approved by designated, trained personnel. We ensure that all testing of materials and products is in line with industry standards and regulatory expectations.

Comprehensive Training

Our team of researchers and developers receive training according to internationally recognized current Good Laboratory Practice (GLP), Good Clinical Practice (GCP), Good Manufacturing Practice (GMP), Good Distribution Practice (GDP) and Good Pharmacovigilance Practice (GVP) standards.

Elements of our QMS are integrated across all GxP areas, such as our global system procedure on employee training programs. All employees involved in clinical trials receive training according to GCP global standards. Protocol-specific and safety-reporting training are also provided to prepare employees to conduct and document experimental drug studies. In addition, new relevant employees receive GxP training when hired, and all relevant employees receive ongoing routine GxP training. We offer our GxP training by live instruction, both in person and virtually, as well as by electronic training modules to provide flexibility to our employees.

Rigorous Supplier Qualification

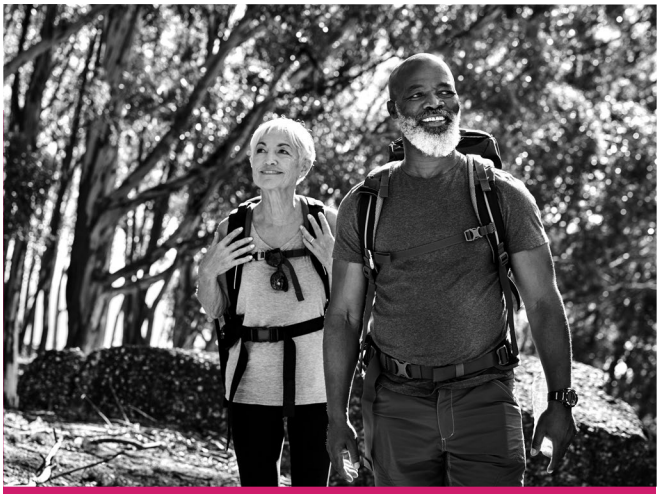
Ionis maintains a rigorous standard for quality, and we uphold the same standard when introducing vendors into our supply chain. This assessment focuses primarily on assuring the GxP compliance of vendor systems, processes and operations.
To mitigate supplier risk, we have an approved GMP vendor list that feeds into our external audit program. A risk-based process determines the frequency of our vendor audits. Our senior management oversees quality in our supply chain, including vendor selection, monitoring and auditing, all of which are part of our quality risk management process.

Clinical Trial Program

Clinical research is a key component of developing safe and effective new medicines to treat diseases where no other therapeutic approaches have proven effective. At Ionis, we require all our clinical studies be conducted in an ethical manner. We have established a series of policies and procedures that govern the ethics of conducting clinical trials and we adhere to applicable standards set by the ICH.

We adhere to GCP guidance and regional laws and regulations for designing and conducting clinical trials and reporting trial results. GCP is an international ethical and scientific quality standard for conducting clinical trials that is provided by the ICH. Compliance with GCP standards, in addition to GLP and GMP standards, provides assurance that the rights, safety and well-being of trial participants are protected and that clinical trial data are credible.

Our VP of Clinical Operations and Data Management has responsibility for ethical conduct of our clinical trials. Additionally, Independent Review Boards (IRBs) monitor the ethical conduct of our trials and have the authority to approve, modify or stop trials. Independent ethics committees, IRBs and health authorities review and approve essential clinical trial documents, such as protocols and informed consent forms before they are used. Our safety data review committees and, for some studies, independent



Health Equity in Clinical Trials

To improve patient access and ensure diverse representation, we are working on initiatives to better match the demographics of our clinical trials with the demographics of patient populations. Working cross-functionally, we have been able to recruit participants who more closely represent the patient population that could benefit most from a medicine.

For example, within CARDIO-TTRansform, our largest clinical trial for transthyretin-mediated amyloid cardiomyopathy (ATTR-CM), we have a comprehensive plan to address barriers to participation. These efforts have translated into a 70% increase in patients of color in the CARDIO-TTransform trial. We believe the programs and partnerships we have established as part of this trial will improve health equity and increase access to novel therapies.

external Data and Safety Monitoring Boards (DSMBs), monitor safety data across all study participants to identify potential issues or concerns, which are handled in accordance with our study plans.

Our Clinical Development and Clinical Operations teams evaluate the benefits and risks associated with our clinical studies. Our annual summary reports and post-approval safety surveillance reports are shared with health authorities. These include Development Safety Update Reports (DSURs), Periodic Benefit Risk Evaluation Reports (PBRERs) and Periodic Adverse Drug Experience Reports (PADERs/PAERs). All identified risks associated with a clinical trial are disclosed in the summary sections of these reports.

All employees in our Clinical Development and Clinical Operations organizations are trained on standard operating procedures and employees working on a clinical trial are trained on the administration of an investigational drug, as well as other relevant materials specific to that trial, as applicable. When we introduce a new protocol in the clinical trial process, we ensure all relevant employees at each site receive the necessary training. To protect patient privacy, patient data are concealed and captured in systems that pass rigorous validation processes. How the study data are to be used and who can access the data are disclosed in the study protocol, informed consent form and study plans.

All clinical trials are disclosed in credible and publicly available databases, including ClinicalTrials.gov. We are committed to following trial requirements when publishing trial results.

Post-Trial Medication

While we know that the best way to access an investigational product is through participation in one of our clinical studies, we understand that there are seriously ill patients with life-threatening diseases who will not be eligible for our studies. To support these patients, we consider expanded access—also referred to as “compassionate use”—to investigational products. We also offer open-label extension (OLE) studies for many of our clinical trials.

Access to Medicine

At Ionis, we believe the goal of making life-changing medicines available to patients in need is achieved through rigorous science, innovation and well-designed clinical studies, followed by regulatory approval. We also recognize that to fulfill this goal, we need to get our medicines to those who need them most. We work closely with patient advocacy organizations and communities around the world to identify and understand the needs of the people we serve.

Our Head of Clinical Development and our SVP responsible for Global Medical Affairs provide oversight to our compassionate use and access programs. We work collaboratively with our partners on pricing mechanisms and the pricing approval process, with reimbursement for the patient as the goal. As we continue to advance plans to become a fully integrated biotechnology company, we are also evolving the approach and design of our access strategy to ensure we deliver our medicines to as many patients who need them as possible.

We also have an Expanded Access Policy that aims to provide access to investigational products based on select criteria and to support those patients with a serious or immediately life-threatening condition who have exhausted all available medical options and are unable to enroll in any ongoing clinical study.

For more information, visit Patients & Community at www.ionispharma.com.

A Culture that Empowers Our Employees

Ionis is where passionate, driven people come together to help patients in need. Our culture is challenging, motivating, rewarding, and designed to foster innovation and scientific excellence. Our success is a direct result of our outstanding employees.

Our programs for attracting talent

Internships

- **Research**
  Pharmacology, Biochemistry, Cellular and Molecular Biology, Genomics and Bioinformatics, Medical Affairs, Toxicology, Pharmacokinetics, etc.
- **Business Operations**
  Finance, Corporate Communications, Alliance Management, Regulatory Affairs, Human Resources, IT, Commercial, etc.

Postdoctoral and clinical fellowships

- Chemistry
- Cell Biology
- Biochemistry
- Toxicology
- Pharmacology
- Pharmaceutical Development
- Clinical Development

Talent Recruitment

Our pursuit of excellence begins with our talent recruitment process. We have a formal talent recruitment strategy and processes in place to ensure fair and equitable recruitment of the best and most qualified candidates. We post our positions to a diverse range of job boards to help ensure a diverse candidate pool.

In addition, Ionis offers internships, post-doctorate fellowships and clinical fellowships to extend the reach of our talent pipeline. Whether we are hiring entry-level, mid-career or executive-level candidates, we look beyond a candidate's academic qualifications to identify valuable experience and skills that will add to our culture and organizational capacity.

Compensation, Benefits and Talent Retention

In addition to our supportive and inclusive culture, we offer employees a combination of robust and meaningful benefits, compensation and well-being programs. Our compensation is awarded based on individual and company performance. We recognize achievements with salary increases, equity awards, promotions and bonus opportunities.

We offer highly competitive benefits to all regular employees who work at least 20 hours per week. Our U.S. benfits include:

- Medical, dental and vision plan options
- 401(k) plan with 100% company match on first 5% of employee contributions

- Employee Stock Purchase Plan (ESPP)
- Stock options/Restricted Stock Units (RSUs)
- Annual performance-based bonus and merit increases
- Paid vacation, sick days, holidays, parental leave and paid time off for volunteering
- Flexible spending accounts for health and dependent daycare needs
- Life, AD&D and long-term disability insurance coverage options

Benefits offered to employees outside of the U.S. are also competitive and tailored based on the market.

In addition to our benefits, we offer a range of industry-leading wellness and stress management initiatives and programs. These include:

- On-site gyms in select locations with group fitness classes, company-wide wellness challenges and virtual fitness options
- Regular wellness tips and resources shared with employees each month
- An Employee Assistance Program (EAP) with phone, online and face-to-face counseling sessions
- Mental and behavioral health benefits through our healthcare insurance
- Online resources through LinkedIn Learning on topics such as work-life integration, avoiding burnout, managing stress and working from home
- Mental health first aid training for Human Resources (HR) team and select employees
- Flexible work schedules

In 2021, we conducted our most recent employee engagement survey. We plan to conduct our next survey in 2023.

Our HR team monitors employee retention and turnover and reports on a quarterly basis to our cross-functional senior leadership team. As a testament to our performance, our average employee turnover in 2021 was 16% and voluntary turnover was 13.3%. In comparison, industry-wide turnover for life sciences and medical device companies over this same period was 19% according to a survey published by Radford, an Aon Hewitt Company.

Training and Development

Beginning with our employees' first day, we aim to provide them with tools and trainings necessary to succeed at every stage of their careers.

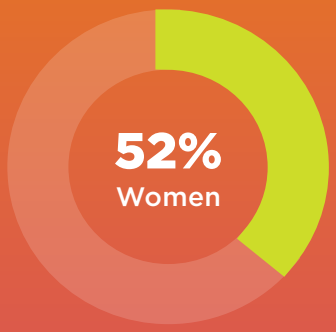
We offer our new employees a peer mentoring buddy program, and comprehensive training and development opportunities are provided for employees at all levels, including job-related and compliance training. Our robust training and development program, referred to as The Learning Continuum, supports the development of our employees as they progress through their careers. For rising Ionis leaders, we have programs such as Supervising at Ionis, Intro to Leadership and a Leadership Conference, each of which are two-day, on-site offerings. In addition, we offer integration programs, science classes for non-scientists, a manager's book club, soft skills training, English language skills training, as well as supervisory capabilities programs. Most of the training sessions are co-facilitated by a member of the HR team and a functional area leader from across the organization.

In 2021, we offered 165 hours of instructor-led Learning Continuum sessions. More than 60% of employees attended at least one of these sessions, averaging eight hours of training per employee.

Diversity, Equity and Inclusion

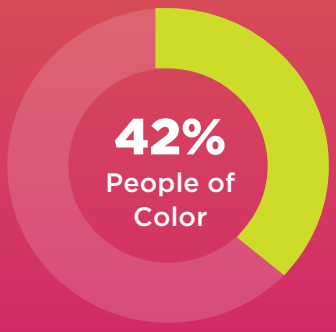
Diversity, equity and inclusion (DEI) is embedded within our culture at Ionis. We have a corporate objective to enhance and improve DEI initiatives across our organization supported by our employee-led DEI Advisory Council to our CEO. Our Executive Director of Human Resources has leadership responsibility for our DEI programs and policies. Our senior management regularly monitors performance against our objectives and our Board of Directors oversees our DEI programs through semi-annual reporting and discussion.

We offer a three-part diversity training series, which focuses on unconscious bias, inclusion and belonging, and allyship and advocacy. We also provide mandatory anti-discrimination and anti-harassment training for all employees.



Gender Diversity

TOTAL	Female	Male	Total	% Female	% Male
Total	332	308	640	52%	48%
Executive/Senior-Level Leaders and Managers	13	37	50	26%	74%
First/Mid-Level Leaders and Managers	81	97	178	46%	54%
Professionals	192	146	338	57%	43%
Support Workers	46	28	74	62%	38%



Ethnic Diversity

TOTAL	People of Color	White	Total	% People of Color	% White
Total	267	373	640	42%	58%
Executive/Senior-Level Leaders and Managers	12	38	50	24%	76%
First/Mid-Level Leaders and Managers	65	113	178	37%	63%
Professionals	158	180	338	47%	53%
Support Workers	32	42	74	43%	57%

Data as of December 31, 2021

Employee Resource Groups

To promote DEI within our organization, we have employee-led, executive-sponsored Employee Resource Groups (ERGs). Our ERGs are designed to build cultural awareness, promote an inclusive and supportive culture and support our business goals. Many of our ERG employee leaders also serve on the CEO's DEI Advisory Council.

Ionis' ERGs include:

- **LGBTQIA+**: Supports our LGBTQIA+ community
- **empowHer**: Empowers women at Ionis
- **DEI Advocates:** Champions DEI initiatives and programs across the organization
- **Mental Health & Wellness**: Promotes employee mental health and wellness
- **The Parent Network:** Connects our employees who are parenting young children
- **Ionis NEXT:** Engages with middle- and high-school students to nurture the NEXT generation of minority science leaders
- **New Employee Opportunity Network**: Creates community for new Ions (employees) as they integrate into the company
- **Veterans:** Supports our veteran and military family community

Workplace Health and Safety

At Ionis, we strive to protect the health and safety of all employees, contractors and visitors. We are also committed to providing an injury-free workplace. We have implemented a safety management system that uses monitoring, auditing and target setting to continuously improve our occupational health and workplace safety. Regular safety training is provided to all laboratory and manufacturing employees, and health and safety compliance is audited routinely. We regularly assess health-related risks to employees, contractors and visitors and proactively manage those risks across our operations.

	2020	2021
Recordable Injury Rate (per 200,000 hours worked)	1.00	0.94
Lost Time Injury Rate (per 200,000 hours worked)	0.50	0.47

Data as of December 31 in the applicable calendar year

Pay Equity

We are committed to paying our employees fairly, regardless of their gender, race or other personal characteristics. To ensure we are achieving our objective, we benchmark and evaluate pay based on market data and consider factors such as an employee's role and experience, employee performance and internal equity. We also regularly review our compensation practices, both in terms of our overall workforce and in terms of individual employees, to ensure our pay is fair and equitable.

In 2021, we engaged an independent third-party expert to perform a pay equity analysis that reviewed pay equity by gender, race and age. The results of this analysis showed that our pay practices are fair and equitable. We are committed to continuing to regularly review our pay practices and report the results of this analysis.

A Commitment to Our Communities

We are committed to having a positive influence on the communities in which we live and work.

Corporate Alliances

Uplifting the Healthcare Communities

Every year we provide support—from financial assistance to employee volunteerism and beyond—to various organizations that have a positive impact in our communities. We seek sustainable partnerships and initiatives that encourage scientific innovation and help address unmet patient needs, including disease awareness, education and support. In 2021, we donated approximately $2 million to charitable groups, including about $500,000 to the n-Lorem Foundation, a nonprofit organization established by Ionis' Founder and former Chairman and CEO, Stanley T. Crooke, M.D., Ph.D. Ionis' financial and in-kind scientific support to n-Lorem directly contribute to the funding and development of free antisense treatment to patients with nano-rare diseases.

We also coordinated volunteering days and provided in-kind support to a range of organizations, including:

- **ALS Association, Greater San Diego Chapter:** dedicated to finding a cure for ALS and to improving the lives of those living with and affected by ALS
- **ADAPT Functional Movement Center:** providing a complete integrative recovery experience for individuals with chronic neurological conditions
- **Life Science Cares**: leveraging the influence of the life science industry to address issues of poverty and inequality in Boston, San Diego, Philadelphia, and the San Francisco Bay Area and virtual options

Contributing to the Scientific Community

We are guided by world-class scientists whose passion to innovate is matched by their commitment to discover, develop and deliver transformational medicines to those who need them most. We share our scientific research in peer-reviewed industry publications and we expect our scientists to publish and present their work to peers, both internally and externally. Our employees are also encouraged to explore new ideas and interact with the broader scientific community.

ADAPT X Ionis — Hope Scholarship

In collaboration with Adapt Functional Movement Center, the Ionis Hope Scholarship grant program provides fully sponsored care services, rehabilitation programs and education to individuals impacted by ALS. Hope Scholarship grants support ALS patients' participation in group classes, massage therapy, meditation and functional movement therapy offered by Adapt Functional Movement Center located in Carlsbad, CA. Since its inception, the program has seen a 40% increase in the number of active participants and issued more than $125,000 in grants.

A Respect for the Environment

Ionis is committed to operating responsibly and sustainably while providing transformative medicines to our patients. We strive to minimize our impact on the environment, including our emissions, and efficiently use resources at our facilities.

Environmental Management System

We are committed to conducting our operations in an environmentally responsible manner to protect our employees, the environment and the communities in which we operate. We have established an environmental management system (EMS) that serves as a systematic approach to managing and continuously improving our environmental performance across company operations. The EMS is designed in accordance with the U.S. Environmental Protection Agency's guidance standard, Environmental Management Systems: An Implementation Guide for Small and Medium-Sized Organizations, and based upon the ISO 14001:2015 standard.

Our Environmental Management System manual establishes policies and procedures, outlines processes for identifying risk and implementing preventative measures, assigns roles and responsibilities and sets performance standards to improve our environmental performance. Our Environmental Policy is included in the EMS manual and provides the framework for setting and reviewing environmental objectives and targets. This policy is communicated to all relevant employees.

Our Executive Director of Health, Safety and Environment (HSE) serves as the EMS Officer, providing oversight of our EMS and reporting our annual HSE Scorecard (Scorecard) to our VP of Manufacturing. The Scorecard includes many facets of HSE, including injury rates, ongoing environmental monitoring and emerging environmental legislation. The EMS supports monitoring and measuring our greenhouse gas emissions, hazardous waste output, leak and spill emissions and specifically regulated solvents. We perform an annual internal audit of our EMS and hold an external audit every three years.

Our EMS Officer works collaboratively with our Safety Committee to ensure a cross-functional approach for our HSE activities, including assessing and reviewing our HSE programs and progress.

On an annual basis, we identify, record and monitor our products and activities that may have a significant impact on the environment. In the unlikely event an environmental incident occurs, we have in place procedures to investigate incidents and implement corrective actions with a focus on continuous improvement and prevention. Incident reports are included in our HSE Scorecard which is then reviewed with our Safety Committee.

EMS program training is provided to all members of HSE staff and EMS team members. All employees and contractors in job functions that have the potential to create an environmental impact also receive additional training that our HSE staff prepare and track. This training ensures all relevant employees and contractors are aware of the procedures and requirements of the EMS and their role and responsibility to follow the Environmental Policy.

Energy Consumption

Our Carlsbad, California, headquarters was designed and built to meet energy-efficient Leadership in Energy and Environmental Design (LEED) standards, a green building rating system. Our conference center was also built to the U.S. Green Building Council's Green Building Codes and Standards in alignment with LEED standards. In addition, we are in the process of constructing a new research and development facility and we recently began work on a new state-of-the-art manufacturing facility, both of which will include advanced sustainability and environmental protection features.

The energy efficiency performance of our buildings is monitored through a building management system. In addition, we have several solar photovoltaic systems in place. We monitor and report their output annually. Our investment in technology and infrastructure, including the implementation of solar energy and energy efficiency plans, has helped us reduce our electricity consumption over time. We also offer several electric vehicle charging stations at our Carlsbad headquarters that are available to employees and visitors.

Water and Waste Management

We are committed to efforts to reduce our water use and waste generation to minimize our environmental impact. We regularly monitor and evaluate our water usage to identify opportunities for reducing and minimizing consumption. Conservation measures include using recycled water for landscaping.

We also have programs to minimize waste, and review waste disposal alternatives, such as reuse and recycling. We recycle paper, cardboard, plastics and glass waste, and we provide training in waste management to all relevant employees and contract workers at our facilities. We conduct audits on procedures and practices at third-party waste management sites regularly.

2021 Greenhouse Gas (GHG) Emissions, Energy Use, Water Consumption and Waste

	2021
Greenhouse Gas Emissions (Metric tons CO_2e)	
Scope 1 (fuels, natural gas, refrigerants)	2,566
Scope 2 (electricity use)	2,052
Total Scope 1 & 2	4,618
Electricity Use (MWh)	
Total electricity use from non-renewable sources	6,466
Total electricity use from renewable sources	4,482
Total Electricity Use	10,948
Energy Generation (MWh)	
Total electricity generated onsite	1,535
Water Consumption (Million Gallons)	
Water Use	16.84
Non-hazardous Waste Disposal (Tons)	
Non-hazardous waste (landfilled)	254
Non-hazardous waste (recycled)	148
Total Non-hazardous Waste	402
Hazardous Waste Disposal (Tons)	
Hazardous Waste	277

Data as of December 31,2021

Governance and Integrity

At Ionis, we are committed to high legal and ethical standards and adhering to those standards is of the utmost importance to us and our employees. A clear governance structure oversees every aspect of our operations and ensures we act with integrity while pursuing our business objectives.

Corporate Governance

Our Board of Directors is committed to effective corporate governance and represents the interests of Ionis' stockholders by providing guidance and strategic oversight to optimize long-term value. Seven of nine directors are independent, and three of nine directors are gender and/or racially diverse. Our Board also has an Independent Lead Director and has established six committees, including Audit, Compensation, Compliance, Finance, Nominating, Governance and Review and Science and Medical Committees.

For more information on Ionis' commitment to corporate governance, including Board duties and criteria, Board committee charters and committee composition, visit Investors & Media/Governance at www.ionispharma.com.

Code of Ethics and Business Conduct

Ionis strives to achieve and maintain the highest level of integrity and ethics across all our business operations and interactions with our stakeholders. We are guided by our Code of Ethics and Business Conduct (Code), which applies to all employees, including executive officers and all members of our Board of Directors. The Code also applies to all employees of our subsidiaries and affiliates worldwide. We launched new annual training for our Code of Ethics and Business Conduct in March 2022.

Moving forward, all employees will receive training on the Code and must sign their acknowledgment of the Code on an annual basis.

Anti-Bribery and Anti-Corruption

We are committed to upholding a comprehensive and rigorous ethics program, including anti-bribery and anti-corruption commitments as detailed in our Code and our anti-bribery and anti-corruption policy. Our SVP and Chief Compliance and Quality Assurance Officer and our Chief Legal Officer, General Counsel and Corporate Secretary provide oversight for all anti-bribery and anti-corruption matters. We use a risk-based approach to perform internal audits. We conduct compliance risk assessments on an as-needed basis covering subjects such as anti-bribery and anti-corruption.

If an employee is interested in advice on any ethics-related issues, they are encouraged to contact our SVP and Chief Compliance and Quality Assurance Officer or contact our confidential Ionis Helpline. Our annual employee Code training and acknowledgement includes the subject of anti-bribery and anti-corruption.

Ionis Helpline

We maintain a confidential 24/7 helpline, hosted through a third-party provider, which is available by phone or web and provided in local languages. We proactively communicate the availability of the Ionis Helpline to employees on our external website, on our internal intranet site and on posters in our buildings. The Ionis Helpline is also available to our vendors, customers and other third parties. We have a structure in place to ensure reports of any issues are logged, reviewed, assigned for investigation as appropriate and tracked until resolved.

Drug Promotion Standards

We are committed to developing ethical and responsible marketing strategies with our patients in mind. Our Promotional Review and Medical Review Committees have oversight of drug promotion standards at Ionis to ensure materials about products or conditions meet regulatory and medical guidelines. As stated in our Code of Ethics and Business Conduct, we interact with healthcare professionals in accordance with applicable laws, regulations, codes and our policies. All relevant payments made to healthcare professionals are disclosed as required at the U.S. national and state level.

Appendix

Sustainability Accounting Standards Board (SASB) Index

The following table provides data and information for Ionis utilizing the Sustainable Accounting Standards Board's (SASB) Health Care - Biotechnology and Pharmaceuticals industry standard. The data represents full-year 2021 performance.

Categories	Accounting Metric	Code	Information
Safety of Clinical Trial Participants	Discussion, by world region, of management process for ensuring quality and patient safety during clinical trials	HC-BP-210a.1	For details, see Clinical Trial Program in the Our Focus on Patients section of this report.
	Number of FDA Sponsor Inspections related to clinical trial management and pharmacovigilance that resulted in: (1) Voluntary Action Indicated (VAI) and (2) Official Action Indicated (OAI)	HC-BP-210a.2	All data reported to relevant national regulators.
	Total amount of monetary losses as a result of legal proceedings associated with clinical trials in developing countries	HC-BP-210a.3	Not applicable.
Access to Medicines	Description of actions and initiatives to promote access to health care products for priority diseases and in priority countries as defined by the Access to Medicine Index	HC-BP-240a.1	For details, see Access to Medicine in the Our Focus on Patients section of this report.
	List of products on the WHO List of Prequalified Medicinal Products as part of its Prequalification of Medicines Programme (PQP)	HC-BP-240a.2	No Ionis products are on the WHO List at the time of reporting.
Affordability & Pricing	Number of settlements of Abbreviated New Drug Application (ANDA) litigation that involved payments and/or provisions to delay bringing an authorized generic product to market for a defined time period	HC-BP-240b.1	Not applicable.
	Percentage change in: (1) average list price and (2) average net price across U.S. product portfolio compared to previous year	HC-BP-240b.2	Not applicable.
	Percentage change in: (1) list price and (2) net price of product with largest increase compared to previous year	HC-BP-240b.3	Not applicable.

Drug Safety	List of products listed in the Food and Drug Administration's (FDA) MedWatch Safety Alerts for Human Medical Products database	HC-BP-250a.1	There were no Ionis products listed on U.S. FDA MedWatch at the time of reporting.
	Number of fatalities associated with products as reported in the FDA Adverse Event Reporting System	HC-BP-250a.2	There were no fatalities associated with Ionis products listed on U.S. FDA Adverse Event Reporting System (FAERS) Public Dashboard at the time of reporting.
	Number of recalls issued, total units recalled	HC-BP-250a.3	Ionis did not issue any recalls in 2021.
	Total amount of product accepted for takeback, reuse, or disposal	HC-BP-250a.4	Not reported.
	Number of FDA enforcement actions taken in response to violations of current Good Manufacturing Practices (cGMP), by type	HC-BP-250a.5	No FDA enforcement actions taken in 2021 in response to violations of current Good Manufacturing Practices (cGMP).
Counterfeit Drugs	Description of methods and technologies used to maintain traceability of products throughout the supply chain and prevent counterfeiting	HC-BP-260a.1	For details, see Product Quality and Safety in the Our Focus on Patients section of this report.
	Discussion of process for alerting customers and business partners of potential or known risks associated with counterfeit products	HC-BP-260a.2	For details, see Product Quality and Safety in the Our Focus on Patients section of this report.
	Number of actions that led to raids, seizure, arrests, and/or filing of criminal charges related to counterfeit products	HC-BP-260a.3	No raids, seizure, arrests, and/or filing of criminal charges occurred related to counterfeit products.
Ethical Marketing	Total amount of monetary losses as a result of legal proceedings associated with false marketing claims	HC-BP-270a.1	To date, Ionis has incurred no monetary losses as a result of legal proceedings associated with false marketing claims.
	Description of code of ethics governing promotion of off-label use of products	HC-BP-270a.2	For details, see the Governance and Integrity section of this report and our Code of Ethics and Business Conduct.

Employee Recruitment, Development & Retention	Discussion of talent recruitment and retention efforts for scientists and research and development personnel	HC-BP-330a.1	For details, see Compensation, Benefits and Talent Retention in the A Culture that Empowers Our Employees section of this report.
	(1) Voluntary and (2) involuntary turnover rate for: (a) executives/senior managers, (b) midlevel managers, (c) professionals, and (d) all others	HC-BP-330a.2	Our average employee turnover in 2021 was 16% and voluntary turnover was 13.3%.
Supply Chain Management	Percentage of (1) entity's facilities and (2) Tier I suppliers' facilities participating in the Rx-360 International Pharmaceutical Supply Chain Consortium audit program or equivalent third-party audit programs for integrity of supply chain and ingredients	HC-BP-430a.1	Not reported.
Business Ethics	Total amount of monetary losses as a result of legal proceedings associated with corruption and bribery	HC-BP-510a.1	To date, Ionis has incurred no monetary losses as a result of legal proceedings associated with corruption and bribery.
	Description of code of ethics governing interactions with health care professionals	HC-BP-510a.2	For details, see the Governance and Integrity section of this report and our Code of Ethics and Business Conduct.
Activity Metrics	Number of patients treated	HC-BP-000.A	To date, more than 13,000 patients have been treated with SPINRAZA globally.
	Number of drugs (1) in portfolio and (2) in research and development (Phases 1-3)	HC-BP-000.B	For details, visit the Ionis Pipeline at www.ionispharma.com.

Task Force on Climate-related Financial Disclosures (TCFD) Index

We recognize the importance of ESG and climate-related initiatives as they relate to our business strategy and risk assessment. We are committed to providing transparency on our climate-change risk management, governance and performance. The Task Force on Climate-related Financial Disclosures (TCFD) has developed voluntary, consistent climate-related financial risk disclosures for use by companies in providing information to stakeholders. A summary of our response to the TCFD-recommended disclosures is below.

Governance

Board Oversight — Our Board oversees an enterprise-wide approach to risk management considering various factors, which can include environmental and climate-related issues, for guiding the long-term success of our business. ESG risks, including those related to climate and environmental performance, are a priority of the Board and are reviewed by the Board periodically.

Management Oversight — Our senior management, including our Executive Director of Health, Safety and Environment and SVP of Manufacturing, regularly discusses risks and opportunities including those related to environmental issues, as well as how to apply policies and strategies to address these issues in each area of our business.

Strategy

While we do not believe climate change poses a material business risk, we have identified potential climate change-related risks that may impact our business over the short-, medium- and long-term, which include the following:

Physical Risks — As a biopharmaceutical company, our products face few climate-related risks, with little potential for such risks to have a significant financial impact on our business. However, extreme weather events and changing weather patterns have become more common in recent years. As a result, we are potentially exposed to varying natural disaster or extreme weather risks such as hurricanes, tornadoes, earthquakes, fires, droughts, floods or other events that may result from the impact of climate change on the environment. The potential impacts of climate change might also include increased operating costs associated with additional regulatory requirements and investments in reducing energy, water use and greenhouse gas emissions. In addition, we manufacture most of our research and clinical supplies in a manufacturing facility located in Carlsbad, California. Currently, we manufacture the finished drug product for marketed products at third-party contract manufacturers. The facilities and the equipment we and our contract manufacturers use to research, develop and manufacture our medicines would be costly to replace and could require substantial lead time to repair or replace. Our facilities or those of our contract manufacturers might be harmed by natural disasters or other events outside our control and our development and commercialization efforts may be impacted.

Regulatory Risks — We do not currently view climate change as a significant business risk. However, climate change could pose regulatory risks due to potential future carbon disclosure and compliance requirements or reputational risks due to not proactively addressing climate change issues. Possible carbon tax or regulatory incentives to encourage the use of renewables could affect energy costs. We do not expect this would have a significant impact on our business and financial performance.

Risk Management

Our process for integrating risk management throughout the business includes identifying, evaluating and addressing ESG risks and opportunities on a regular basis. The risks and impacts associated with our business require effective collaboration among departments, business units and external stakeholders. Our senior management and Board are focused on ensuring business continuity and managing and mitigating various risks to our business and financial performance, including climate change-related risks.

Metrics

We are currently reviewing our disclosure of carbon emissions.

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FORWARD-LOOKING STATEMENTS

This report and the information incorporated herein by reference includes forward-looking statements regarding our business and the therapeutic and commercial potential of SPINRAZA (nusinersen), TEGSEDI (inotersen), WAYLIVRA (volanesorsen), eplontersen, olezarsen, donidalorsen, ION363, pelacarsen, tofersen and our technologies and products in development. Any statement describing our goals, expectations, financial or other projections, intentions or beliefs, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, including those related to the impact of COVID-19 could have on our business, and particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this report. Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors currently known by us. As a result, you are cautioned not to rely on these forward-looking statements.

Ionis Pharmaceuticals, Inc.
2855 Gazelle Court
Carlsbad, CA 92010
www.ionispharma.com

If you have any questions regarding this Corporate Responsibility Report, please contact us at corporateresponsibility@ionisph.com.