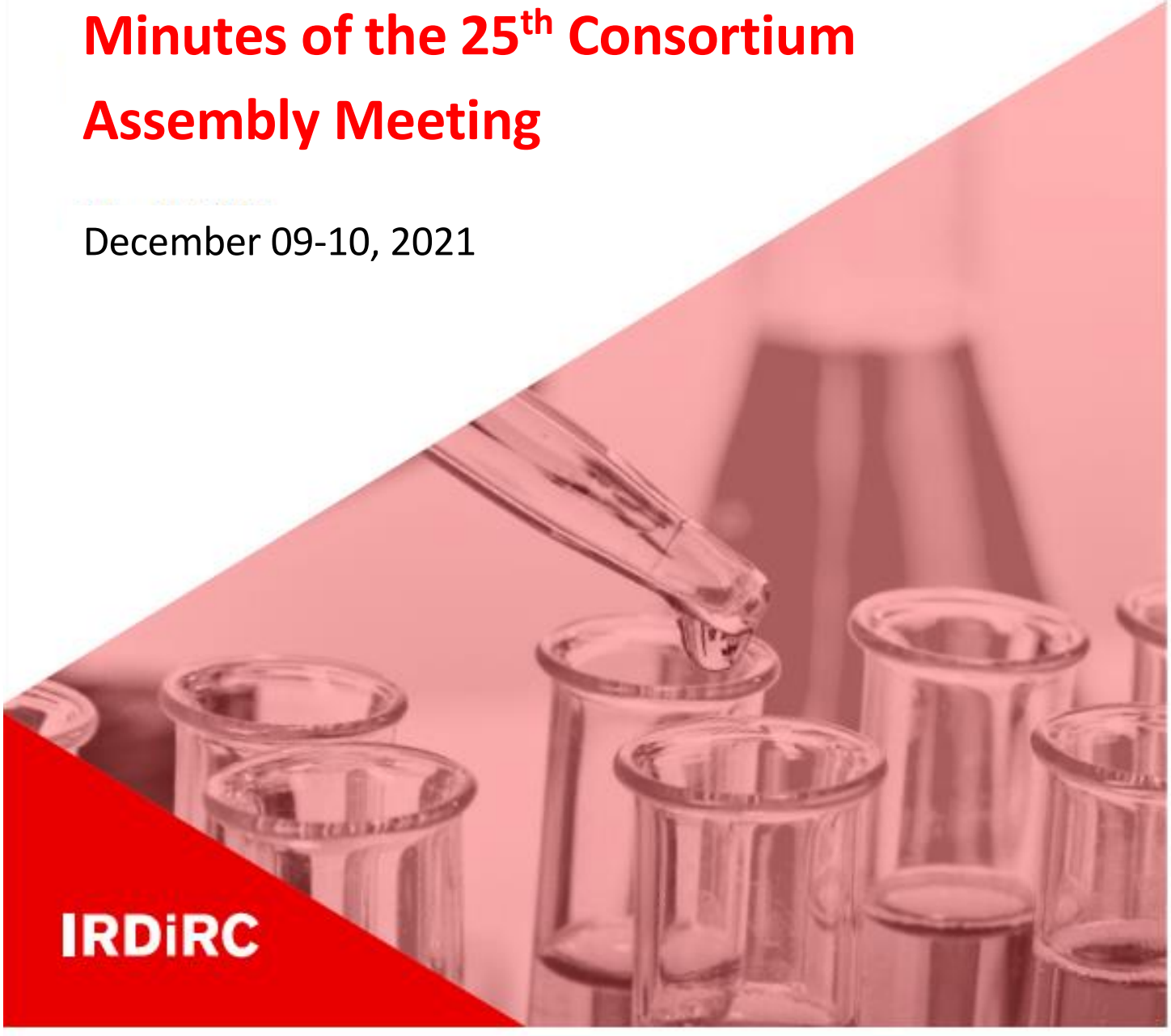
INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

# Minutes of the 25th Consortium Assembly Meeting

December 09-10, 2021



IRDiRC

# EXECUTIVE SUMMARY

The Consortium Assembly (CA) of the International Rare Diseases Research Consortium (IRDiRC) held a two-days hybrid meeting on December 09 & 10, 2021, via web/teleconference and Face-to-Face (F2F) in Paris, France. It was attended online by 39 participants representing 28 member organizations and the Scientific Committees (SC), and on-site in Paris by 15 participants representing 8 member organizations and the Scientific Secretariat (Sci Sec).

**December 09, 2021:**

1. Changes in Representation
   - EURORDIS appointed Dr. Virginie Hivert (Therapeutic Development Director) to replace Dr. Virginie Bros-Facer as their representative for PACC.
   - Fondazione Telethon appointed Dr. Stefano Benvenuti (Public Affairs Manager) to replace Dr. Lucia Monaco as their representative for FCC.

2. IRDiRC's Ten Years of Activity
   - A commentary paper was submitted by IRDiRC to Nature Review Drug Discovery Journal last November 2021 to present the past ten years activities of IRDiRC.
   - Lucia Monaco, the CA Chair, addressed that IRDiRC is overall growing in activities and encourages the CA to attract more new members.

3. How to Better Address the Vision of the Consortium?
   - More activities have emerged under the IRDiRC theme of "Stimulating Multistakeholder Engagement" and "Access to Care, and Impact Methodologies".
   - Miro Session: The CA members were invited to provide suggestions and comments on how to better address the vision of the Consortium through the Miro board online.

4. New Process for Task Force Preparation and Validation
   - Flexibility in the timeline of the submission of Task Forces proposals.
   - Provision of the State of the Art with each Task Force proposal.
   - Inclusion of different proposal evaluators (based on their expertise) from the whole IRDiRC assembly.
   - Open submission of Task Force proposals between January and September, and proposal evaluations performed in fourth quarter of each year.

**December 10, 2021:**

5. Update on IRDiRC Activities: Task Forces and Working Groups
   - Rare Diseases Treatment Access Working Group (in collaboration with RDI)
   - Chrysalis (led by the FCC and CCC)
   - Sustainable Economic Models in Drug Repurposing (led by the TSC and PACC)
   - Machine Readable Consent and Use Conditions (led by the ISC and ULEIC)
   - Shared Molecular Etiologies (led by the ISC)
   - Integrating New Technologies for Rare Diseases Diagnosis (led by the DSC)
   - Primary Care (collaboration between FCC, ISC, and DSC)
   - Enabling and Enhancing Telehealth for Rare Diseases Across the Globe (will be led by the FCC)
   - MedTech Working Group (will be led by the University of Twente)
   - Pluto Project on Disregarded Rare Diseases (will be led by the CCC and TSC)
   - Repurposing Guidebook (will be led by the TSC)

6. IRDiRC 2019-2021 in a Nutshell
   - 9 New Members
   - 14 Task Forces/Working Groups
   - 3 Collaborations
   - 12 CA Meetings
   - 10 Publications
   - 3 Recognized Resources

7. IRDiRC's Leadership Transfer
   - Lucia Monaco, the current CA Chair, will be on retirement and is ending her mandate in December 2021. David Pearce, the current CA Vice Chair, was elected by the CA as the next Chair starting January 2022.
   - Samantha Parker, the current CCC Vice Chair, was elected by the CA as the next Vice Chair and will replace David Pearce on his former role starting January 2022.
   - The CCC will elect a new Vice Chair this year 2022 to take over Samantha Parker's previous role.

8. Upcoming CA Meetings in Year 2022
   - March (online)
   - June (Face-to-Face)
   - October (online)
   - December (Face-to-Face)

9. Actions and Deliverables
   - Monthly Reporting by CA Members
   - MIRO Session Result

# REPORT

## 1. Changes in Representation

- Dr. Virginie Bros-Facer informed the IRDiRC Sci Sec that she will not be a part of EURORDIS starting December 23, 2021. Dr. Virginie Hivert will take over her role at EURORDIS and be the organisation's representative for the PACC. We warmly welcome Dr. Virginie Hivert to the CA.
- Dr. Lucia Monaco announced her retirement in August 2021. As of January 2022, Dr. Stefano Benvenuti will take her role at Fondazione Telethon and be the organisation's representative for the FCC. We warmly welcome Dr. Stefano Benvenuti to the CA.

## 2. IRDiRC's Ten Years of Activity

- A commentary paper with extensive supplemental information was submitted last November 2021 to Nature Review Drug Discovery Journal to present IRDiRC's past ten years activities and accomplishments.
- Post-meeting Note: The manuscript received positive feedback from the Editor and requires some editing mainly to reduce its length. Submission of the revised version will take place in January 2022.

## 3. How to Better Address the Vision of the Consortium?

- The implementation of the strategic vision and the redefinition of IRDiRC goals in 2017 opened the path towards engagement into other thematic actions which address not only basic, translational clinical research, but also health care system infrastructures, multistakeholder engagement, access to care, and measuring impact.
- The CA Chair reminded the members of the vision and goals of the Consortium for 2027 and to contemplate whether the Consortium is on its way to achieving the set goals.
- An online Miro session was initiated by the Sci Sec and requested the CA members to participate via the online link. Members were asked to provide online their input on "How to better address the vision of the Consortium". Lucia Monaco (CA Chair) and Galliano Zanello (member of the Sci Sec) read through some of the provided inputs by the members:
  - Increase in participation and engagement of IRDiRC members has been addressed a few times. IRDiRC's ability to establish multinational stakeholder collaboration and influence has been its greatest asset since its establishment and must be continuously strengthened.
  - Improve communication, consistent dialogue, and intersectoral collaboration with ERNs, regulatory agencies, payers, HTA bodies, health ministries, and other global institutions such as WHO and UN were some of the propositions.
  - Increase dissemination and regular updates of activities, access to tools, and outcomes of Task Forces, including published guidelines, recommendations, and best practices

through various platforms, including social media, to strengthen IRDiRC's visibility and influence.
    - Data sharing and standardization across countries. This is a rapidly evolving field and requires specific competencies. This field can bridge different technical experts and allow collaborations to provide meaningful solutions.
    - Training and Education, with short, dedicated courses for new researchers.
    - Clear positioning of IRDiRC to define targeted priorities and deliver its value coherently to stakeholders and the rare diseases ecosystem.
    - Increase in activities related to Natural History and economic impact of untreated rare diseases
- The CA Chair invited IRDiRC members to promote IRDiRC and highlight their contribution to the Consortium when invited as speakers externally.

## 4. New Process for Task Force Preparation and Validation

- The weaknesses in the current process of Task Forces validation and implementation were addressed to the CA. Flexibility in the timeline of the submission of Task Force proposals and activities was suggested, including the provision of the State of the Art with each Task Force proposal submitted and the inclusion of different proposal evaluators (based on their expertise) from the IRDiRC assembly. The CA Chair proposed an open submission of Task Force proposals between January and September. All Task Force proposals were suggested to be evaluated in the fourth quarter of each year, ensuring that proposers of a Task Force shall abstain from any evaluation.
- A call for a review of the proposed solutions regarding new processes for Task Force preparation and validation was raised by the CA Chair to all members, including the need to standardize the evaluation process of Task Force proposals and be further defined in the year 2022.
- Adam Hartman, the FCC Chair, mentioned that various technology-driven topics evolve quickly and would require an immediate strategic decision from experts. Two tiers of proposals were suggested: The limited scope proposals are submitted twice a year, and others with a broader scope are submitted once a year.
- New Task Force proposals are expected to be received by September 2022.

## 5. Updates on IRDiRC Activities: Task Forces and Working Groups

- Updates on ongoing and foreseen activities were presented by Task Force/Working Group leaders.
- Daria Julkowska, the Sci Sec Coordinator, addressed to the CA that the EJP RD General Assembly is in favour of the 12 months extension of all IRDiRC-related activities. However, it will take a few months for its validation by the European Commission. A justification for the 12 extra months (with no expected provision of additional budget) is required by the Commission, and their response is expected to be received in the second quarter of 2022. Once the response is received, it will be known if all IRDiRC activities can be extended until the end of 2024.

- The EJP RD is lobbying the IRDiRC Scientific Secretariat to be a part of the next phase of its project, the Rare Diseases Partnership.

- **Eleven Activities are Ongoing and/or Foreseen for the Year 2022 (Task Forces and Working Groups):**
  - Rare Diseases Treatment Access Working Group (in collaboration with RDI)
  - Chrysalis (led by the FCC and CCC)
  - Sustainable Economic Models in Drug Repurposing (led by the TSC and PACC)
  - Machine Readable Consent and Use Conditions (led by the ISC and ULEIC)
  - Shared Molecular Etiologies (led by the ISC)
  - Integrating New Technologies for Rare Diseases Diagnosis (led by the DSC)
  - Primary Care (collaboration between FCC, ISC, and DSC)
  - Enabling and Enhancing Telehealth for Rare Diseases Across the Globe (will be led by the FCC)
  - MedTech Working Group (will be led by the University of Twente)
  - Pluto Project on Disregarded Rare Diseases (will be led by the CCC and TSC)
  - Repurposing Guidebook (will be led by the TSC)

- **Rare Diseases Treatment Access Working Group (WG)**
  - Presentation: Durhane Wong-Rieger and Mary Wang from RDI presented the objectives, methodology, and summary of their progress and results. This WG is a collaboration with RDI. It was emphasised that oncology nor cardiology is not covered in this study.
  - Objective: The goal is to improve access to rare disease medicines by creating a list of standard-of-care medicines, looking at innovative schemes, and identifying the systemic and idiosyncratic barriers to access (e.g., barriers in screening, treatment, aftercare, cost, and exclusivity expiration, etc.), especially in low-and-middle-income countries.
  - Foreseen: This WG is considering creating an ongoing list of drugs that are in short supply and maybe include drugs that will potentially be in short supply. How to predict the potential shortness of supply in terms of raw materials, manufacturing capabilities, sites, etc., needs to be further studied.

- **Chrysalis**
  - Presentation: Adam Hartman from NIH/NINDS presented the objectives, methodology, and summary of their progress and results. This Task Force is led by the FCC (Adam Hartman) and the CCC (Katherine Beaverson).
  - Objectives: Identify key criteria that would make Rare Diseases research more attractive to industry and find the gaps in the current funding opportunity landscape, including other non-financial factors.
  - Status: The group has sent out surveys to 70 companies and received 39 responses predominantly from large private pharma and biotech companies. Four Writing Groups were formed covering different themes such as commercial viability, payer/pricing, regulatory, and stakeholders. Writeups from the different Writing Groups were

completed last November 19, 2021. Currently, the final manuscript is being expanded and reviewed by the Chairs and simultaneously being edited by the different Writing Group members.

- Result: Attitudes towards Rare Diseases research were mainly influenced by regulatory factors, return of investment, and availability of Rare Diseases natural history studies.
- Foreseen: The final manuscript would be released by Q1 of 2022 and will then be submitted to a journal as a commentary.

- **Sustainable Economic Models in Drug Repurposing**
  - Presentation: Virginie Hivert presented the objectives, methodology, and summary of their progress. This Task Force is led by the TSC (Daniel O'Connor) and the PACC (Virginie Hivert).
  - Objectives: To understand the key features of successful drug repurposing projects and its corresponding business and/or funding models, and to create IRDiRC recommendations on the most successful approaches to support drug repurposing.
  - Status: The questionnaire is composed of 11 questions focused on the expert groups' repurposing research activities, sources and mechanisms of funding, barriers and challenges, sustainable economic model chosen, and recommendations for a successful drug repurposing process. Ten expert groups were selected with various economic model approaches (eight provided answers; two did not answer).
  - Foreseen: The group will collect and analyse the survey results, build-up the collected case studies, and will then be the basis in creating an IRDiRC recommendation on the most successful economic models approaches for drug repurposing that would be useful for funders and drug developers.

- **Machine Readable Consent and Use Conditions**
  - Presentation: Anthony Brookes from University of Leicester (ULEIC) presented the objectives and summary of their progress/results. This Task Force is led by Esther van Enckevort (from ISC) and Anthony Brookes (from ULEIC). The team comprises of approximately 40 international scientists.
  - Objectives: To create machine-readable profiles for consent and use for registries and biobanks by building on GA4GH+IRDiRC standard data structures and semantics.
  - Status: Consent form templates are designed for the EU Clinical Patient Management System and the ERN registries. This work has been adopted and the group is now working on ontologizing that and putting it into a flexible data structure/profile (Digital Use Conditions) for consent and use consent metadata. Many organizations (EJP RD, BBMRI, FAIR Genomes) are assessing this data structure and giving feedback.
  - In the EJPRD registries and biobanking setting, 14 core elements of consent and core conditions (Common Consent of Use - CEE) have been identified, defined, and now alpha tested. A software was established to create the profiles for these 14 CCEs.
  - Foreseen: The group plans to work with ontology developers such as Orphanet to define new classes and properties that are not yet defined in the ontologies, and to extend the

Common Conditions of Use (CCE) concept for more complete description of consent and use conditions in the Digital Use Condition (DUC) format. The group aims to integrate the use of DUC and CCE as part of the European Joint Program on Rare Diseases (EJPRD) research activity.

- **Shared Molecular Etiologies (SaME)**
  - Presentation: PJ Brooks from NIH/NCATS presented the activity's objectives, methodology, and summary of their progress and results. This Task Force is led by the ISC (PJ Brooks and Marc Dooms).
  - Objectives: To assess the global landscape of clinical trials of drugs with SaME, including approaches to identify and include patients, and to identify potential clusters of rare diseases that may benefit from the SaME approach. The group would also like to explore the applicability of tissue-agnostic oncology basket trials framework for basket trials of drugs targeting SaME underlying multiple rare diseases and identify the roadblocks, potential regulatory pathways, and ethical issues for such trials.
  - Status: The group is currently identifying rare diseases that may benefit the SaME approach, including regulatory and methodological challenges.

- **Integrating New Technologies for Rare Diseases Diagnosis**
  - Presentation: Gareth Baynam from Western Australia Department of Health presented the activity's objectives, methodology, and summary of their progress and results. This Task Force is led by the DSC (Sarah Bowdin, Clara van Karnebeek, and Gareth Baynam).
  - Objectives: To identify new technologies in development or in experimental use which would likely increase the diagnostic rate of rare diseases patients, and to develop a clinical framework or guideline for the implementation of combined diagnostic approach of metabolomics, genomics, and AI.
  - Status: A mini online symposium was held last October 21, 2021, where each member presented their latest research that are potentially or are currently being applied in clinical care.
  - Foreseen: A state-of-play and technology mapping accomplished through surveys will be done in Q1-Q2 of 2022, and a workshop will be organised for Q3 of 2022.

- **Primary Care**
  - Presentation: Gareth Baynam from Western Australia Department of Health presented the activity's objectives. This Task Force is led by the DSC (Gareth Baynam), FCC (Adam Hartman), and Stephen Groft (from NIH/NCATS). The call for nominations was opened for one month and ended last October 29, 2021. The Sci Sec received 35 applicants from North and South America, Europe, Africa, Asia, Middle East, and Australia.
  - Objectives: To bring together representatives from different stakeholders to identify the current state of play, priority research areas, and the challenges and opportunities in rare diseases research in primary care.
  - Status: 17 candidates were selected from different regions (North and South America, Europe, Africa, Asia, Middle East, and Australia). With the three proposers, this Task

Force has 20 members with various backgrounds such as genetic counselor, general practitioners, nurse, pharmacist, a patient advocate with children who are rare disease patients, care pathways and research network coordinator, clinical psychologists, researcher, etc. which meets the first objective of bringing together representatives from different stakeholders.

- Foreseen: The first virtual team meeting was held last December 20, 2021.

- **Enabling and Enhancing Telehealth for Rare Diseases Across the Globe**
  - Presentation: Melissa Parisi from NIH/NICHD presented the activity's objectives and background. This Task Force is led by the FCC. The call for nominations ended last November 30, 2021, and received 35 applicants from North America, Europe, Middle East, Asia, Africa, and Australia.
  - Objectives: To conduct survey and systematic review of existing telehealth models and identify its barriers and opportunities to improve access to rare diseases diagnosis, care, and research, and leverage the output to develop best practices for introducing telehealth services into the rare diseases' community.
  - Questions: Few questions were raised regarding the insurance coverage and how it can be adapted to different national healthcare systems, including potential difficulties from a regulatory perspective in terms of clinical trial data. Melissa Parisi mentioned that many of the past and current clinical studies in NIH were converted to virtual assessments of enrolled subjects. It is evident that there has been some willingness and flexibility from the funders perspective about accommodating virtual assessments and evaluations. She also defined telehealth for this study as the delivery of health-related services, information, and education virtually and remotely.

- **MedTech Working Group**
  - Presentation: Anneliene Jonker from University of Twente presented the activity's objectives and background. This Task Force is initiated by the University of Twente (Netherlands). The call for nominations will end on January 15, 2021.
  - Objectives: To understand and map the current incentives, supportive frameworks, and unmet technical and functional needs for developing medical devices for rare diseases. The group would also like to determine the possibilities for patient involvement in the medical device design process.

- **Pluto Project on Disregarded Rare Diseases**
  - Presentation: Daniel O'Connor from MHRA presented the activity's objectives and background. This activity will be open for nominations in January 2022.
  - Objectives: To use an integrated database search approach to identify and classify groups of rare diseases that are currently underrepresented by academic research and industries and to determine their common characteristics through analysis to help understand the roadblocks in developing effective treatments for such diseases.
  - Foreseen: A call for collaboration was raised by Daria Julkowska, the Scientific Secretariat Coordinator.

- **Drug Repurposing Guidebook**
  - Presentation: Anneliene Jonker from University of Twente presented the activity's objectives and background. This activity will be open for nominations in February 2022.
  - Objectives: To create a guidebook focused on repurposing approaches (incentives, regulatory tools, initiatives, development tools, etc.).

## 6. IRDiRC 2019-2021 in a Nutshell

- New Members
  - 3 FCC: INSERM, NRDRS, CZI
  - 3 CCC: Illumina, Congenica, Innoskel
  - 3 PACC: APARDO, ALIBER, RD Ghana Initiative

- Task Forces/Working Groups
  - 9 activities launched, 3 completed
  - 5 activities are in preparation

- Collaborations
  - EJP RD: Machine Readable Consent and Use Conditions
  - RDI: Global Access Working Group
  - University of Twente: MedTech for RD

- Meetings
  - CA: 10 online, 2 in-person
  - OpComm: Monthly
  - SciSec: Every 2 weeks
  - IRDiRC Conference: 1 (with RE(ACT) Congress)

- Publications
  - 10 scientific papers/editorial articles

- Recognized Resources
  - MAARVEL
  - hPSCReg
  - Cellosaurus

## 7. IRDiRC's Leadership Transfer

- CA Election
  - Following a CA election last October to November 2021, David Pearce, President at Innovation and Research at Sanford Health, has been elected by the CA as the Chair for a three-year term, beginning on January 01, 2022, and extending through December 31,

2024. Samantha Parker, Chief Patient Access Officer at Innoskel, has been elected by the CA as the Vice-Chair for a three-year term, beginning on January 01, 2022, and extending through December 31, 2024.

- CCC Vice Chair Election
  - An election process will be held in Q1 of 2022 for the position of Vice Chair.

## 8. Upcoming Meetings

- Year 2022 CA Meetings
  - March (online)
  - June (F2F): This Face-to-Face meeting is open for volunteers to organise and host the meeting. If no volunteers are found, it would be held in Paris (France) where the Scientific Secretariat is based.
  - October (online)
  - December (F2F): This Face-to-Face meeting will take place in Paris (France) where the Scientific Secretariat is based.

## 9. Actions and Deliverables

- Monthly Reporting by CA Members
  - The Sci Sec will collect a monthly update/report from the CA members starting January 2022. The monthly update/report can be from two sentences to two pages on members' key activities, challenges, projects, or questions to the Assembly.

- MIRO Session Result
  - The Sci Sec will complete the categorization of inputs provided by the attendees and will do a summary of the result. The result will be distributed to the CA members in January 2022.