

# REiNS 2019 Winter Meeting

“Clinical Trial Design for Cutaneous Neurofibromas”

*Welcome and Direction*

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Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION

# Disclosures

- SRP: co-founder of NFlection Therapeutics and NF2 Therapeutics; consulting for AstraZeneca



# What is REiNS?

## *Response Evaluation in NF and Schwannomatosis*

- Established in 2011 by team of investigators
- International collaboration to develop standardized response criteria for determining treatment response in patients with NF1, NF2, and schwannomatosis
- Collaboration across institutions and medical specialties; includes experts in NF and other areas (including patient representation)
- Proactive discussion of endpoints with stakeholders will help facilitate approval of, and therefore access to, drugs for these rare conditions
- Response criteria are a work in progress and will continue to be modified as we gain experience in trials for NF
- Criteria will improve our ability to determine and compare treatment efficacy



# Engaging stakeholders

- Investigators
- Patient representatives
- NF Foundations
- Food and Drug Administration
- Cancer Therapy Evaluation Program
- NIH/DOD
- Pharma- Dermavant, NFlection, Pierre Fabre, Springworks



# Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) Collaboration

## Working groups

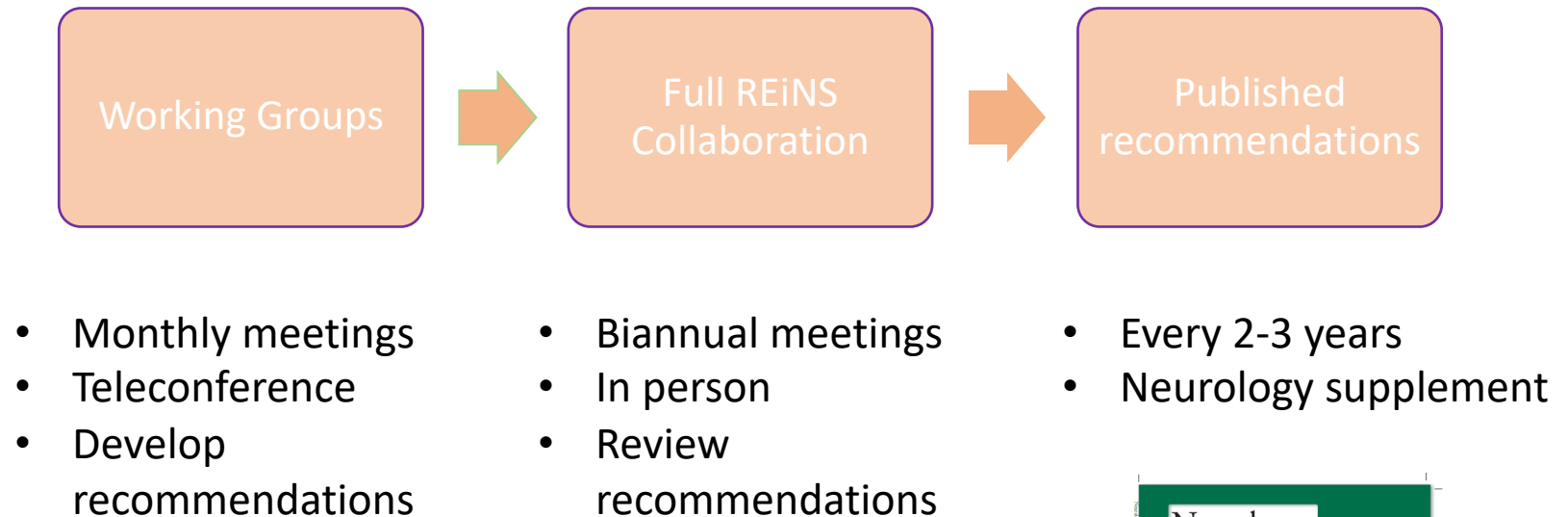
- Tumor Imaging/WBMRI (Ahlawat, Dombi)
- Functional outcomes (Plotkin)
- Patient reported outcomes (Wolters)
- Visual outcomes (Avery, Fisher)
- Disease Biomarkers (Bettegowda/Hanemann)
- Neurocognitive outcomes (Janusz)
- Cutaneous neurofibromas (Cannon/Pichard)
- Patient Representation (Plotkin)

- 9 working groups
- Over 160 active members
- Over 70 institutions and organizations

***The REiNS working groups are open to all participants***

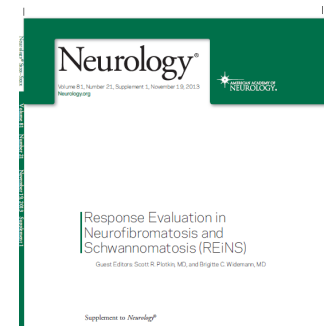


# How REiNS Works



## Collaborators:

- CTF and other foundations
- Food and Drug Administration
- Cancer Therapy Evaluation Program
- National Institutes of Health



# REiNS publications (2013-present)

- Achieving consensus for clinical trials: The REiNS International Collaboration
- Patient-reported outcomes in neurofibromatosis and schwannomatosis clinical trials
- Functional outcome measures for NF1-associated optic pathway glioma clinical trials
- Hearing and facial function outcomes for neurofibromatosis-2 clinical trials
- Recommendations for imaging tumor response in neurofibromatosis clinical trials
- Conclusions and future directions for the REiNS International Collaboration
- Consensus for NF Clinical Trials: Recommendations of the REiNS Collaboration
- Outcomes of Pain and Physical Functioning in NF Clinical Trials
- Sleep and pulmonary outcomes for clinical trials of airway plexiform neurofibromas in NF1
- Neurocognitive Outcomes in Neurofibromatosis Clinical Trials: Recommendations for the Domain of Attention
- Current Whole-Body MRI Applications in the Neurofibromatoses: NF1, NF2 and Schwannomatosis
- Current status and recommendations for biomarkers and biobanking in neurofibromatosis



# 2020 Neurology supplement

## **Use of SkinDex to assess patients with NF1: a report from US and Australian Clinics**

*Christopher Moertel, Mimi Berman for the REiNS Cutaneous Neurofibroma Working Group*

## **Reliability of digital calipers, photography, and ultrasound to measure cutaneous neurofibromas in patients with neurofibromatosis 1**

*Scott Plotkin for the REiNS Cutaneous Neurofibroma Working Group and Neurofibromatosis Therapeutic Acceleration Program (NTAP)*

## **Patient Views Regarding Cutaneous Neurofibromas and Treatment**

*Ashley Cannon and Dominique Pichard for the REiNS Cutaneous Neurofibroma Working Group and Neurofibromatosis Therapeutic Acceleration Program (NTAP)*

## **Evaluating satisfaction, barriers, and successes of patient engagement in REiNS**

*Vanessa Merker, Renie Moss for the REiNS Patient Representative Working Group*

## **Assessing general and disease-specific quality of life in neurofibromatosis clinical trials** (depending on title length restrictions)

*Pamela Wolters for the REiNS Patient Reported Outcomes Working Group*

## **Measures of Quality of Life and function for hearing in patients with neurofibromatosis 2**

*Heather Thompson for the REiNS Patient Reported Outcomes Working Group*



# 2020 Neurology supplement

## **Social skills outcomes for patients with neurofibromatosis 1**

*Jennifer Janusz for the REiNS Neurocognitive Working Group*

## **Measurement of attention as a clinical trials outcome in preschoolers with neurofibromatosis 1**

*Bonnie Klein-Tasman for the REiNS Neurocognitive Working Group*

## **Genotype-Phenotype correlations in neurofibromatosis and their potential clinical use**

*Chetan Bettegowda and Oliver Hanemann for the REiNS Biomarkers Group*

## **Biomarkers for cutaneous neurofibroma**

*Kavita Sarin for the REiNS Cutaneous Neurofibroma Working Group*

## **Reliability of strength testing using hand held dynamometry in patients with neurofibromatosis 1 and 2.**

*Vandana Akshintala, Kaleb Yohay for the REiNS Functional Endpoints Working group*

## **Implementation and performance of REiNS clinical trial endpoints in SPRINT trial**

*Andrea Gross for the REiNS Functional Endpoints Working and PRO Working group*

# How REiNS is supported

- Through volunteerism of hundreds of investigators and patient representatives!
- Grant support (R13) through National Cancer Institute, National Center for Advancing Translational Sciences (NCATS)
- Financial support from Children's Tumor Foundation, NF Midwest, Texas NF, NF Northeast, and Mass General Hospital



# REiNS 2018/2019 Winter Meetings

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- “Designing Clinical Trials for Cutaneous Neurofibromas, an Unmet Need for Patients with Neurofibromatosis Type 1”
- Focus on a longstanding and important unmet need
- Uniquely suited to our work in determining clinical endpoints
- Drawing from multiple groups and prior experience
  - Patient representation
  - Patient Reported Outcomes, Quality of Life
  - Measures of tumor size
- Focus on discussion among stakeholders



# Agenda (1)

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## 8:00 -8:10 am **Welcome and introduction**

Scott Plotkin (Mass General Hospital), Brigitte Widemann (National Cancer Institute)

## 8:10-9:00 am **Review of proposed outcome measures for cNF: tumor size, PROs, global assessment of change**

Dominique Pichard (NCI) and Scott Plotkin (MGH)

## 9:00 -9:30 am **Selumetinib for cutaneous neurofibroma: preliminary findings and lessons learned**

Ashley Cannon (UAB) and Brigitte Widemann (NCI)

## 9:30 – 10:00 am **Proposed design for a pilot activity trial using local therapy (topical formulation/injection): inclusion criteria, endpoints, and go/no go decisions**

Scott Plotkin (Mass General Hospital)



# Agenda (2)

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10:00 - 10:30 am **Group discussion**

10:30 – 11:00 am **Coffee Break**

11:00 – 11:30 am **Proposed design for a screening trial using systemic therapy: inclusion criteria, endpoints, and go/no go decisions**

Brigitte Widemann (National Cancer Institute)

11:30 - 12:00 pm **Group discussion**

12:00-1:00 pm **Sponsored lunch by NF Northeast, NF Midwest, and Texas NF**

1:00 -1:45 pm **Next steps in designing trials for cNF: what do we need as a community?** A panel discussion



# Agenda (3)

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**1:45-2:30 pm      Assessing the strengths and weaknesses of the REiNS patient representation program**

Vanessa Merker (VA) and Andres Lessing (Patient Representative)

**2:15 -2:45 pm      Small group discussions: next steps for the REiNS patient representation program**

**2:45-3:15 pm      Small group debriefing/large group discussion**



# cNF Working Group

- Thanks to Ashley Cannon and Dominique Pichard for their leadership these last 2 years
- Leadership transition
  - Dominique Pichard to become Chief Scientific Officer for International Rett Syndrome Foundation
  - Kavita Sarin to join leadership of Working Group

# Feedback

- We need your feedback to improve the meeting and for grant purposes
- Please fill out survey at the end of the day (or earlier if you leave before the end)





# Future meetings

- Skeletal endpoints
- Gene therapy
- Your thoughts?

# Acknowledgments

- Dr. William Timmer, Program Director, Cancer Therapy Evaluation Program (CTEP)
- Children's Tumor Foundation, NF Northeast, NF Midwest, and Texas NF
- NTAP
- Patient Representatives
- cNF working group
- Jennifer Da
- All attendees

