



# Response Evaluation In Neurofibromatosis Schwannomatosis INTERNATIONAL COLLABORATION

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# REiNS 2020 Summer Meeting

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Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION

# Disclosures

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



# 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

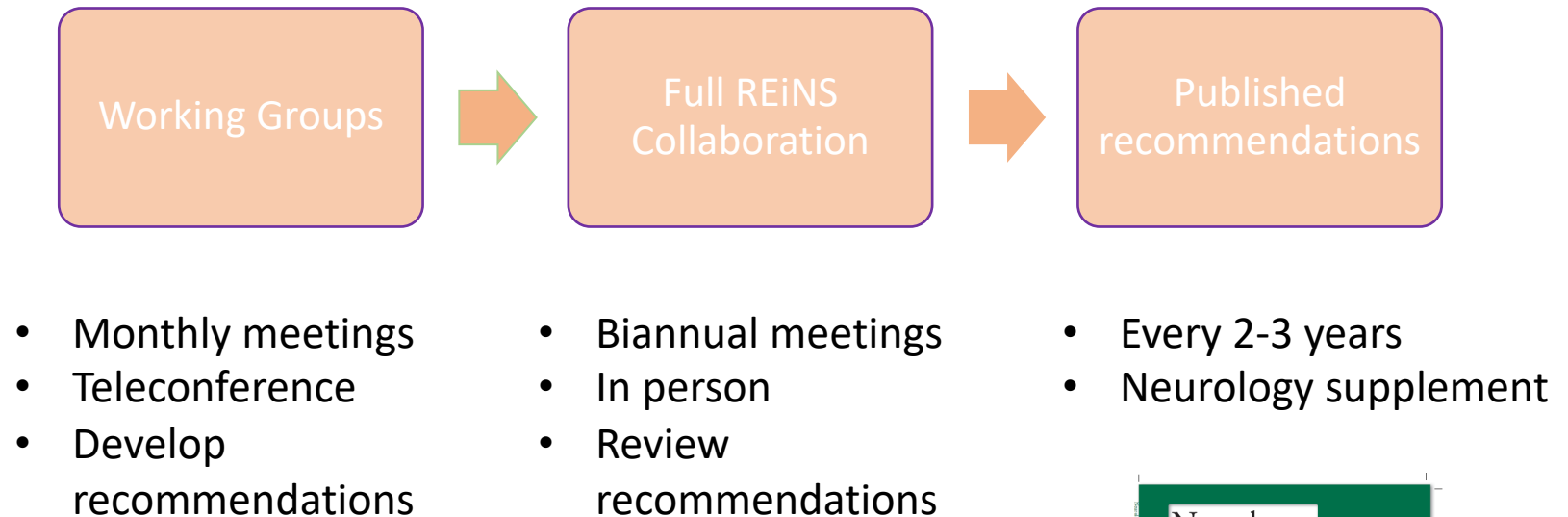
- Tumor Imaging/WBMRI (Ahlawat, Dombi)
- Functional outcomes (Plotkin)
- Patient reported outcomes (Wolters)
- Visual outcomes (Avery, Fisher)
- Disease Biomarkers (Bettegowda/Hanemann)
- Neurocognitive outcomes (Janusz)
- Cutaneous neurofibromas (Cannon/Pichard)
- Patient Representation (Plotkin)

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

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

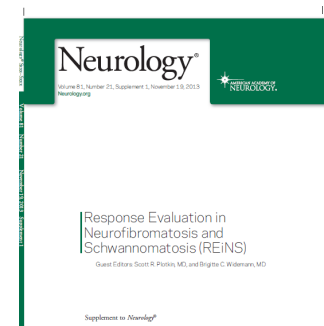


# How REiNS Works



## Collaborators:

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



# REiNS publications

## 2013 *Neurology* Supplement

- 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

## 2016 *Neurology* Supplement

- 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

## **NF Clinical Trials - REiNS Collaboration 2020 Recommendations: Looking Back and Moving Ahead**

*Andrea Gross for the REiNS Leadership Group*

## **Measuring the impact of cutaneous neurofibromas on quality of life in Neurofibromatosis Type 1**

*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)*

## **Perspective of adults with NF1 regarding cutaneous neurofibromas: Implications for clinical trials**

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

## **Enhancing NF clinical trial outcome measures through patient engagement: lessons from REiNS**

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

## **Recommendations for health-related quality of life measures in neurofibromatosis clinical trials**

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

# 2020 Neurology supplement

## **Patient Report of Hearing in Neurofibromatosis Type 2: Recommendations for Clinical Trials**

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

## **Recommendations for social skills endpoints for clinical trials in neurofibromatosis type 1**

*Jennifer Janusz for the REiNS Neurocognitive Working Group*

## **Recommendations for measurement of attention outcomes in preschoolers with neurofibromatosis**

*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*

## **Status and recommendations for incorporating biomarkers for cutaneous neurofibromas into clinical research**

*Kavita Sarin for the REiNS Cutaneous Neurofibroma Working Group*

## **Reliability of hand-held dynamometry for measuring muscle strength in neurofibromatoses**

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

# REiNS 2020 Winter Meetings

Time	Speaker	Topic
7:00am		Breakfast
8:00-8:15 am	Scott Plotkin, MD, PhD (Mass General), Brigitte Widemann, MD (NCI), Jonathan Rios, PhD (UT Southwestern)	Welcome and introduction to REiNS
8:15 - 9:00 am	Noelle Larson, MD (Mayo Clinic)	Developing endpoints for scoliosis: natural history in NF patients and currently used endpoints in sporadic patients
9:00 - 9:45 am	David Stevenson, MD, PhD (Stanford)	Developing endpoints for osteoporosis in NF1
9:45 – 10:30 am	Elizabeth Schorry, MD (University of Cincinnati)	Endpoints for tibial dysplasia and pseudarthrosis
10:30 – 11:00 am	Coffee Break	
11:00 – 12:00 pm		Small group discussion
12:00 – 1:00 pm	Boxed lunch	Informal discussions
1:00 -2:00 pm	Florian Eichler, MD, PhD (Mass General Hospital)	<b>Plenary talk:</b> Hematopoietic Stem-Cell Gene Therapy for Cerebral Adrenoleukodystrophy.
2:00 -2:45 pm	Verena Staedtke, MD, PhD (Johns Hopkins)	Scientific approaches to gene therapy for monogenic disorders and tumor syndromes
2:45-3:15 pm	Vito Grasso	Understanding the patient and family perspective
3:15-3:45 pm	Scott Plotkin, MD, PhD (Mass General Hospital)	Initiating human trials of gene therapy: deciding what? when? who? how?
3:15 – 5:00		St
5:00 pm	Adjourn meeting	

## Skeletal outcomes

## Gene therapy



# Agenda

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**3:30–3:45 pm Introduction and REiNS Updates**

Scott Plotkin, M.D., Ph.D (MGH) and Brigitte Widemann, M.D. (NCI)

**3:45–4:00 pm Taking the REiNS: How REiNS Clinical Trial Recommendations Contributed to the FDA Approval of Selumetinib for NF1**

Andrea Gross, M.D., NCI

**4:00–4:30 pm Developing endpoints for skeletal manifestations of NF1**

Jonathan Rios, Ph.D., UT Southwestern

**4:30–4:45 pm Developing Endpoints Across Multiple Cognitive Domains**

Jennifer Janusz, PsyD., Children's Hospital Colorado

**4:45–5:00 pm Developing endpoints to assess physical disfigurement in NF**

Staci Martin Peron, Ph.D., National Cancer Institute

**5:00–5:15 pm Recruiting patient representatives to REiNS: version 2.0**

Vanessa Merker, Ph.D., Mass General Hospital

**5:15–5:30 pm Plans for December meeting and closing comments**

Scott Plotkin, M.D., Ph. (MGH) and Brigitte Widemann, M.D. (NCI)



# 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

