

# Trials of acetazolamide and dichlorphenamide in the periodic paralyses

- Acetazolamide (ACZ) & dichlorphenamide (DCP) used off-label in hyper (HYP) and hypo (HOP) periodic paralyses
  - Uncertainty whether treatment will prevent the chronic, progressive weakness afflicting patients
  - ACZ initially improves in many cases, but patients often become acetazolamide-resistant and progressively weak
  - DCP may improve weakness.
- DCP taken off the market by Merck due to lack of market viability for glaucoma
  - Never indicated for periodic paralysis. Not currently available to patients
- Working Group on Periodic Paralysis carried out an FDA-funded phase III cross-over trial of DCP (Tawil et al)
  - Showed that the drug was effective over a 9-week period in reducing the number of attacks in subjects with periodic paralysis
- Current phase III, NIH-funded, year-long trial (HYP HOP) of ACZ vs. DCP for attack prevention and treatment/prevention of weakness in the periodic paralyses to:
  - (1) develop standard treatments for the periodic paralyses;
  - (2) defend recommendations for long-term treatments in periodic paralysis
  - (3) provide data for regulatory approval of DCP.

# Taro funded by MDA to bring DCP to Market

- Taro Pharmaceutical Industries, Ltd. (Taro) providing the ACZ and DCP for HYP HOP
- MDA has awarded funding to enable Taro Pharmaceuticals U.S.A., Inc to provide DCP commercially to patients with the periodic paralyses.
- Taro has purchased the NDA from Merck
  - Will develop a synthetic method for the manufacture of pharmaceutically pure DCP to 2008 standards.
  - Will develop a formulation in which DCP is sufficiently bioavailable
  - Will perform clinical studies to establish bioavailability of DCP
  - Rochester will support the clinical arm of the project and provide safety and outcome data necessary for FDA filings
- Plan to bring the drug to the marketplace soon after the Phase III trial is complete.

# HYP-HOP Site Screening/Enrollment Status

Site #	Site	Completed Subjects	Enrolled Subjects	Withdrawn Subjects	Screenings Scheduled	Pre-screening / Under Assessment
001	University of Rochester	1	2	2	0	2
002	Columbia University Medical Center	0	1	1	0	0
020	Ohio State University	0	0	0	0	4
029	University of Kansas Medical Center	0	0	0	0	3
063	Brigham and Women's Hospital	0	1	0	1	0
073	University of California/San Francisco	0	1	0	0	1
102	University of Texas Southwestern - Dallas	0	0	0	0	2
133	Mayo Clinic	0	0	0	0	3
118	London Health Sciences Center					
164	Hospital Pitie-Salpetriere					
166	University of Milan					
167	Institute of Neurology (London, UK)					
	Thomas Jefferson Univ. Hospital					

**TOTAL:**                      1                      5                      3                      1                      15