The TREAT-NMD Advisory Committee for Therapeutics: A multi-disciplinary expert approach to drug development advice

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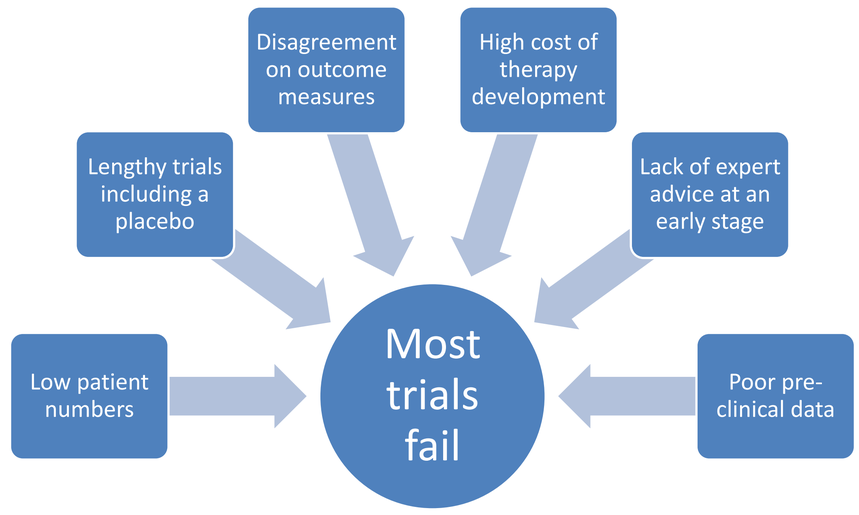
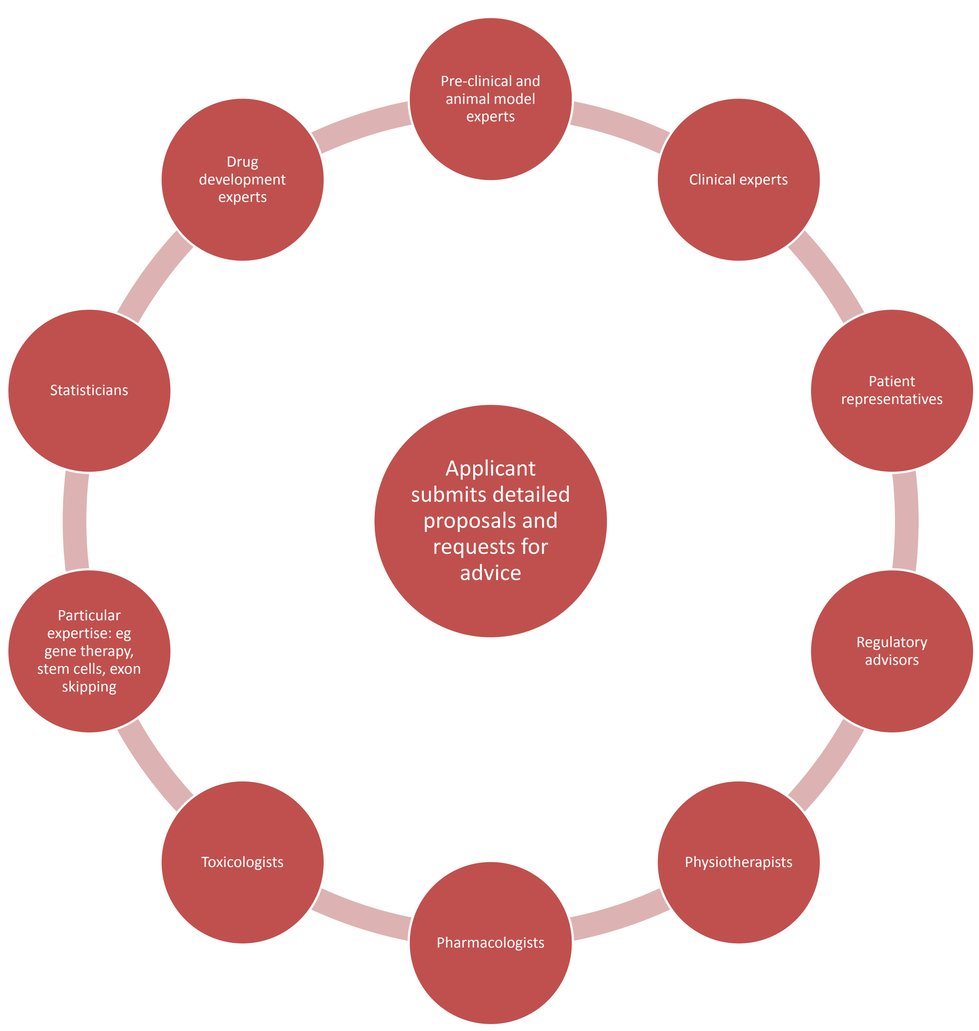
Some Challenges in Therapy Development for Rare Neuromuscular Disease

- Fewer than 90% of compounds that enter Phase 1 clinical trials result in a marketed drug
- Drug development is expensive. Where there are few patients, it is even more expensive
- Patient numbers in rare disease are small and strict inclusion/exclusion criteria alongside competing trials mean recruitment targets for trials need to be low
- For slowly progressing conditions, trials are often longer than average which increases the burden on patients
- Lack of natural history data means a placebo arm is usually required. In long trials for degenerative muscle diseases - often involving children - this is a high burden on patients
- Agreement on clinically meaningful outcome measures, approved by regulators, is difficult
- Groups planning trials in this field may be new to the disease and have little understanding of the condition
- A lack of regulatory guidance early on can make subsequent registration and approval more difficult





Multi-disciplinary experts make up a bespoke review panel for each application with patient-experts always included

Part of the solution to many of the challenges identified in rare disease therapy development is to work directly, closely and early with patients. Input from TACT patient-expert reviewers has covered many areas but is often focussed on:

- Study schedule and burden on families
- Mode of administration
- Risk/benefit considerations
- Inclusion/exclusion criteria and recruitment plans
- Selection of outcome measures that are clinically meaningful and relevant
- Evidence showing justification for potential therapy and the need for placebo
- Questions about study length and extension studies
- The need for biopsies

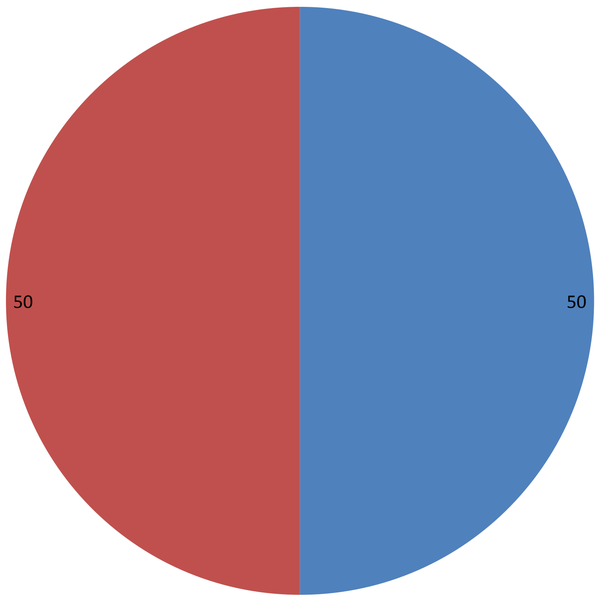
Disease specific patient expert reviewers are selected for each application.

Part of the solution: The TREAT-NMD Advisory Committee for Therapeutics (TACT)

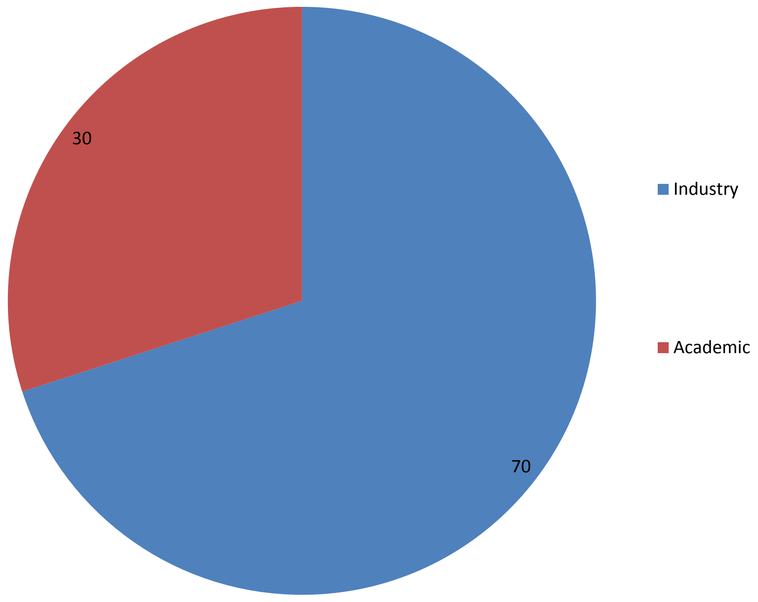
- Established to provide independent and objective guidance on the pre-clinical and development pathway of potential therapies for rare neuromuscular diseases
- A multidisciplinary body of drug development experts that includes patients and/or their advocates
- Works closely with patient organisations in multiple regions to ensure the process meets the needs of the neuromuscular community as a whole
- A bespoke expert panel of world-leading experts from all areas of drug development discuss each application together and with the applicants before formulating comprehensive and confidential advice
- Generates recommendations that have greatly helped investigators in evaluating their potential compounds and in considering their development program in a methodical fashion with clear go/no-go decisions
- So far 46 applications from industry and academics have been received and reviewed over 8 years
- Educates the drug development community via workshops and training: next at ICNMD'18, Vienna

How TACT works

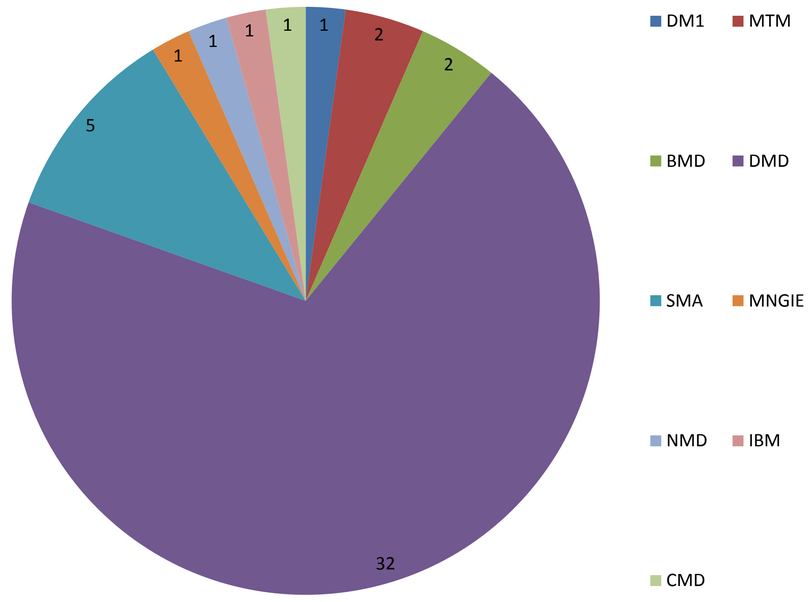
- Applicants working on the development of a therapy in NMD outline their proposals – these can be at a pre-clinical stage right through to phase III or even post-marketing
- Under strict confidentiality agreements and checking for conflicts, a panel of reviewers (10-15) is convened every 6 months in response to the particular needs and questions of applications
- A 6-week online review between the experts is followed by a face-to-face meeting and discussion with the applicant
- A comprehensive and confidential advisory report is sent to the applicant after the meeting
- TACT does not recommend projects to be funded but a review is often used to help support funding applications – indeed, funders often refer applicants to TACT



Applications by stage



Applications by type of applicant



Applications by disease

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