RUNNING CLINICAL TRIALS

RETINA AND BEYOND

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COLUMBIA | COLUMBIA UNIVERSITY IRVING MEDICAL CENTER

WHAT IS A CLINICAL TRIAL

1) Clinical trials are research studies conducted to evaluate the effectiveness and safety of medical treatments, drugs, or devices.
2) These trials help determine if new treatments work as intended and are safe for public use
3) Clinical trials are essential for developing new treatments and improving patient care.
4) They involve careful planning, regulation, and ethical considerations.
5) Participation in clinical trials is vital to advancing medical science

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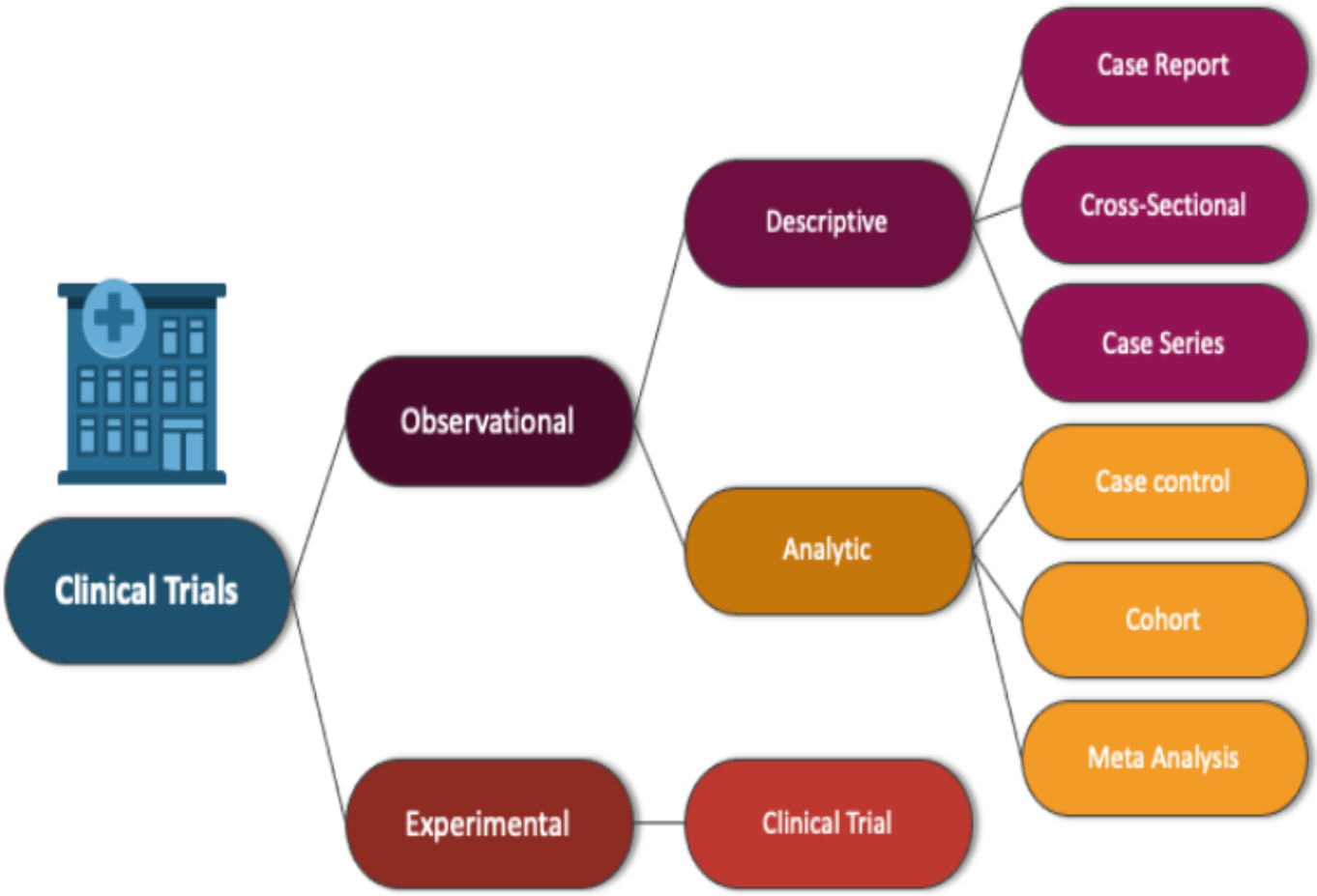
PURPOSE OF CLINICAL TRIALS

- To evaluate new treatments, drugs, or medical devices.
- To discover how effective a treatment is compared to existing options.
- To determine potential side effects or risks.
- To improve public health and contribute to medical knowledge.

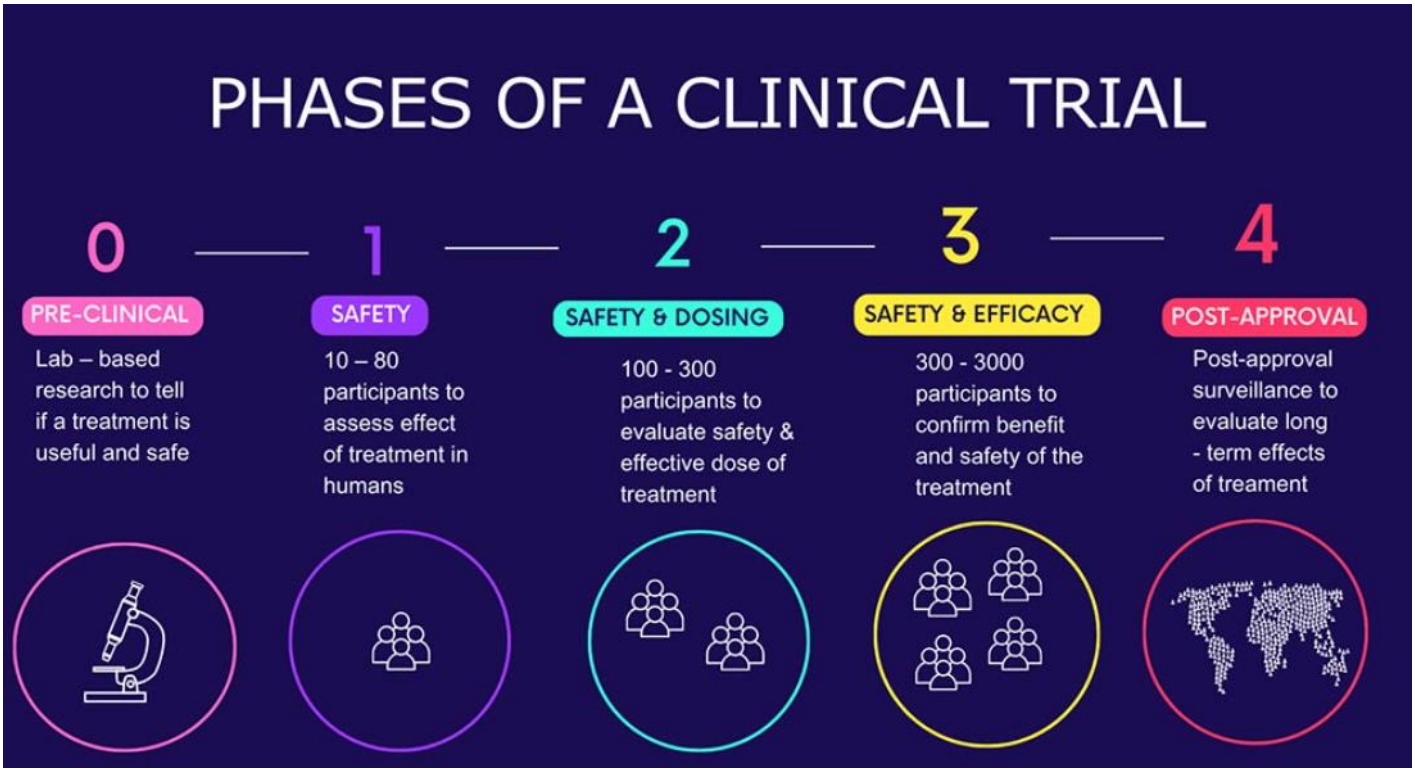
TYPES OF CLINICAL TRIALS

- **Interventional Trials:** Participants receive specific treatments or interventions.
- **Observational Trials**: Researchers observe participants without intervention.
- **Prevention Trials**: Evaluate ways to prevent diseases or health conditions.
- **Treatment Trials**: Focus on testing new therapies or drugs.
- **Diagnostic Trials:** Evaluate methods to diagnose diseases.
- **Quality of Life Trials:** Assess ways to improve the quality of life for people with certain conditions.

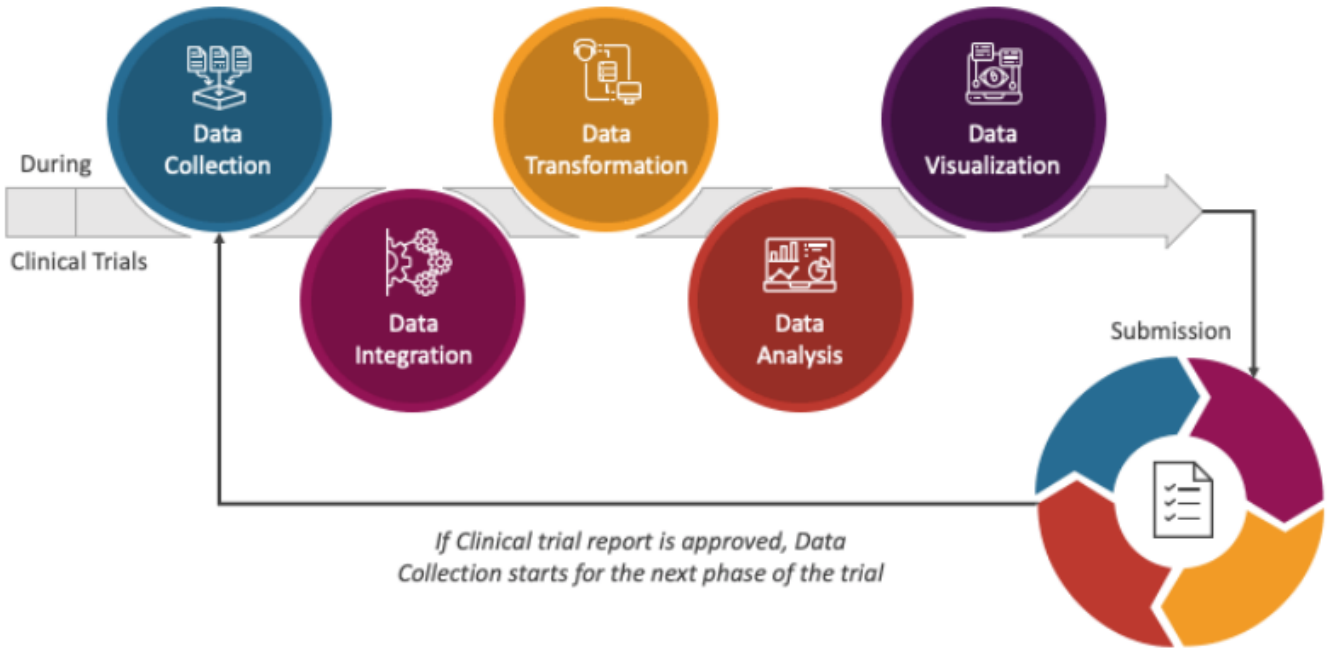


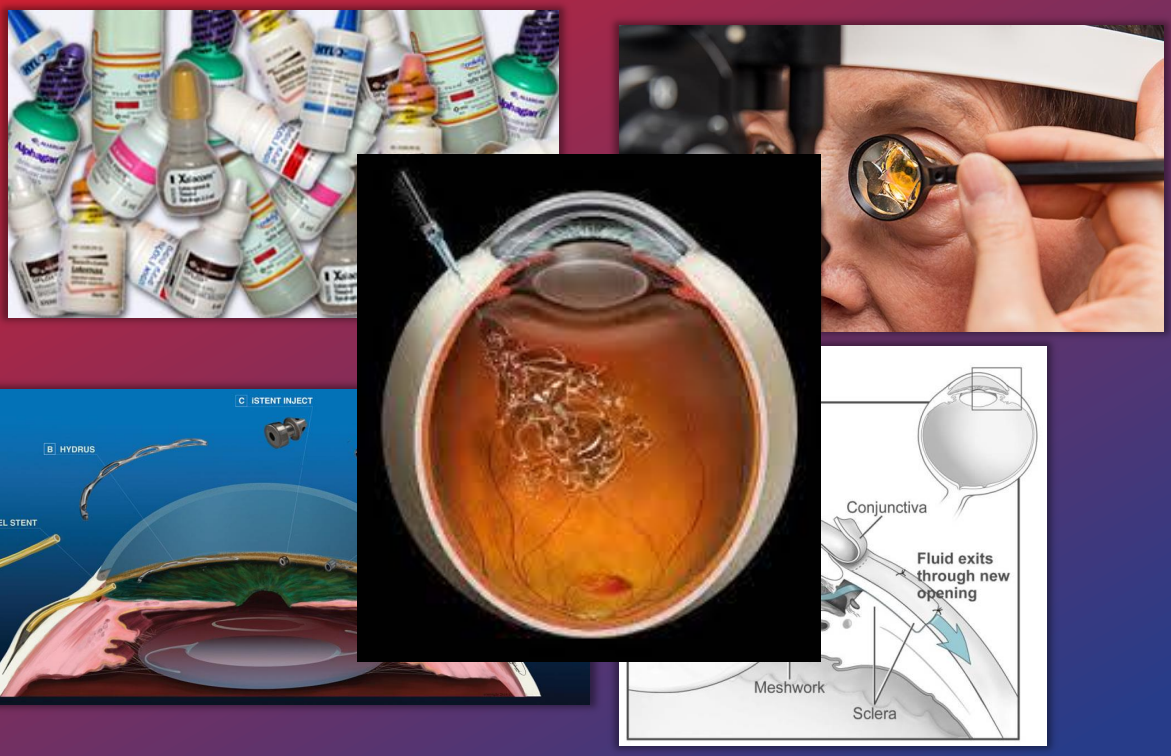
PHASES OF A CLINICAL TRIAL

- **Phase 1:** Safety and dosage; small group of participants.
- **Phase 2:** Testing the effectiveness and side effects (larger group of patients).
- **Phase 3**: Larger trials to confirm effectiveness, monitor side effects, and compare to standard treatments.
- **Phase 4:** Post-market studies to gather additional information after a drug is approved.




Planning & Budget
Finances & Contract
Funding Application
Document Management
Approvals
Develop Protocol
Peer Review
Ethics Application, Site impact & Health Canada Approval
Clinical Trial Registration
Clinical Trial Operations


During
Clinical Trials
Data Collection
Data Integration
Data Transformation
Data Analysis
Data Visualization
Submission
If Clinical trial report is approved, Data Collection starts for the next phase of the trial



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IMPACT OF OPHTHALMOLOGY CLINICAL TRIALS ON PATIENT CARE

- **Improved Outcomes:** Clinical trials lead to new treatments that improve quality of life and vision for patients.
- **Faster Access to Breakthrough Treatments:** Bringing promising therapies to market faster through successful trials.
- **Expanded Access Programs:** Enabling patients with no treatment options to access investigational drugs.
- **Reduced Healthcare Costs:** Preventing blindness and eye-related diseases can reduce overall healthcare expenses.

OPHTHALMOLOGY CLINICAL TRIALS UNIT
WHAT IS A CLINICAL TRIAL

- Clinical trials test new treatments, drugs, devices, or procedures aimed at improving eye health and vision.

- Purpose: To evaluate the safety, effectiveness, and potential benefits of interventions in treating ocular conditions.

- Importance: Essential for the development of innovative therapies for vision-related diseases.

IMPORTANCE OF CLINICAL TRIALS
WHY DO CLINICAL TRIALS MATTER?

- Clinical trials provide crucial data to approve new treatments.

- They help determine whether a new drug or therapy is more effective than existing options.

- They ensure treatments are safe for wider use.

- Participation in clinical trials can advance medical research and patient care.

BENEFITS OF PARTICIPANTNG IN CLINICAL TRIALS FOR OPHTHALMOLOGISTS AND PATIENTS

- Access to new and potentially life-saving treatments.
- Contribution to scientific and medical knowledge.
- Close monitoring by healthcare professionals.
- The opportunity to help others by advancing research.
- Participation in clinical trials can advance medical research and patient care.

RECENT BREAKTHROUGHS IN OPHTHALMOLOGY CLINICAL TRIALS

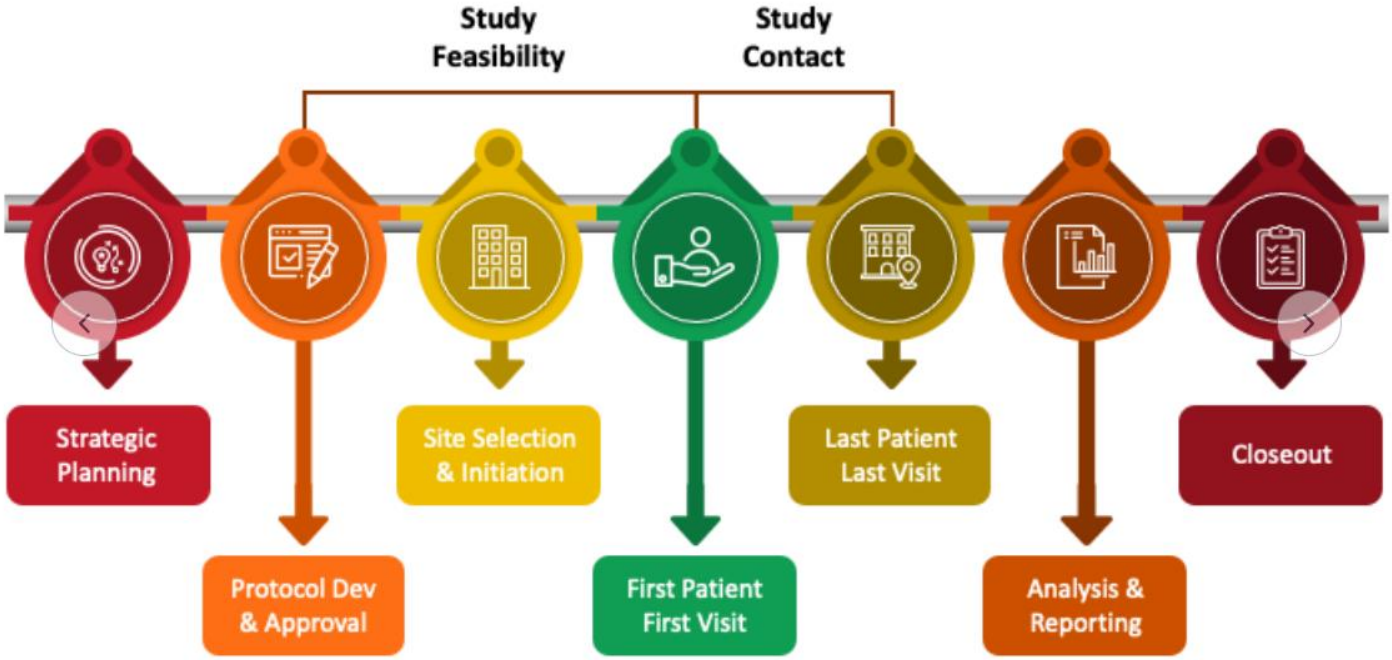
- **Gene Therapy for Retinal Diseases:** Voretigene neparvovec (Luxturna) for inherited retinal dystrophies.
- **New Drugs for Glaucoma:** Latest medications like latanoprostene bunod, aimed at lowering IOP.
- **Stem Cell-Based Retinal Implants:** Progress in clinical trials for retinal degeneration treatments.
- **AI for Retinal Disease Detection:** Machine learning systems being used in clinical trials to improve early diagnosis of retinal diseases.

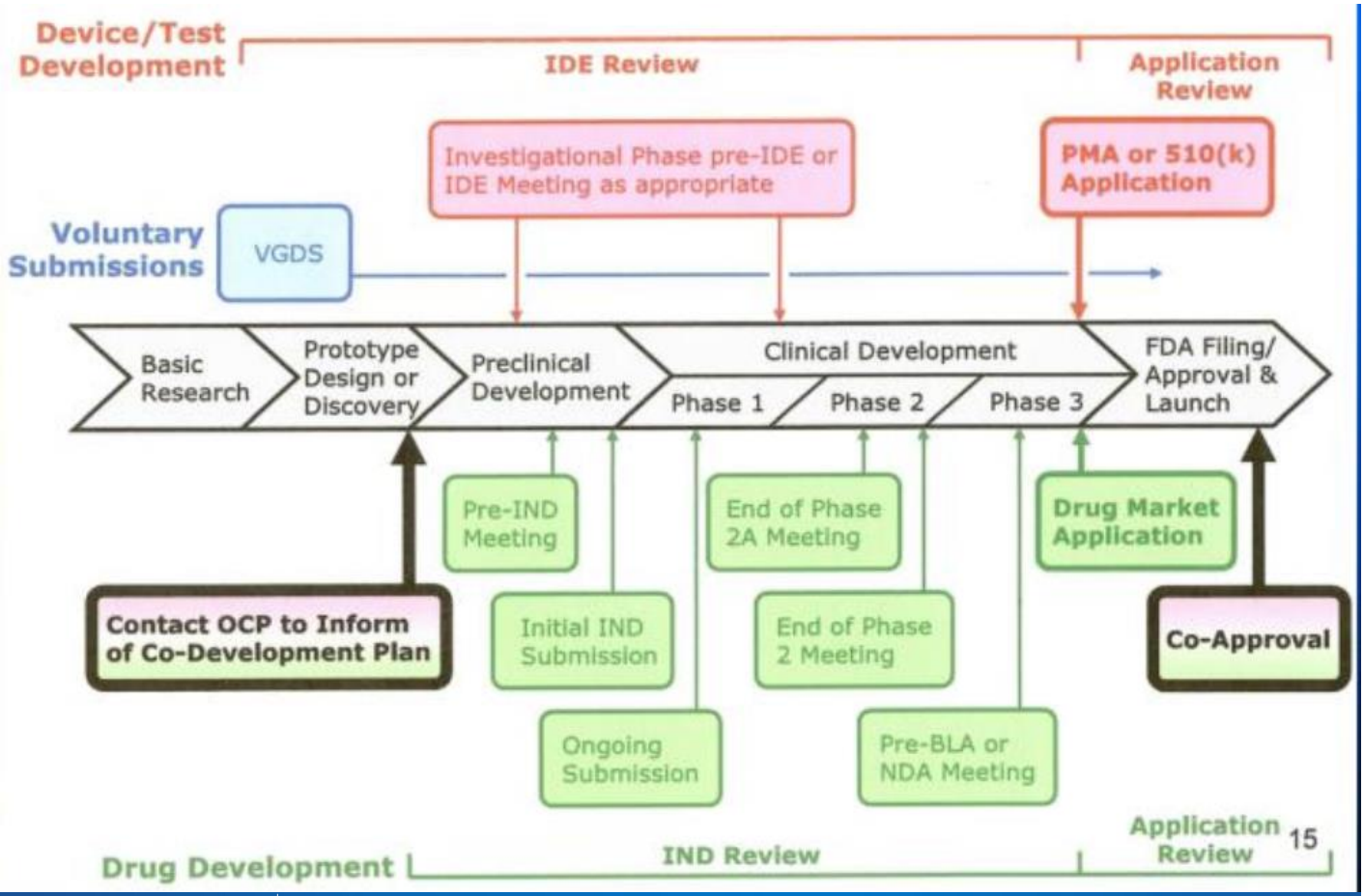
COMMON OCULAR CONDITIONS IN OPHTHALMOLOGY CLINICAL TRIALS

- Glaucoma: Trials for new medications and surgical interventions.
- AMD: Testing of new drugs and gene therapies.
- Diabetic Retinopathy: Evaluation of novel treatments for controlling blood vessel growth.
- Cataracts: Innovations in lens replacement surgery and intraocular lenses.
- Retinal Diseases: Gene therapy, cell-based therapies, and retinal implants.
- **Thyroid Eye Disease:**

CLINICAL TRIAL DESIGN AND METHODOLOGY

- Randomized Controlled Trials (RCTs): Gold standard for testing new treatments.
- Blinding (Masking): Single or double blinding to minimize bias.
- Placebo-Controlled Trials: Assessing the true efficacy of treatments.
- Endpoints: Defining clinical endpoints such as visual acuity, intraocular pressure, or quality of life.
- Data Collection: Use of specialized tools like OCT (optical coherence tomography), visual field testing, and fundus imaging.


Study Feasibility
Study Contact
Strategic Planning
Protocol Dev & Approval
Site Selection & Initiation
First Patient First Visit
Last Patient Last Visit
Analysis & Reporting
Closeout


Device/Test Development
IDE Review
Application Review
Investigational Phase pre-IDE or IDE Meeting as appropriate
PMA or 510(k) Application
Voluntary Submissions
VGDS
Basic Research
Prototype Design or Discovery
Preclinical Development
Clinical Development
Phase 1
Phase 2
Phase 3
FDA Filing/ Approval & Launch
Pre-IND Meeting
End of Phase 2A Meeting
Drug Market Application
Contact OCP to Inform of Co-Development Plan
Initial IND Submission
End of Phase 2 Meeting
Co-Approval
Ongoing Submission
Pre-BLA or NDA Meeting
Drug Development
IND Review
Application Review
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TED: TOURMALINE: Glass

Title: A Multicenter Phase 2b Randomized, Double-Masked, Placebo-Controlled Dose-Ranging Study of TOUR006 in Participants with Thyroid Eye Disease

Sponsor: Tourmaline Bio, Inc.

Subjects: 100 subjects. **CUIMC Recruitment Goals**: 1 to 2 subjects.

Eligibility: Age 18-80 y/o. Moderate to severe TED patients w/ lid retraction, soft tissue involvement, proptosis (exophthalmos), and/or intermittent/constant diplopia.

Study Duration: ~78 wks + [optional 2 wk prescreening + 4 wk screening period]

Treatment:

Subcutaneous. TOUR006 is a highly selective fully human mAb of the IgG2 isotype that binds with high affinity to human IL-6 and neutralizes its functions; it is being developed for the treatment of TED.

TED: TOURMALINE: Glass

Study Design: To investigate the efficacy, safety, PK, and PD of TOUR006 in the treatment of TED.

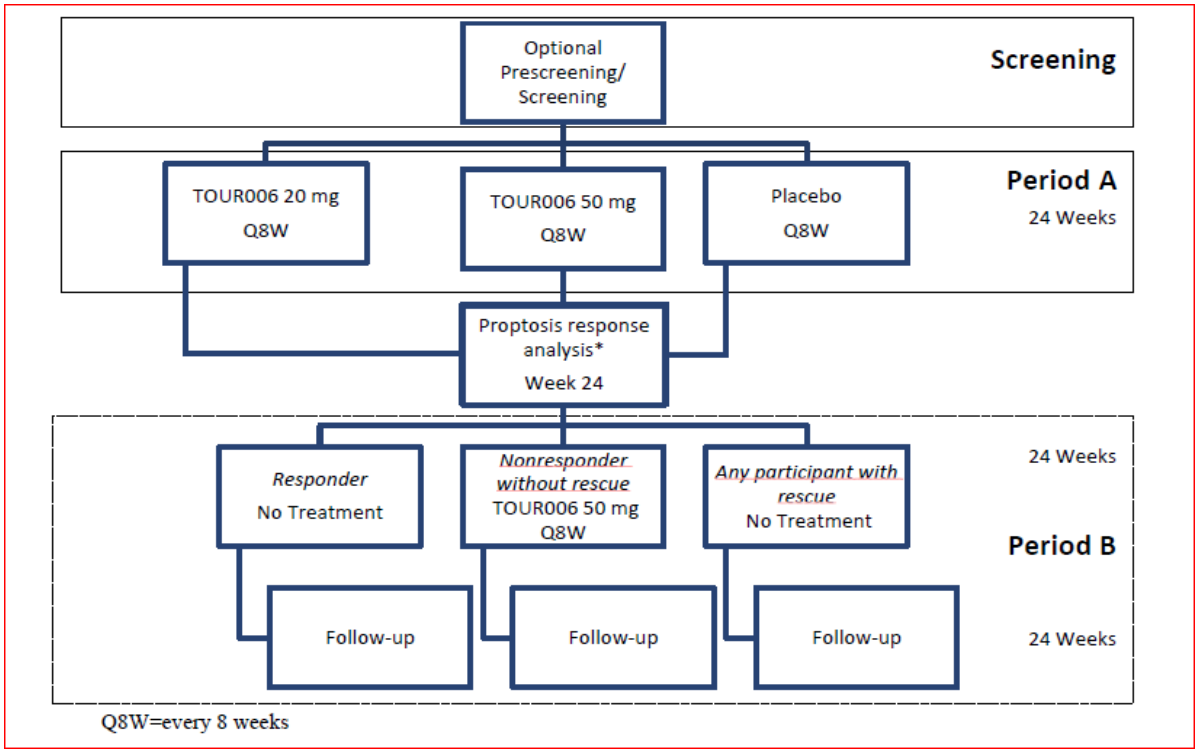
Primary Outcome: A ≥2 mm proptosis reduction from baseline in the study eye, without deterioration (≥2 mm increase) of proptosis in the fellow eye and without need for rescue therapy/intervention.

Benefits: Both active dose levels may provide benefit in terms of the disease. Meaningful effects in participant outcomes may include reductions in proptosis, diplopia, and CAS. Medical evaluations, w/ ophthalmic exams, related to their general health and TED and rescue therapy if deemed medically necessary.

Staffing Needs: PI (L. Glass); Regulatory & Start-up (M. Atakulova); Coordinator (E. Bautista)

Budget: $18.5k Start up; ~~$30k/subject for 17 visits APPROVED 1/15/25

IRB Timeline/Approval: Site selected. Pending IRB approval.



Questions/Concerns/Recommendation

INCLUSION AND EXCLUSION CRITERIA
PAY CAREFUL ATTENTION
TYPICALLY EXTENSIVE

- Age, gender
- Diagnositc criteria
- BCVA criteria- what is this and why.
- Able to provide informed consent #1
- Exclusion: has other ocular conditions
  - History of liver disease
  - Elevated liver enzymes

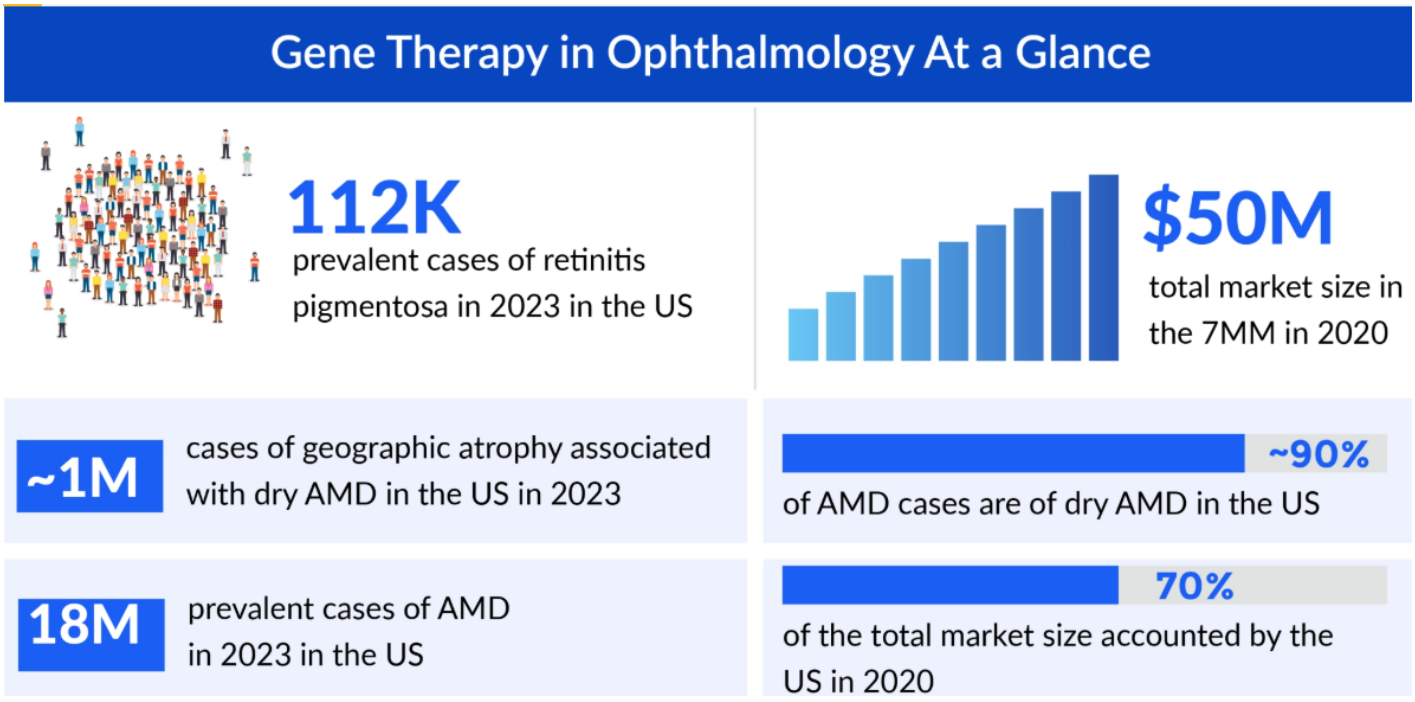
GLAUCOMA CLINICAL TRIALS

https://eyeguru.org/blog/landmark-trials-ophthalmology/

Study Name	***Key Contribution***
Ocular Hypertension Treatment Trial (OHTS)	Looked at efficacy of treating glaucoma **before** it appears
Early Manifest Glaucoma Trial (EMGT)	Looked at efficacy of treating glaucoma **after** it has appeared
Collaborative Initial Glaucoma Treatment Study (CIGTS)	Compared incisional surgery vs meds as initial glaucoma treatment
Glaucoma Laser Trial (GLT)	Compared laser surgery vs meds as initial glaucoma treatment
Advanced Glaucoma Intervention Study (AGIS)	Compared laser vs incisional surgery in advanced glaucoma
Collaborative Normal -Tension Glaucoma Study	Evaluated role of IOP in NTG

INNOVATIONS IN OPHTHALMOLOGY CLINICAL TRIALS

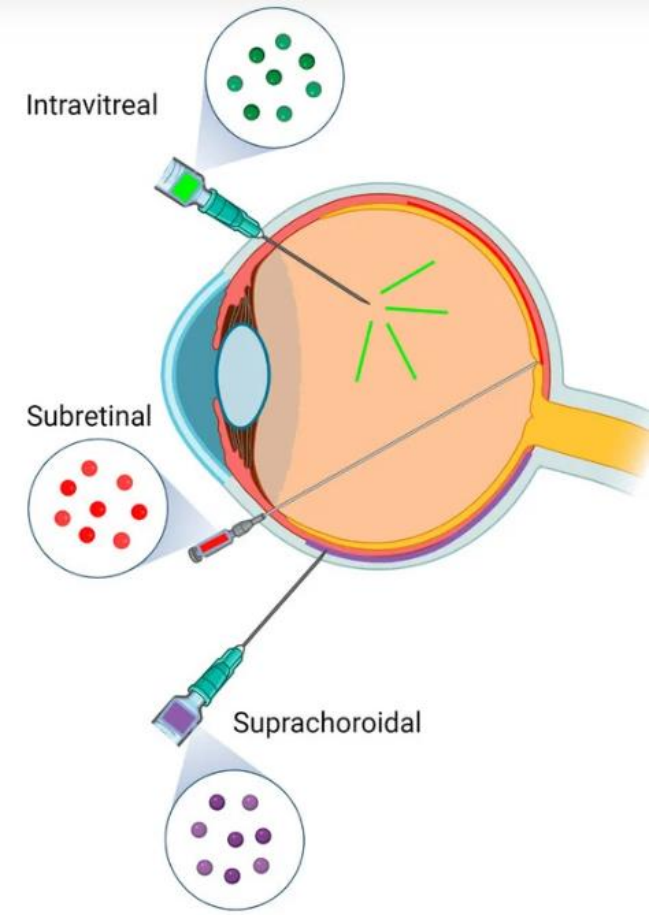
- **Gene Therapy**: Exploring genetic modifications to correct inherited eye diseases like retinitis pigmentosa.
- **Stem Cell Therapy**: Investigating stem cells to regenerate damaged retinal cells or corneal tissue.
- **Drug Development:** New medications for glaucoma, AMD, and diabetic retinopathy.
- **Minimally Invasive Surgery**: Trials focused on laser therapies, robotic surgeries, and less invasive surgical techniques.
- Diagnostic Technologies: Development of advanced imaging techniques and AI for better disease detection.

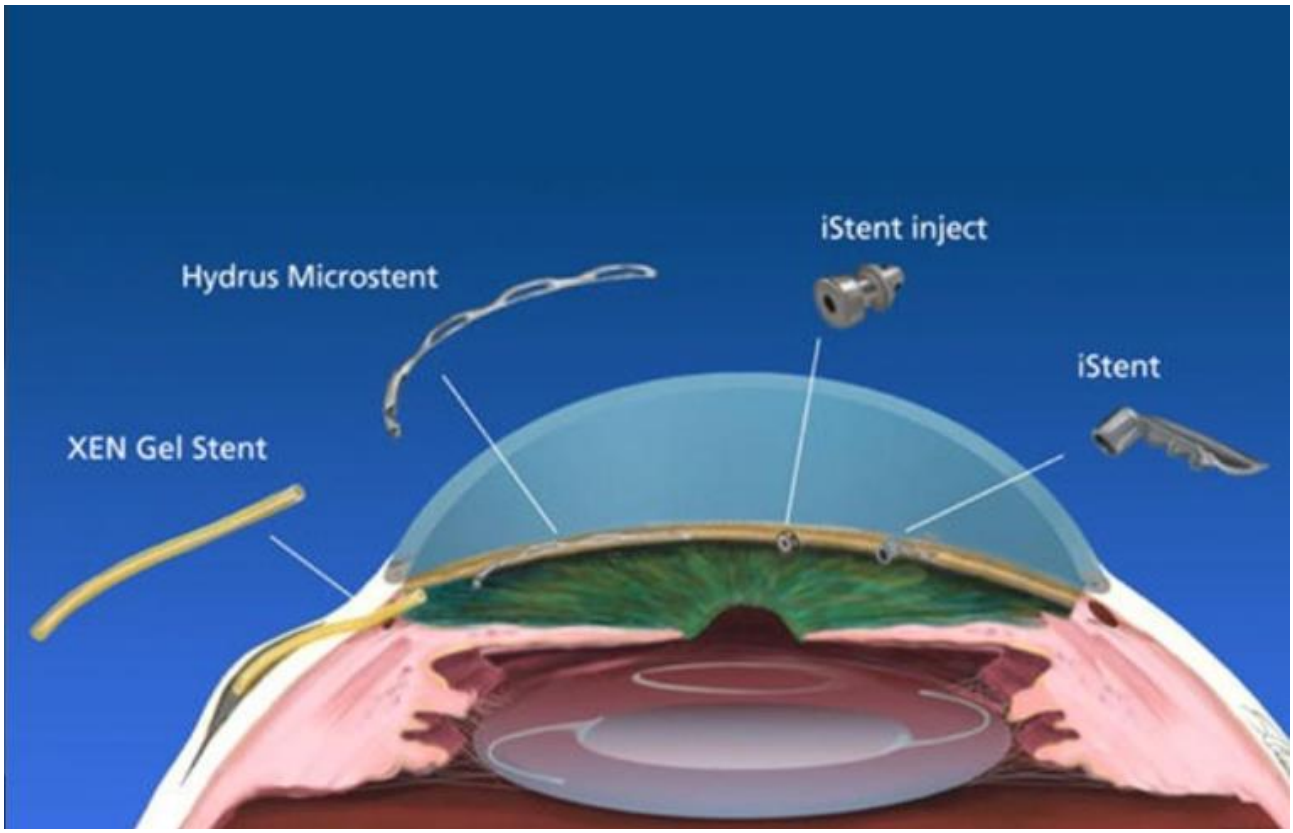


Source: University of Pennsylvania Scheie Eye Institute

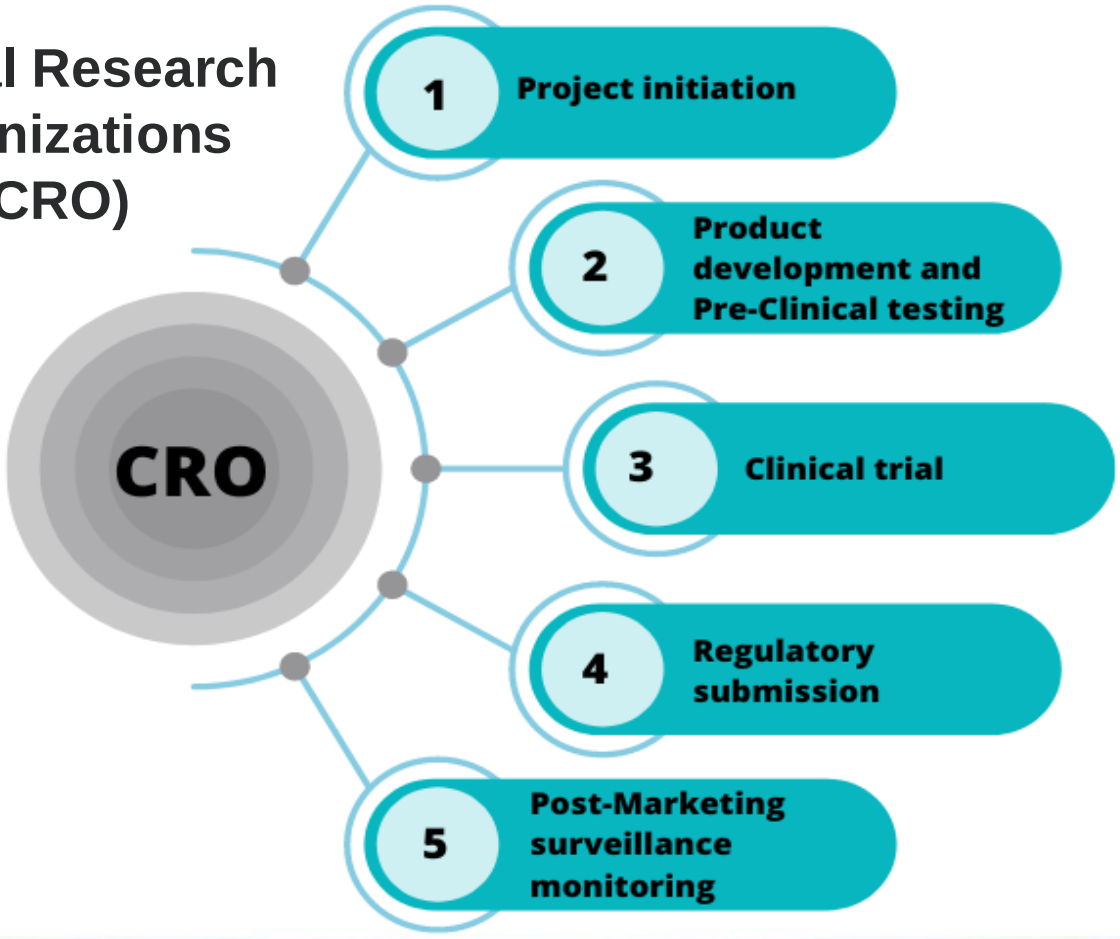
Gene Therapy:

Exploring genetic modifications to correct inherited eye diseases like retinitis pigmentosa.





Clinical Research Organizations (CRO)



STUDY SCHEDULE (TESTS + #VISITS)

	Screen Day –28 to –1	CRU Admission (Baseline)	Day 1			Day X to X	Prior to Discharge (Day X)	Follow-up ≥3 days and ≤5 days after Discharge
			Pre-dose	Dosing	Post-dose	Post-dose		
Informed Consent Form Signed	X							
Eligibility Review and Confirmation	X	X	X					
Medical History	X							
Physical Examination	X	X					X	X
Height Assessment	X							
Weight Assessment	X	X	X				X	
Urine Drug Test	X	X						
HIV & Viral Hepatitis Screen	X							
Vital Signs	X	X	X		X	X	X	X
12-lead ECG	X	X	X		X	X	X	
Clinical Laboratory (Blood) and Urinalysis	X	X	X		X	X	X	
Prior Medication Assessment	X	X	X					
Serum Pregnancy Test	X							X
Urine Pregnancy Test		X						
CRU Admission		X						
Randomization			X					
Administer Study Drug				X				
Pharmacokinetic Sampling (Blood)			X		X	X	X	
Pharmacokinetic Sampling (Urine)			X		X	X	X	
Treatment-Emergent Adverse Events				X	X	X	X	X
Concomitant Medication Assessment				X	X	X	X	X
CRU Discharge							X	X

INNOVATIONS IN OPHTHALMOLOGY CLINICAL TRIALS

- **Gene Therapy**
- **Stem Cell Therapy**:
- **Drug Development:**
- **Minimally Invasive Surgery**:
- **Diagnostic Technologies:**

RISK AND CHALLENGES OF CLINICAL TRIALS

- Potential side effects or adverse reactions to treatments.
- Uncertainty of outcomes; new treatments may not always work.
- Time commitment and frequent visits to medical centers.
- Emotional and physical stress during the trial process
- Recruitment: Difficulty in finding suitable participants, especially for rare eye diseases.
- Long Trial Durations: Many ophthalmology trials require long-term follow-up.
- Costs: High financial costs for conducting large-scale studies.
- Outcome Measures: Establishing reliable and consistent outcome measures for visual improvement.
- Regulatory Hurdles: Navigating complex regulatory requirements for new treatments.

ETHICAL CONSIDERATIONS FOR CLINICAL TRIALS

Study Design:

Informed consent is a legal and ethical requirement.

Privacy and confidentiality of participant information.

Participant safety is a top priority.

Trials must adhere to ethical guidelines and regulations.

REGULATORY/IRB CONSIDERATIONS FOR CLINICAL TRIALS

- Overview of the FDA's role in approving new ophthalmic treatments.
- Informed Consent: Ensuring participants understand the risks and benefits.
- Ethical Guidelines: Importance of participant safety, privacy, and fair recruitment practices.
- Data Integrity: Ensuring accuracy and transparency in trial results

THE FUTURE OF CLINICAL TRIALS

- **International Collaborations:** Joint trials between institutions and countries for diverse patient populations.
- **Funding Sources:** Government agencies, private pharmaceutical companies, and non-profit organizations funding ophthalmology research.
- **Multi-Center Trials:** Large-scale studies across various locations to increase sample size and generalizability of results.
- **Precision Medicine:** Trials focused on personalized treatment approaches for eye diseases

ENDOINTS IN OPHTHALMOLOGY

- Dry Eye Disease: Symptom (questionnaires) and Sign (Schirmer's, corneal staining) at P<5%
- Wet AMD and PDR: BCVA change > 2 lines (ETDRS)
- NPDR: 2-step change in DRSS score
- Geographic atrophy: FAF growth area / Ellipsoid zone
- Glaucoma: visual field progression*