Altasciences' Proactive Drug Development Solution

Large Molecules

ALTASCIENCES

Altasciences' Proactive Drug Development Solution—Large Molecules

The process of large molecule drug development, from lead molecule identification to approval, can be long and complicated. Altasciences is here to help streamline the process and accelerate you through it—from discovery to preclinical, clinical, and beyond.

Altasciences' extensive variety of services are outlined in the table below and discussed in more detail in the sections that follow.

	DISCOVERY	PRECLINICAL IND/CTA-Enabling	CLINICAL Phase I	CLINICAL Phase II	CLINICAL Phase III	BEYOND Phase IV/ Commercialization
PROGRAM MANAGEMENT		Dedicated Cross-Functional Program Manager				
REGULATORY SUPPORT	Gap Analysis/"You Are Here" Report; Pre-IND Meeting; Design and Execution of Effective Regulatory Strategy	IND/CTA Preparation and Submission and IND Meeting		NDA/BLA Preparation and Submission		
		Preparation and Maintenance of Investigator's Brochure (IB)				
SCIENTIFIC LEADERSHIP	Design and Execution of Effective Drug Development Strategy					
		Post-submission Regulatory Request Management				
SAFETY ASSESSMENT		PK/PD				
		Pre-IND Toxicology Study Packages				
		Phase I Dosage Support				
		First-in-Human (FIH) Risk Assessment				
CLINICAL PHARMACOLOGY			FIH Studies			
				POC Studies		
				Customized Studies—NDA-/BLA-Enabling		
BIOANALYTICAL SERVICES/ BIOMARKERS	Discovery and Exploratory Samples	GLP and Non-GLP	Regulated and Exploratory GxP Clinic Sample Analysis			
RESEARCH SERVICES	CRO Services, Including Organizational, Scientific, and Trial Services					

Program Management

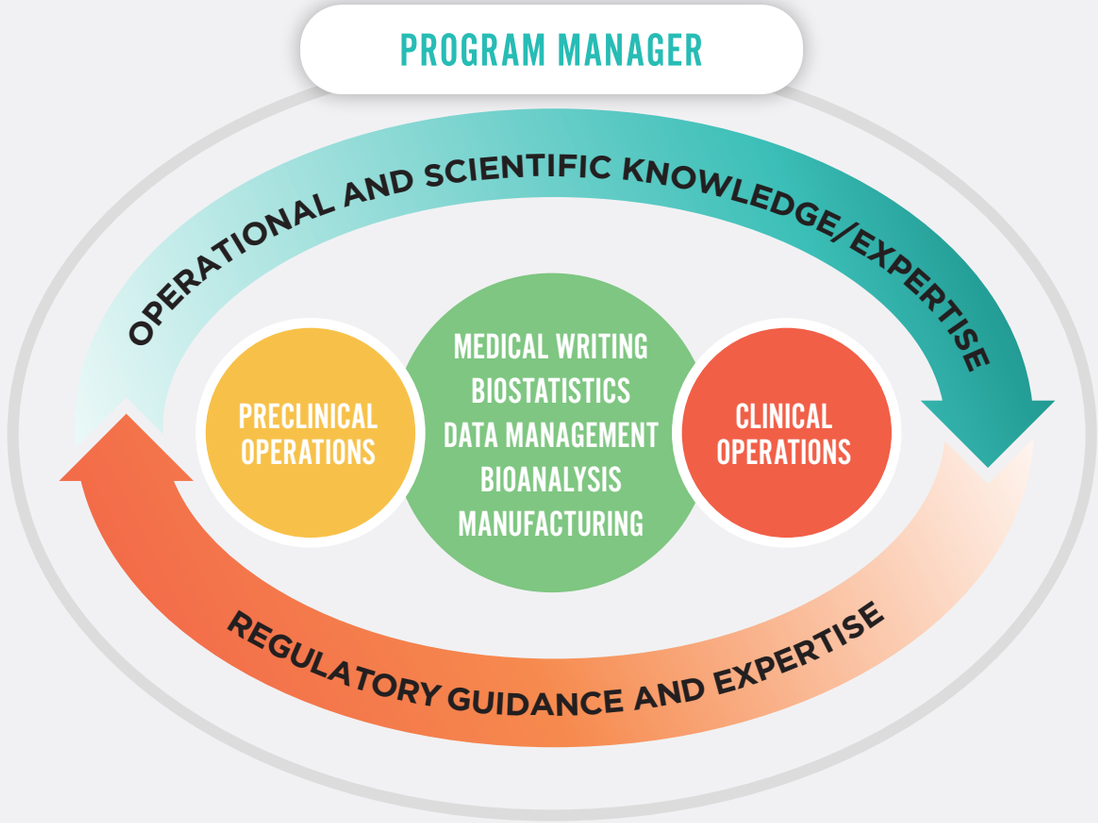
With Altasciences, your entire program is managed by one organization and overseen by a **single, cross-functional program manager**, dedicated to your studies.

Our team seamlessly advances your molecule from preclinical testing to first-in-human clinical trials, and beyond, with a tailored, proactive approach that unites bioanalytical services, preclinical safety evaluation, and clinical testing to proof of concept (POC).

One partner guiding your drug development means that some activities can occur in parallel, rather than sequentially, saving you time and costs.

Your dedicated, cross-functional program manager:

- **Provides** you with a centralized point of contact to improve speed and efficiency.
- **Manages** your study timelines proactively.
- **Leverages** our team of experts to review your emerging data and support your needs.
- **Responds** to your program challenges with solutions, in real time.
- **Shares** all your information across departments and sites proactively, so you only have to Tell Us Once™.



Regulatory Support and Scientific Leadership

Altasciences helps you navigate the complex regulatory environment by preparing study designs that best accommodate your large molecule program specifications and goals, while ensuring compliance with regulatory agencies internationally. Our team works in close collaboration with you to define your program needs, prepare your Investigator's Brochure, and facilitate a successful transition between the preclinical and clinical stages of development.

	DISCOVERY	PRECLINICAL IND/CTA-Enabling	CLINICAL Phase I	CLINICAL Phase II	CLINICAL Phase III	BEYOND Phase IV/ Commercialization
REGULATORY SUPPORT/ SCIENTIFIC LEADERSHIP		Pre-IND Meeting Request/Package				
		IND/CTA Preparation and Submission				
	Gap Analysis/"You Are Here" Report				NDA/BLA Preparation and Submission	
	Design and Execution of Effective Regulatory Strategy	Preparation of Investigator's Brochure				
		Investigator's Brochure Maintenance				
	CMC					
		Proof-of-Concept (POC) Support				
		Post-submission Regulatory Request Management				

High-Level Checklist: International Regulatory Documents and Meetings

Large Molecule Program Support

- Design and execution of effective nonclinical and clinical regulatory strategy
- Identification of program gaps, risks, and potential risk mitigation
- Toxicology consulting and strategic advice
- Investigator's Brochure preparation and/or review

IND only (FDA)

- Communication with FDA on your behalf
- Pre-IND gap analysis
- Pre-IND meeting request
- Pre-IND briefing package preparation and FDA meeting support
- IND preparation and submission

CTA only (Health Canada)

- Pre-CTA gap analysis
- Pre-CTA package preparation and Health Canada meeting support
- CTA preparation, submission, and maintenance
- BLA preparation and submission
- Post-submission regulatory request management/independent review
- Annual reports, safety reports, and amendments (CTA-A, CTA-N)
- Briefing book preparation and/or review
- End-of-phase 2a (EOP2A) meeting representation

International Guidelines Experience

Health Canada	Canada
Food and Drug Administration (FDA)	United States
European Medicines Agency (EMA)	European Union
Medicines and Healthcare products Regulatory Agency (MHRA)	UK
Therapeutic Goods Administration (TGA)	Australia
Brazilian Health Regulatory Agency (ANVISA)	Brazil
Pharmaceuticals and Medical Devices Agency (PMDA)	Japan

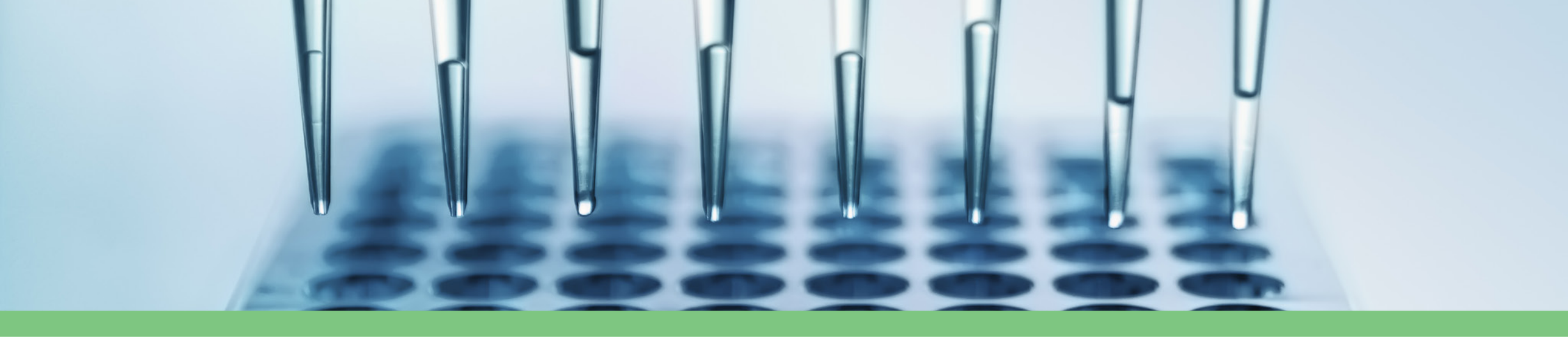
Safety Assessment

Altasciences has a comprehensive offering of *in vivo* GLP and non-GLP preclinical evaluation studies in both nonhuman primates and other species as appropriate, to thoroughly assess the safety of large molecules. We have dedicated and diversified cynomolgus monkey supply agreements in place to allow for faster start-up, and a continuously maintained and backfilled population of hundreds of naïve NHPs at our preclinical facilities.

Our solution offering includes IND/CTA-, NDA-, and BLA-enabling toxicology, safety pharmacology, and laboratory services that meet global regulatory requirements.

	DISCOVERY	PRECLINICAL IND/CTA-Enabling	CLINICAL Phase I	CLINICAL Phase II	CLINICAL Phase III	BEYOND Phase IV/ Commercialization
PK/PD	Primary/Secondary PD					
	Toxicology/Safety Pharmacology Screens					
		Pre-IND Study Packages				
PIVOTAL STUDIES		Rodent Single dose/DRF*	Pivotal Rodent GLP Toxicity with Safety Pharmacology Endpoints*	Subchronic/Chronic Rodent Toxicity*		
		Nonrodent Single Dose/DRF*	Pivotal Nonrodent GLP Toxicity with Safety Pharmacology Endpoints*	Subchronic/Chronic Nonrodent Toxicity*		
OTHER SERVICES		Laboratory Sciences				
		Standalone Safety Pharmacology**				

*As appropriate
** When safety pharmacology is required but cannot be added to the pivotal toxicity study



Safety Assessment Expertise

Altasciences' over 500 team members conduct more than 700 large molecule safety studies each year in 585,000 square feet of purpose-built facilities. Our state-of-the-art laboratories are BSL-2 certified, AAALAC and USDA accredited, and OLAW assured. Altasciences performs safety assessment studies of six-months' duration and longer (if required), in line with the ICH S6 guidance from single-dose acute to chronic studies, including dosing rodents and non-rodents.

Investigational Products

- Monoclonal antibodies
- Vaccines
- Proteins and peptides
- Antibodies
- Cell and gene therapy
- Oligonucleotides
- mRNA/siRNA
- Antibody Drug Conjugates

- GLP-compliant analytical support is available, including analytical and bioanalytical method development and validation, and assessment of a compounds' potential immunogenic or immunotoxic effects.

Routes of Administration

- Intravenous bolus
- Subcutaneous
- Intrathecal
- Intrarticular
- Ocular

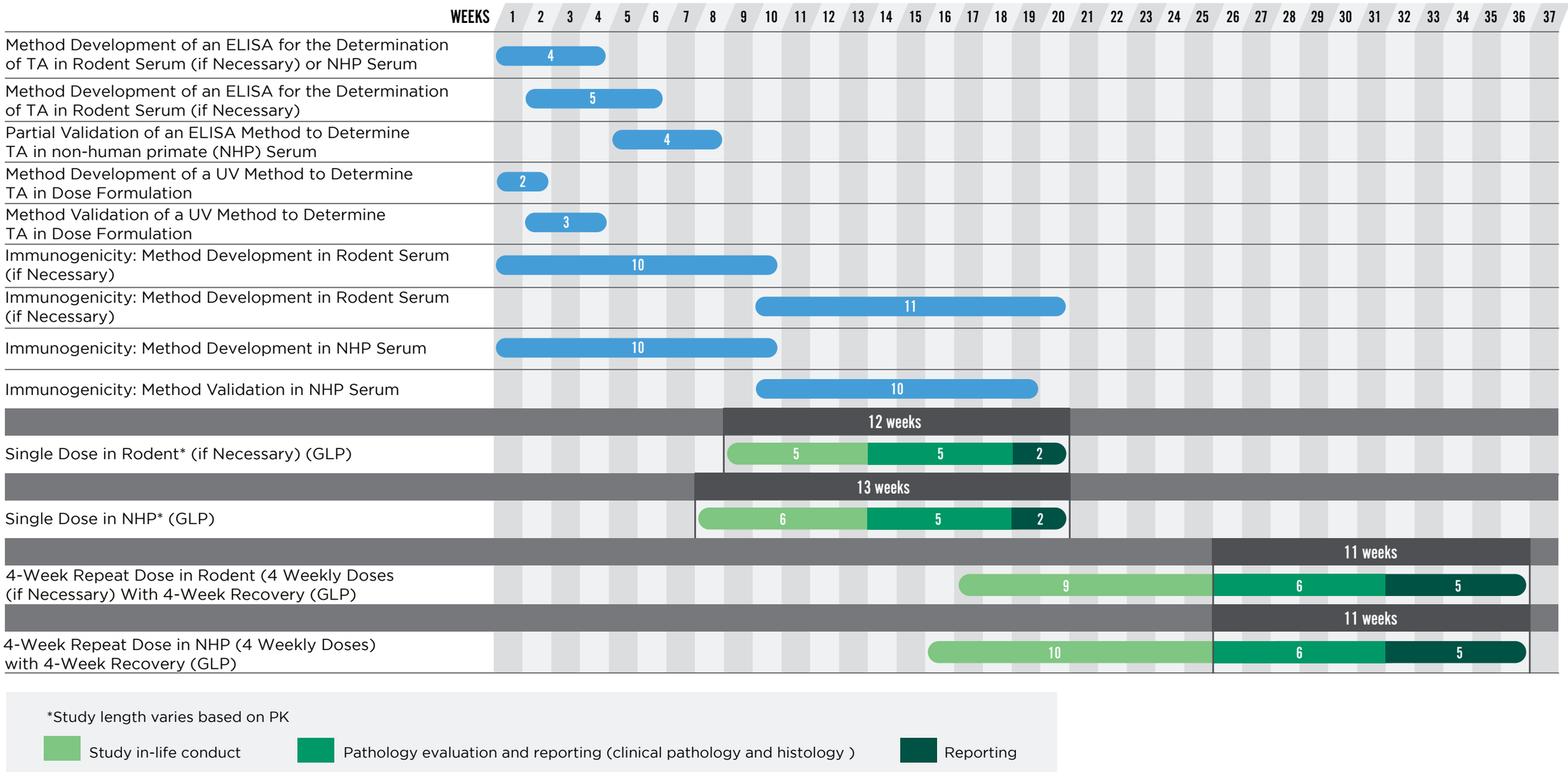
	Large Molecule
Species selection	• Pharmacology as a primary factor • May be only one species
Dose selection	Based on pharmacology or maximum feasible dose
Pivotal toxicology	One species — up to six months in duration
Safety pharmacology	• Part/all may be in toxicology studies • May also be standalone
Genetic toxicology	May not be required

Study designs may be enhanced with pharmacodynamic and immunogenicity analyses, local tolerance evaluation (Draize measurement), and immunomodulating assessment via KLH challenge (TDAR). Additional investigations include TCR/immunohistochemistry, flow cytometry, biodistribution, and tissue biopsies.

Accelerate Your Program

We work in close collaboration with you to accelerate your timeline. We can complete your large molecules program in approximately six months by using the program management approach proposed in the chart below for the *in vivo* portion of the IND/CTA program. This chart represents only one proposed approach. Each program is different, and will be assessed to address its unique requirements. Our unique preclinical, clinical, and bioanalytical platform enables you to work with a single, integrated partner to develop large molecules through to human proof of concept, resulting in shorter timelines and reduced costs.

To learn more about our approach, consult Issue 11 of ***The Altascientist, "Navigating the IND Submission Process."***



Commitment to Animal Welfare

The unique position of the Chief Animal Welfare Officer oversees Altasciences' commitment to exemplary animal care and welfare practices. Our staff members are specifically selected for their compassion toward animals, and are fully trained to the highest standards of laboratory animal care. We are focused on environmental enrichment, and understand the importance of compassion, sensitivity, and adherence to regulatory guidelines.

Our methodologies, procedures, and equipment are refined to decrease stress on the animals, improve workflows for technicians, and ensure the success of your study. As part of our **C.A.R.E. program**, we are committed to the 3Rs (replacement, reduction, and refinement).

C.A.R.E.

- A contract signed by every employee to iterate their commitment to prioritizing the humane care of animals used in research

Animal Welfare Council

- Made up of veterinarians, scientists, and members from the community

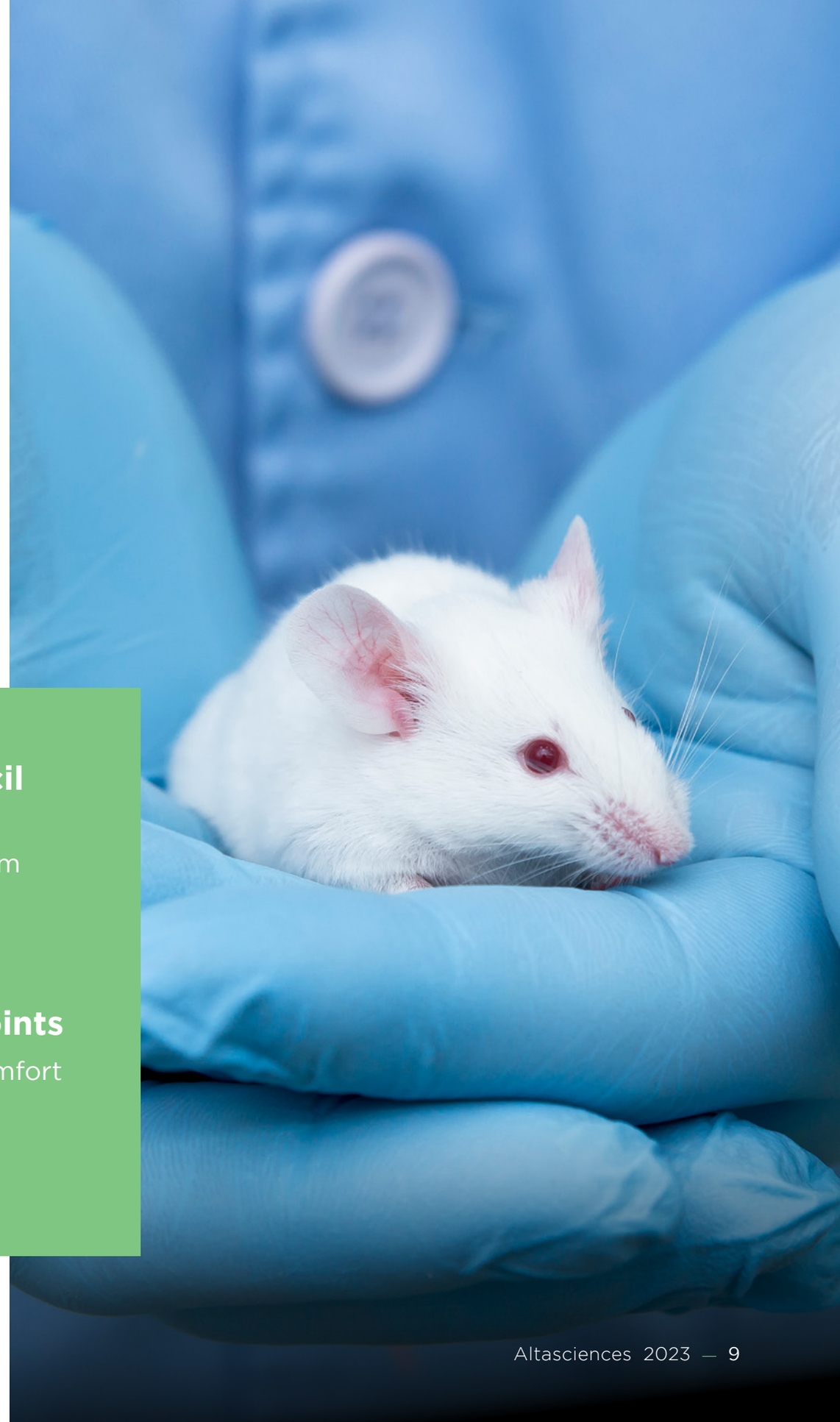
Veterinarian Committee

- For decision-making in difficult euthanasia situations

Use of Humane Endpoints

- To minimize pain and discomfort

Feel the love



Clinical Pharmacology

Altasciences' team designs, conducts, and reports on large molecules clinical pharmacology studies required for regulatory submissions across a wide range of therapeutic areas. We use a centralized medical/operation triage system to review all protocols and choose the optimal path forward for your study. Our purpose-built clinical pharmacology units house over 500 beds, and our seamless processes deliver safety and quality combined with speed and ease, with strong focus and significant expertise in large molecule drug development regulations, processes, and procedures.

Our integrated approach allows us to efficiently leverage preclinical data to design your clinical trials.

	DISCOVERY	PRECLINICAL IND/CTA-Enabling	CLINICAL Phase I	CLINICAL Phase II	CLINICAL Phase III	BEYOND Phase IV/ Commercialization
FIH/POC STUDIES			First in Human (FIH)			
			Proof of Concept (POC)			

THE SPECIALIZED ASSESSMENTS BELOW ARE NOT REQUIRED FOR BIOLOGIC DRUG DEVELOPMENT, BUT MAY BE RELEVANT DEPENDING ON THE DRUG MECHANISM OF ACTION/INDICATION.

CUSTOMIZED STUDIES—NDA-/BLA-ENABLING					Human Abuse Potential (HAP)	
					Driving Simulation	
			Bioavailability/Bioequivalence			
			Formulation/Route Bridging			
			Drug-Drug/Alcohol Interactions			
			PK Special Populations			
			QT Assessment			
				Renal/Hepatic Impaired		
			Imaging			
			Ethnobridging			

Clinical Pharmacology Expertise

First in Human, Proof of Concept, and Clinical Pharmacology

We have expertise in large molecule dosing and administration procedures, including stringent safety protocols. Participants are seen daily by a Principal Investigator, and monitored on a constant basis for serious adverse events (AEs).

- Scientific and regulatory consulting
- Dedicated program manager
- Cross-functional team
- Large molecules quantitation by mass spectrometry and ligand binding assays
  - Biomarkers
  - Flow cytometry
  - Cell-based assays
  - ELISpot
  - Immunogenicity assays
- Rapid turnaround of PK/PD analysis between cohorts
- Rapid participant/patient recruitment with retention rate of over 95%
- Medical monitoring
- Clinical monitoring
- USP 797 research pharmacies compliant to FDA
- Harmonized standard operating procedures
- Electronic source data capture

Areas of Expertise

Altasciences' integrated large molecule drug development solutions include key study types for regulatory submissions, as well as many specialized assessments depending on the particulars of your program.

- First in human (including SAD/MAD) and proof of concept
  - Altasciences' integrated large molecule drug development solutions include key study types for regulatory submissions, as well as many specialized assessments depending on the particulars of your program.
  - More than 400 FIH trials conducted
  - Extensive experience with injectables, complex sterile compounding, monoclonal antibodies, and immunology
- Bioavailability/bioequivalence
  - Study design database of over 1,200 products/combinations
- Drug-drug/alcohol interactions
  - Hundreds of studies conducted, including cocktail and single challenge
- PK in special and patient populations
  - Testing of different BMIs, sexes, genotypes, and ages
  - Testing in targeted patient types and patients of concern
- QT assessment
  - Can be done during FIH studies or post-Phase II as dedicated thorough QT (TQT)
  - Over 50 studies conducted
  - Clario-certified
- Renal/hepatic impaired
  - Over 10 studies performed in partnership with leading external sites
- Imaging
  - Over 20 studies performed with nearby partners
  - X-ray, CT scan, MRI, ultrasound, DEXA, endoscopy, and colonoscopy
- Ethnobridging
  - Reduction of drug development timelines by streamlining process of meeting international regulatory requirements
  - Over 200 ethnobridging studies since 2004
  - Over 9,000 Asian participants in our database
- CNS Center of Excellence
  - Human abuse potential (HAP), abuse-deterrent formulation (ADF), and substance abuse
    - Over 50 studies conducted since 2008
  - Driving simulation
    - Over 15 pivotal studies
    - More than 13,000 simulated drives

Bioanalytical Services

We offer a broad range of of large molecule bioanalytical services from discovery to preclinical to Phase IV, conducted in state-of-the-art, purpose-built laboratories at our locations in the U.S. and Canada, with designated containment Level 2 areas for work with Risk Group 2 pathogens. Staffed by highly skilled analysts, with shifts running 24/7 (as needed), we can process over 60,000 study samples per month. Bioanalytical services are available as standalone solutions, or as part of an end-to-end development package.

Capabilities at a Glance

- Over 25 years of experience with large molecules
- Ligand binding assay (LBA) equipment, including BD Fortessa flow cytometer, CTL ImmunoSpot S6 Analyzer (ELISpot), and MSD Sector Imager S600
- Hybrid LC-MS/MS capabilities for large molecules
- Approximately 450 validated methods developed for large molecule assays
- Over 25 research and development scientists
- Over 300 highly skilled bioanalytical experts
  - Over 30 liquid mass spectrometers, including SCIEX 6500 and Q Exactive
- Assigned bioanalytical Principal Investigator
- Microsampling expertise with a variety of collection devices (liquid and dry matrices) as and if appropriate for large molecule programs
- Qualified vendors to facilitate synthesis of stable label internal standards
- Wide array of biological matrices in both humans and animal species:
  - Serum
  - Plasma
  - Blood
  - Urine
  - Feces
  - Animal tissues
  - Cerebrospinal fluid
  - Human tissue biopsies
  - Tears
  - Saliva
  - Vitreous humor

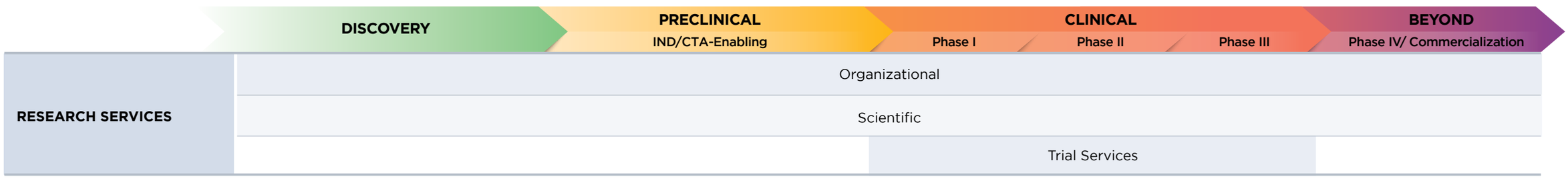
	DISCOVERY	PRECLINICAL IND/CTA-Enabling	CLINICAL Phase I	CLINICAL Phase II	CLINICAL Phase III	BEYOND Phase IV/ Commercialization
METHOD DEVELOPMENT AND VALIDATION	Method Development					
		Validation (All Types: Cross-Validation, Partial Validation, Fit-for-Purpose)				
SAMPLE ANALYSIS		GLP and Non-GLP				
			Regulated and Exploratory GxP Clinic Sample Analysis			

Research Support Services

Altasciences offers a wide variety of complementary CRO support services for each stage of your large molecule drug development program. These are available as standalone offerings or as part of an integrated drug development program, all customizable to your specific request.

Complementary CRO Support Services

- Organizational:
  - Full-time equivalent agreement (FTE) capabilities
  - Due diligence assessment
  - Post-acquisition integration
  - Vendor/subcontractor qualification and management
- Scientific:
  - Strategic scientific publication guidance and development
  - Regulatory science
  - Clinical protocol development
  - Clinical program design and strategy
- Trial services:
  - Project/program management
  - Biostatistics
  - CDISC/SEND
  - Data management
  - Clinical monitoring
  - Site feasibility and qualification
  - Clinical sample management
  - PK/PD
  - Preparation of clinical study reports



Proactive Drug Development Solution

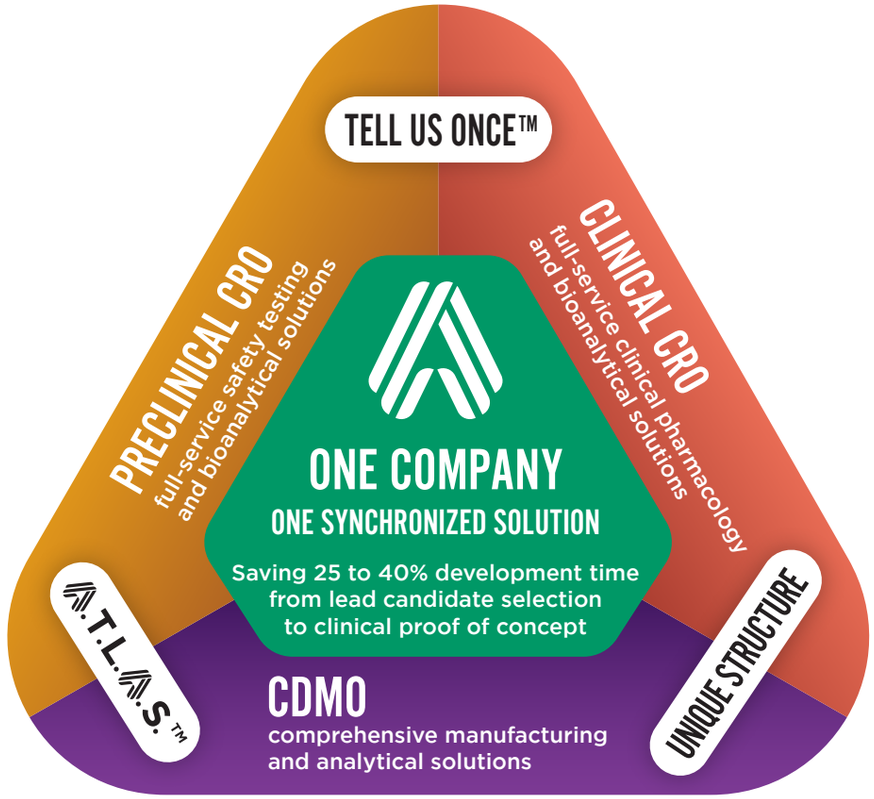
Altasciences accelerates decision-making by offering expert guidance and synchronized early-phase services to reduce timelines by up to 40%. Our integrated solution drives success at each milestone with a tailored program that unites bioanalytical services, preclinical safety evaluation, formulation development, clinic-ready manufacturing, on-demand clinical pharmacy, and clinical testing to proof of concept, all within one organization. With drug development managed by one partner, activities can occur in parallel, rather than sequentially. Altasciences can support your entire drug development programs end to end, or you can partner with us for just one study—we offer you complete flexibility using the same approach.

Learn more about our integrated solution.

Proactive Drug Development is based on three core pillars.

- **How we communicate**—Tell Us Once™
- **How we bring a project to life**—A.T.L.A.S.
- **How we organize ourselves**—A unique organizational structure

CEO Explains Proactive Drug Development



How We Communicate

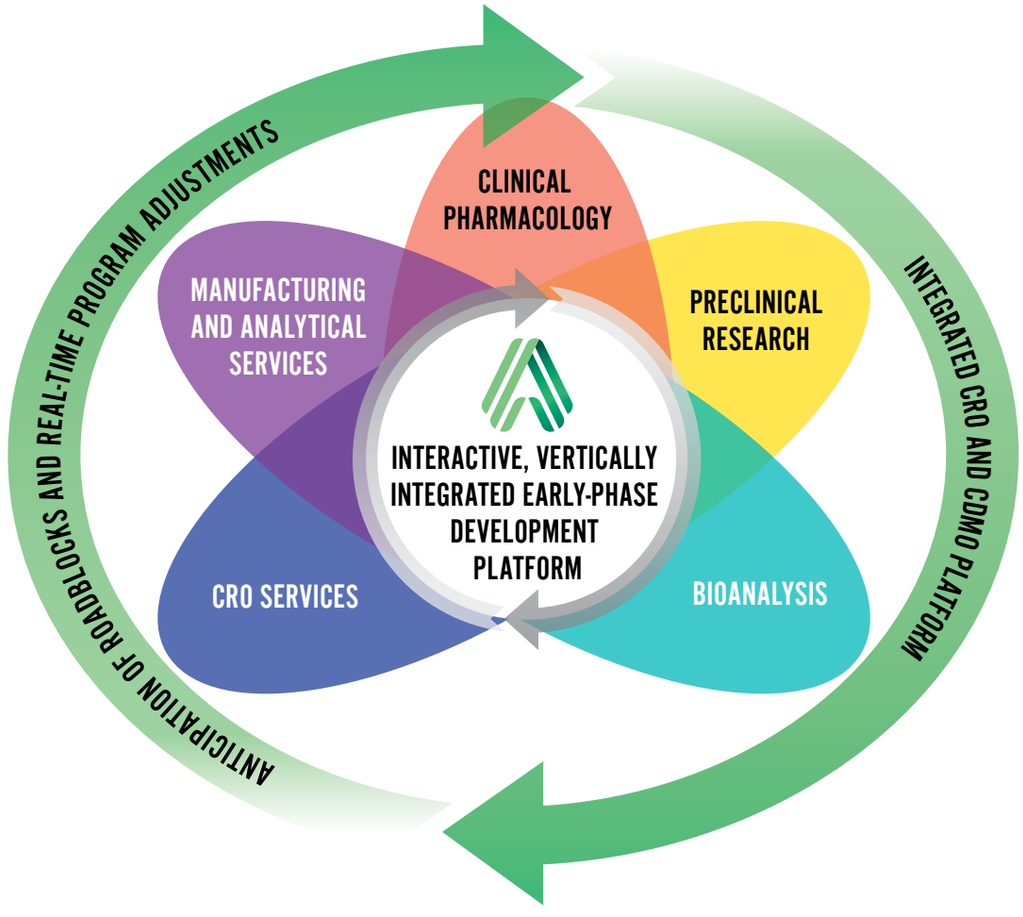
Ask Albert, Altasciences' proprietary client database, is the backbone of our integration and information-sharing capability, allowing us to conceptualize your entire program and adapt to any new information as your small molecule advances through the development process. So, you only have to **Tell Us Once™**.

Discover our Tell Us Once™ Commitment

How We Bring a Project to Life

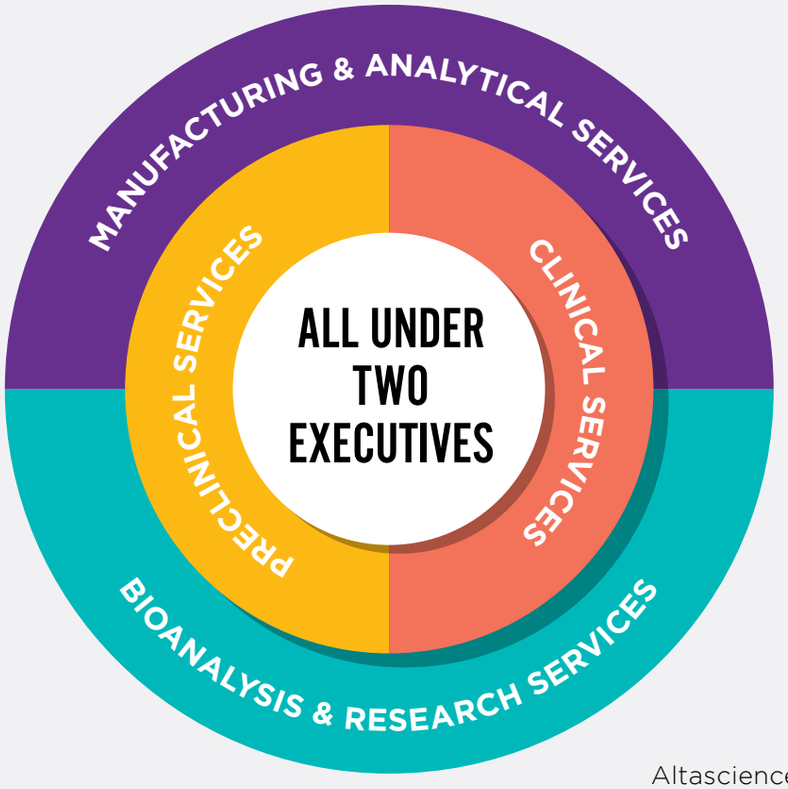
A.T.L.A.S.™ is our interactive, vertically integrated approach to managing study conduct and our workflow. We provide strategic scientific guidance to your program, and use our program management and proprietary scheduling system to centrally coordinate all activities between services and phases of development.

Learn more



How We Organize Ourselves

Our **unique organizational structure** begins with two executives leading all scientific and operational teams, integrating study phases and departments to eliminate silos, ensure communication, and move your small molecule through development quickly and safely.



ALTASCIENCES

Altasciences is a forward-thinking, drug development solution company offering pharmaceutical and biotechnology companies a proven, flexible approach to **preclinical** and **clinical pharmacology** studies, including **formulation, manufacturing, and analytical services**. For over 25 years, Altasciences has been partnering with sponsors to help support educated, faster, and more complete early drug development decisions. Altasciences' integrated, full-service solutions include **preclinical safety testing**, **clinical pharmacology and proof of concept**, **bioanalysis**, **program management**, **medical writing**, **biostatistics**, **clinical monitoring**, and **data management**, all customizable to specific sponsor requirements.

Altasciences helps sponsors get better drugs to the people who need them, faster.

CONTACT US

DISCOVER THE DIFFERENCE