

Development of a Model Precision Cancer Therapies Program in a Community Setting





An enduring partnership between Ochsner Health System and TGen on a phase I clinical trials program

Cancer in Louisiana is a significant problem, with both incidence and death rates from the disease far surpassing national averages.¹ In fact, the problem is so pervasive that the region between Baton Rouge and New Orleans through which the Mississippi River flows is commonly referred to as “Cancer Alley.” The etiology of the problem is multifactorial and includes environmental exposure, lifestyle issues, and hereditary predispositions.

Physicians and non-clinical leaders at Ochsner realized that progress in the fight against cancer can only be made through research and that patients in the region had very limited access to a full range of cancer clinical trials. Ochsner had been an early National Cancer Institute Community Oncology Research Program site, bringing cooperative group and late-phase pharmaceutical cancer trials to its patients for decades. But in order to access early phase clinical trials at a dedicated center, patients had to travel to either Houston or Birmingham—a five- to six-hour drive in both directions. This option was impossible for most and impractical for all patients in the area. As a result, the Ochsner Precision Cancer Therapies Program was born of great necessity.

We recognized early on that the many challenges and nuances of running early phase trials required a dedicated center. Early phase trials are different for several reasons, including:

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In Brief

Two years ago, Ochsner Health System, the leading healthcare provider in Louisiana, made a bold move in opening the region’s only early phase cancer clinical trials program. From the beginning, it was clear that identifying a partner with complementary experience and expertise was critical to accelerating the program’s development. After much research and consideration, Ochsner partnered with the Translational Genomics Research Institute (TGen) of Phoenix, Ariz., a leading innovator in the field. The Ochsner Precision Cancer Therapies Program has rapidly grown to be an outstanding success.



View of the Mississippi River from the fifth-floor infusion suite lobby of the Benson Cancer Center.



The infusion suite at the Benson Cancer Center has 42 infusion chairs.

- **Many unknowns.** Often the proper dose of a new drug has not been defined, nor have the toxicities
- **Intense monitoring.** Phase I trials require intense monitoring and heavy oversight from sponsors and the U.S. Food and Drug Administration
- **Demanding protocols.** Protocols are often very demanding for staff and patients, including:
 - Intense pharmacokinetic measurements (i.e., 15-minute lab draws)
 - Multiple required consults (i.e., weekly eye exams, frequent cardiology evaluations)
 - Intense imaging schedules
 - Triplicate electrocardiograms with every dose of drug for some trials
 - Time-intensive functions (i.e., near-daily follow-up for most, weekly visits for others)
 - An overwhelming amount of computer and/or paperwork
 - Extensive discussions to convince sponsors to bring their best new agents to our program.

Despite the challenges, we were motivated to bring the best possible clinical care to our patients, and we quickly identified the resources and infrastructure that would be required to sustain the Ochsner Precision Cancer Therapies Program. These included:

- Medical expertise
- Nursing expertise
- Regulatory affairs expertise
- Specimen processing expertise
- Experimental pharmacy (frequently audited)
- Dedicated physical facilities with space for monitors
- Administrative support
- Special equipment for specimen processing and labs
- Interventional radiology cooperation for specimen acquisition
- Budget and contracts
- Legal infrastructure that understands the limits of intellectual property
- Networks of contacts and industry partners.

Early Initiatives

When the Ochsner Precision Cancer Therapies Program was in its planning phases and early after its launch, we took several important steps to set a tone for success. First, we arranged regular steering committee meetings between Ochsner, TGen, and other stakeholders to guide oversight and strategy. We also set up regular pipeline meetings to discuss new leads for interesting studies, potential partnerships with scientists and pharmaceutical companies, and the progress of the studies during initiation. We made a concerted team effort to convince sponsors to bring new agents and new trials to us, and we undertook extensive staff training at every level.

One of the most important actions we took, which continues today, was to establish weekly Phase I rounds. During these meetings, every member of the team—including lab technicians,

data coordinators, pharmacists, nurses, supervisors, physicians, investigators, and the director—meet to discuss each study open and in the pipeline and every patient enrolled on an early phase study or potentially eligible for a study. We also review every upcoming site initiation visit and site qualification visit and make relevant general announcements. Every team member’s voice is heard and valued.

Early Organizational Structure and Site Description

As part of our efforts to establish an early phase cancer trials program, Ochsner Cancer Institute research staffing was organized into two distinct pathways: general oncology (core industry-sponsored and cooperative group studies) and Ochsner Precision Cancer Therapies Program (early phase studies, novel reagents, precision therapy trials). When we began our partnership with TGen, we were very fortunate to already have a robust, well-staffed clinical research program in general oncology. In year one of the Ochsner Precision Cancer Therapies Program initiative, we hired two nurses, a data coordinator, a regulatory coordinator, and a lab technician.

Marc Matrana, MD, a member of Ochsner’s Hematology-Oncology Department who had trained at MD Anderson Cancer Center, was recruited as medical director of the Ochsner Precision Cancer Therapies Program with 40 percent protected research time. He was joined by two other physicians—Drs. Laura Finn and Robert Ramirez (20 percent protected research time each)—and a nurse practitioner who also devoted 40 percent time to the Ochsner Precision Cancer Therapies Program and supported Dr. Matrana in the clinic. Key additional support—without which the program could not have been developed—was provided by the nurses, cancer registry coordinators, and other anatomic site-specific general oncology team members that provided guidance and expertise to the new Ochsner Precision Cancer Therapies Program staff. It would not have been possible to launch a successful early phase program of this magnitude without a prior established robust research program.

Due to space limitations in clinical areas, the workspace for Ochsner Precision Cancer Therapies Program research staff was centralized in a building adjacent to the Benson Cancer Center. The oncology clinics are within Benson Cancer Center, as is the infusion area and oncology clinical laboratory.

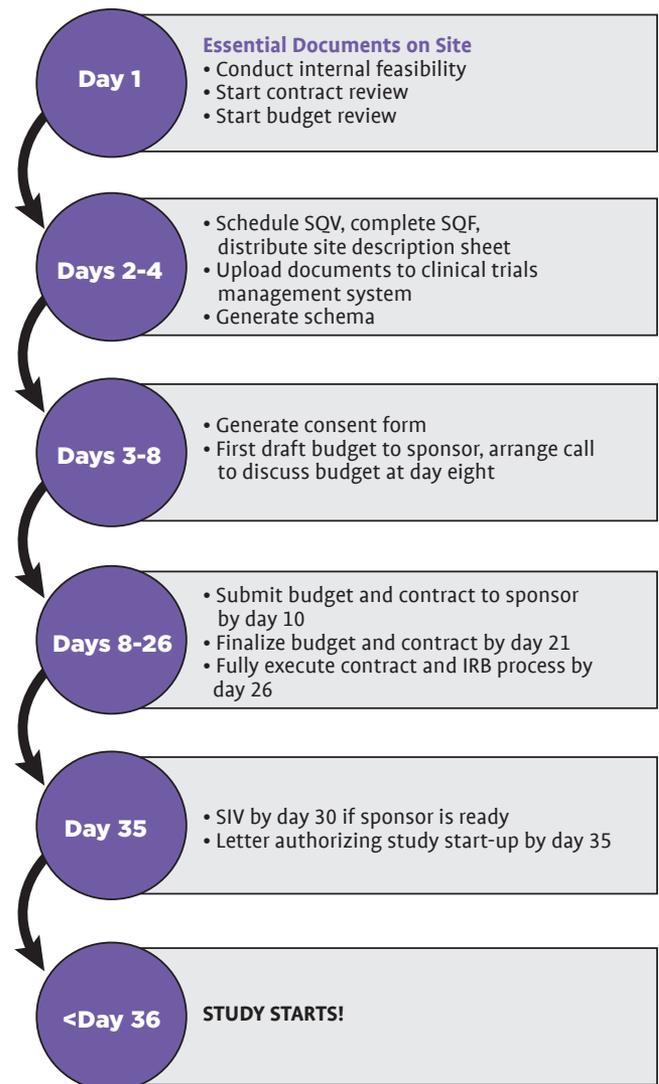
Process Optimization: The Budget and Contract Office

At the inception of the partnership, our TGen colleagues worked with us to review and optimize our processes. They reviewed our job descriptions, audited our prescreening logs, reviewed our study budgets, and evaluated our infusion center and investigational pharmacy, among other roles.

At that time, our centralized budget and contract office (which serves research across the organization) was typically completing contracts within 90 to 120 days. We worked with our partners and our internal office to devise a plan to reduce turnaround time to 36 days from the time that all essential documents are loaded

into our clinical trials management system to the time that the study launches (see Figure 1, below). We hired one additional staff member for the budget/contract office to selectively accelerate Ochsner Precision Cancer Therapies Program study activation without compromising turnaround time for non-Ochsner Precision Cancer Therapies Program studies.

Figure 1. Contract and Budget Time to Study Start-Up Working days



Typical time to study start-up for Ochsner Precision Cancer Therapies Program is less than 40 days from receipt of all sponsor materials. SQV = site qualification visit; SQF = sponsor feasibility; SIV = site initiation visit.



One of two private rooms at the Precision Cancer Therapies Program for administration of complex infusions.



The Precision Cancer Therapies Program laboratory, where patient blood and tissues are processed.



The Ochsner Precision Cancer Therapies Program office entrance area from the first floor of the Benson Cancer Center. These rooms were added in year two of the initiative.

Process Optimization: Site Description for Sponsors

The Ochsner Precision Cancer Therapies Program initiative led us to re-evaluate, revise, and refine our site description and presentation for sponsor site qualification visits. The current material is in a branded, glossy two-pocket folder and contains key program elements and practical materials, including:

- A map of Benson Cancer Center
- A map of the Ochsner campus
- General site specifications for the oncology clinic, chemotherapy infusion, electronic health record, and record retention
- Protocol training
- Institutional Review Board (IRB) statement of compliance
- Association for the Accreditation of Human Research Protection Programs accreditation certificate
- IRB roster
- IRB panel meeting dates and submission deadline dates
- Informed consent process
- Research education requirements for study staff
- IRB external serious adverse events reporting
- Research pharmacy
- Study drug destruction guidance
- Intravenous bag and administration information
- Chemotherapy infusion—pharmacy site blinding guidance
- Radiology specifications
- Laboratory send-out equipment
- College of American Pathologists accreditation and Clinical Laboratory Improvement Amendments certification.

The site description folder has been very popular with our sponsors and adds to the overall perception of an organized and professional clinical trials site.

Process Optimization: Sponsor Feasibility Form

Sponsors typically require that provider organizations like Ochsner complete information in a feasibility form that assures sponsors that we have the appropriate physicians, patient population, and resources to partner effectively on a given study protocol. Within a few months of launch, it became apparent that the Ochsner Precision Cancer Therapies Program (and Ochsner Cancer Institute as a whole) also needed an internal form to ensure that trials we were considering were reasonable for Ochsner and that the sponsoring partners were reliable and of high caliber. Some of the specific problems that led to the conclusion that we should better evaluate our partners and trials included the following:

- Several studies closed at the national level immediately after we opened them at Ochsner—launching new studies requires significant time and resource input (budget and contract office, research office, regulatory coordinator, physician, and lead nurse time).
- Sponsor medical monitors were not always readily available—we found them to be difficult to track and slow to respond, and contact information was not always correct.
- Sponsor research monitors were not always optimally informed regarding studies.

- Concerns were expressed by our pathology department and laboratory—they required a more substantial advance notification to prepare for trials in which their participation was required.

In response to these challenges, we generated a feasibility form that must be completed by the industry sponsor for our consideration before we agree to accept a study. The questions on the form include, but are not limited to, the following:

- Expected enrollment for trial (all phases/cohorts)
- Current number of subjects enrolled (all phases/cohorts)
- Rate of enrollment
- Study start date
- Date of first subject enrolled
- Proposed “closed to enrollment” date
- Total number of sites planned
- Total number of sites currently open (nationally or internationally)
- Number of additional sites projected to open
- Is the medical monitor located in the United States? If not, where is it located?
- What central IRB is used?
- Are computed tomography/positron emission tomography/magnetic resonance imaging/labs conducted within standard of care?
- Are there any special requirements for scans, labs, etc.?
- Are there any pending amendments to the IRB or protocol?
- When are the new documents expected?
- Are there any special pathology requirements (fresh tissue, slides, etc.)?
- Is an ophthalmologist required?

Completion of this form by our sponsors before the site qualification visit has improved our selection process and greatly reduced frustrations caused by decisions made with inadequate information.

Process Optimization: Internal Feasibility and Trial Selection

It is challenging to enroll patients into cancer clinical trials. Enrollment, even to those trials that would seem on the surface to be good study matches based on disease status and patient population, may be difficult due to the precise and detailed intricacies of the enrollment criteria. The challenge is greater yet for precision studies in which genetic criteria are restricted. Therefore, a robust internal feasibility assessment is critical to reduce non-enrolling trials, which are costly mistakes for both the provider organization and the sponsor.

For several years, Ochsner General Oncology held protocol review and monitoring committee meetings that reviewed all incoming trial opportunities for pertinence to the program. The cover sheet included questions related to disease relevance, patient population, sponsor, research category, and therapeutic intent. The review process functioned well for about two years, after which the meetings lost momentum—in part because the com-

mittee members had competing priorities and in part because the disease-specific expertise required in cancer, given its many disease subspecialties, was difficult to adequately capture in a static review team. An alternative review process was clearly needed for both the Ochsner Precision Cancer Therapies Program and general oncology areas.

Consequently, a group of physicians, administrators, and research leaders worked together to create a virtual protocol review committee in which study protocols are forwarded with a circulation document to key stakeholders. The recommendation from each party is recorded on the form (Figure 2, page 28), and the time frame for the circulation is five working days. If, at the end of five days, there is concordance from stakeholders, the regulatory coordinator will inform the primary investigator (PI) and move to next steps with the sponsor. If there is discordance, the medical director provides guidance. This new process has led us to reduce the number of trials that we commit to initiating and focus on trials that better serve our patients.

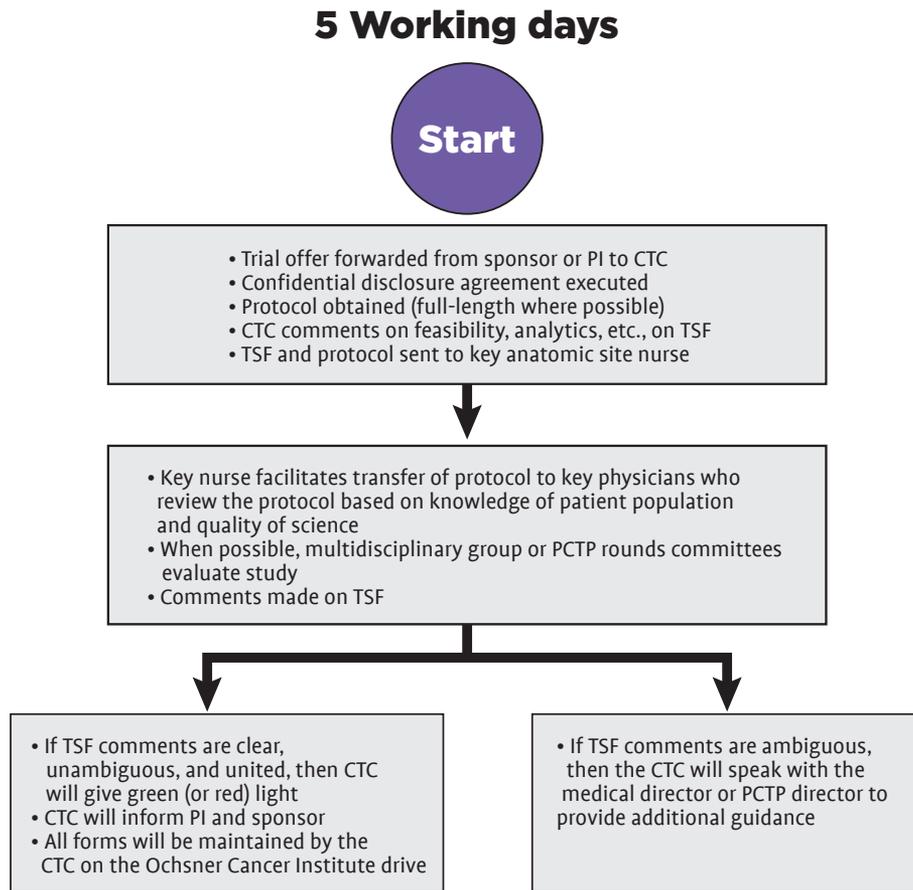
Year One: Trials and Enrollment

Though the official launch of the Ochsner Precision Cancer Therapies Program occurred in April 2017, our internal program clock started on Jan. 1, 2017. We fell slightly short of our goal of 48 patient accruals in early phase novel studies, enrolling only 42 in year one (Figures 3a and 3b, page 29). However, we opened 28 Precision Cancer Therapies Program trials in 2017, exceeding our goal of 25. These trials covered many different subspecialties, including hematologic malignancies, solid tumors with specific defined mutations, squamous cell carcinoma of the lung, metastatic pancreatic cancer, renal cell carcinoma, ovarian and fallopian cancers, melanoma, and breast cancers, among many others. Our average patient enrollment over the first year was 3.5 patients per month, ranging from 2 to 8 patients per month (Figure 3b, page 29). A total of 38,427 pre-screening events were required to enroll 42 patients in these highly specialized trials (0.1 percent). Note that, within a given pre-screening session, individual patients were pre-screened for many studies.

Year One: Philanthropy

Obtaining philanthropic support was an important goal to offset the high costs of starting and maintaining the Ochsner Precision Cancer Therapies Program. An inaugural \$1 million gift from former Entergy chief executive officer and Ochsner Precision Cancer Therapies Program patient Wayne Leonard set the tone for further gifts. In order to recognize Leonard and his wife, Jackie, our Ochsner Precision Cancer Therapies Program clinic was named in their honor. A \$1 million gift from environmental attorneys Stuart Smith and Barry Cooper followed. This money was earmarked for an endowed professorship in experimental therapeutics to help support the Ochsner Precision Cancer Therapies Program medical director’s research time. An additional \$350,000 gift for experimental therapeutics research and 450 smaller gifts were received during the program’s first year. Days before his death, Wayne Leonard gave an additional \$250,000 to further support the initiative. A close working relationship

Figure 2. Trial Selection Process: Five Working Days



Trial selection process is five working days from protocol receipt to final decision regarding interest and suitability of study for the PCTP. Note: Budget may still be a barrier to trial launch. CTC = regulatory coordinator; PCTP = Precision Cancer Therapies Program; TSF = trial selection form.

between Ochsner Precision Cancer Therapies Program staff and our cancer center philanthropy officer was vital to successful fundraising.

Year One: Marketing and Outreach

Spreading the word to patients and providers that “new hope” had arrived in our region was crucial. We worked with our marketing, communications, and business development teams to execute detailed plans for outreach. These included physician presentations through field trips to satellite sites and outside practices in order to meet providers and introduce the Ochsner Precision Cancer Therapies Program. We engaged in speaking tours through various forums and venues across the region. We conducted television and radio interviews, launched ads in various publications, created online videos, engaged social media outlets, and published articles about the Ochsner Precision Cancer Therapies Program. We also hosted a full-day off-site CME event around issues of precision cancer medicine and early phase trials

that was attended by about 85 providers, nurses, and other stakeholders from the region. We further created a website, dedicated email address, and a toll-free hotline to centralize contact from interested individuals. Our scheduler/concierge continually works with the research nurses to follow up every inquiry.

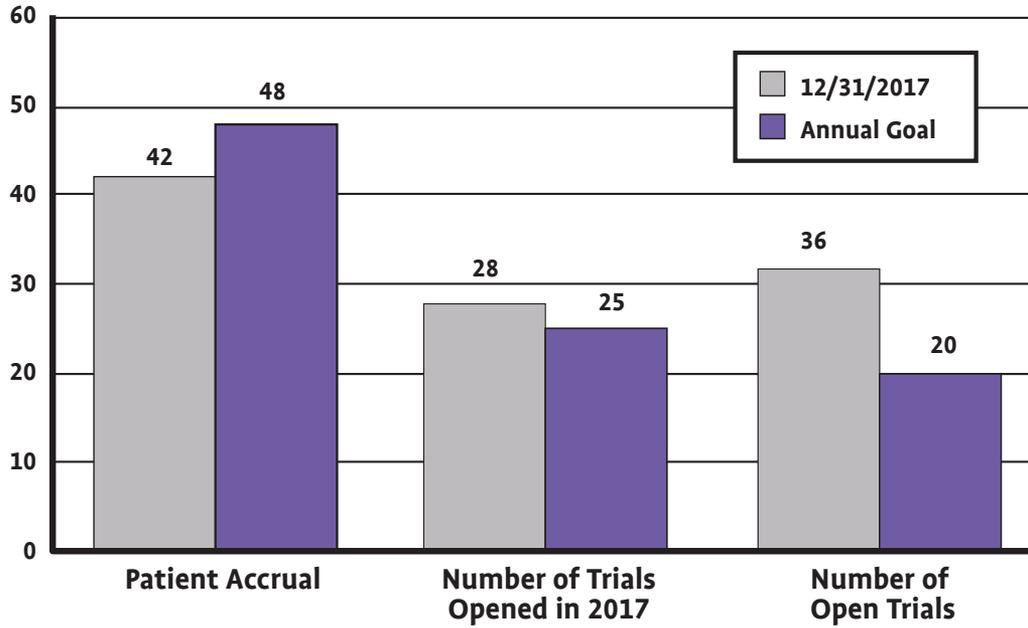
Year Two: Programmatic Updates

In year two, Ochsner Precision Cancer Therapies Program offices were repurposed from existing space on the first floor of Benson Cancer Center, marking the first Ochsner Precision Cancer Therapies Program-dedicated space. The Ochsner Precision Cancer Therapies Program was also enhanced with the addition of new staff and sites. We added a third investigational pharmacist for research; additional pharmacy assistance was required to manage the increasing number of studies opened within the program.

Moreover, in year two, we began opening select Ochsner Precision Cancer Therapies Program studies at other Ochsner

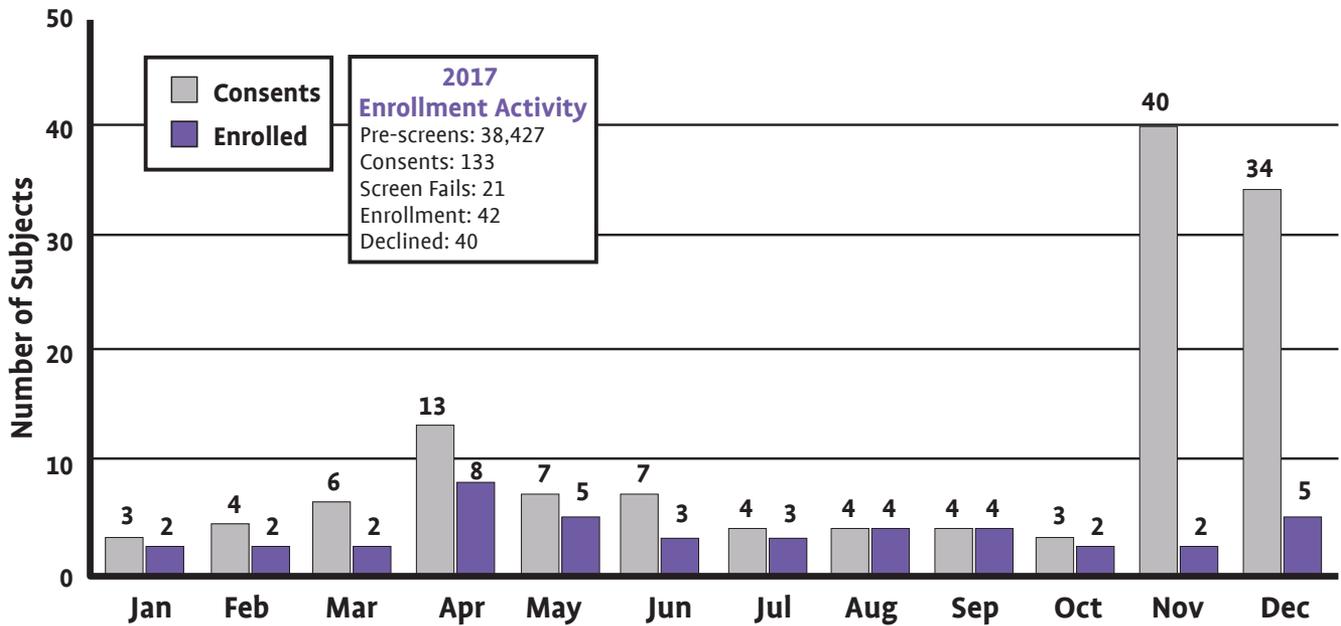
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Figure 3a. Precision Cancer Therapies Program Trials and Accruals vs. Annual Goals: Year One (2017)



“Open Trials” reflects some trials that were opened in Ochsner General Oncology and moved under the Ochsner Precision Cancer Therapies Program umbrella after program launch. “Trials Opened” refers only to those opened initially as Ochsner Precision Cancer Therapies Program studies.

Figure 3b. Monthly Patient Enrollment in Precision Cancer Therapies Program: Year One (2017)





Ochsner Precision Cancer Therapies Program reception area where guests and families are interviewed for early-phase study participation.



Ochsner Precision Cancer Therapies Program conference room, where patient cases are reviewed and future directions are determined.

(continued from page 28)

campuses, Kenner and Baton Rouge, requiring additional pharmacy assistance. The laboratory assistant was upgraded to a laboratory technician to better manage complex studies. Ochsner Precision Cancer Therapies Program Rounds was formalized in year two, and attendance substantially increased. Trial selection decision support tools were developed for key areas—including breast, gastrointestinal, genitourinary, gynecologic, hematologic, lung, and solid tumors—and updated and distributed to providers monthly.

Year Two: Trials, Enrollment, and Academics

Though we failed to meet our enrollment goal in year one of the initiative, we far exceeded our goal in year two (see Figures 4a and 4b, page 31). Our goal for 2018 was to enroll 60 patients

in Ochsner Precision Cancer Therapies Program studies; we actually enrolled 106 (76 percent positive variance). Our 2018 goal for new trials was lower than our 2017 goal, because our plan was to strategically open studies that both filled trial gaps and were optimized for our patient population. In fact, due to physician enthusiasm for the many early phase trial opportunities presented to our program, we opened 38 trials in 2018. In the second year of the program, therefore, our patients have had opportunities to participate in more than 60 novel trials across a wide range of cancer areas.

Our academic efforts also grew significantly in year two. Our physicians co-authored 11 abstracts and three full-length publications related to early phase novel therapies under investigation at Ochsner in 2018, compared to two abstracts in 2017. For each of these, Ochsner investigators participated as a full partner in these studies and made significant academic contributions.

Future Directions

As the Ochsner Precision Cancer Therapies Program grows and expands to new areas, our goals remain patient focused. We plan to:

- Greatly accelerate the development of new, more effective, less toxic, and more personalized therapies for cancer patients in the Gulf South and beyond.
- Expand precision medicine and routine free or low-cost next-generation sequencing across our network and region and expand to other medical disciplines as appropriate.
- Continue to build our world-class team and identify the best talent at every level, including recruiting new physician talent to meet the needs of our growing research patient population.
- Create new partnerships with scientists and industry to increase innovative breakthroughs and clinical trial opportunities for Ochsner patients.
- Identify additional philanthropic opportunities to further support our work and accelerate the growth of our program.

The Precision Cancer Therapies Program will continue to get the word out to patients and providers in the Gulf South region that “new hope” in the future of cancer care and research is here. 

Marc R. Matrana, MD, MS, FACP, is medical director, Ochsner Precision Cancer Therapies Program, and Julia L. Cook, PhD, is director, Institute for Clinical Research-Oncology, Ochsner Cancer Institute, New Orleans, La.

Reference

1. American Cancer Society. Cancer Statistics Center: Louisiana. Available online at: cancerstatisticscenter.cancer.org/#/state/Louisiana. Last accessed January 7, 2019.