SHIELDS
HEALTH SOLUTIONS

WHITE PAPER

# Advancements in Rare Disease Treatment and Management

## SHIELDS MONITORS ORPHAN DRUG PIPELINE, DEVELOPS CLINICAL PROGRAMS FOR RARE DISEASES

## KEY CONCEPTS

- While the incidence of any given rare disease is low, about 30 million people in the U.S. have been diagnosed with a disease defined as rare.
- Legislation providing incentives for developing rare disease therapies has been successful in increasing the number of orphan drugs.
- Recently, gene therapy has been an area of major growth in rare disease treatment.
- Integrated health system specialty pharmacy (HSSP) offers an ideal paradigm for helping patients and their families manage a rare disease diagnosis and adhere to treatment.
- Shields Health Solutions (Shields) partners with health systems to monitor the drug pipeline, build access to medications, and develop clinical programs.

## INTRODUCTION

The prospect of a rare disease diagnosis presents numerous challenges to patients and their families, beginning at the earliest stages of the patient journey. Likewise, rare diseases are a challenge for providers to accurately diagnose and treat throughout the patient's lifetime. Nevertheless, there have been many advancements in the diagnosis and treatment of rare diseases. Contributing factors include:

- financial incentives put in place by the Orphan Drug Act;
- scientific breakthroughs in genetics and precision medicine;
- streamlined and collaborative care by health systems;
- and integrated specialty pharmacy, where available.

Collaborations such as those between Shields, its health system partners, and manufacturers help to facilitate and optimize these advancements for better patient treatment and outcomes in an HSSP context.

## WHAT IS A RARE DISEASE?

A rare disease, according to the Orphan Drug Act of 1983 (and the Rare Disease Act of 2002), is one that affects fewer than 200,000 Americans.[1] Approximately 7,000 diseases currently meet this definition, including diseases such as hereditary angioedema (HAE), spinal muscular atrophy (SMA), duchenne muscular atrophy, sickle cell disease (SCD), and pulmonary arterial hypertension (PAH). While the number of people within each given rare disease is low, the number of individuals overall who are diagnosed with a rare disease is high—about 30 million, or one in every ten people in the U.S.[1]

A rare disease is a disease or condition that impacts less than 200,000 people in the U.S.

## SUPPORT FOR ORPHAN DRUG DEVELOPMENT

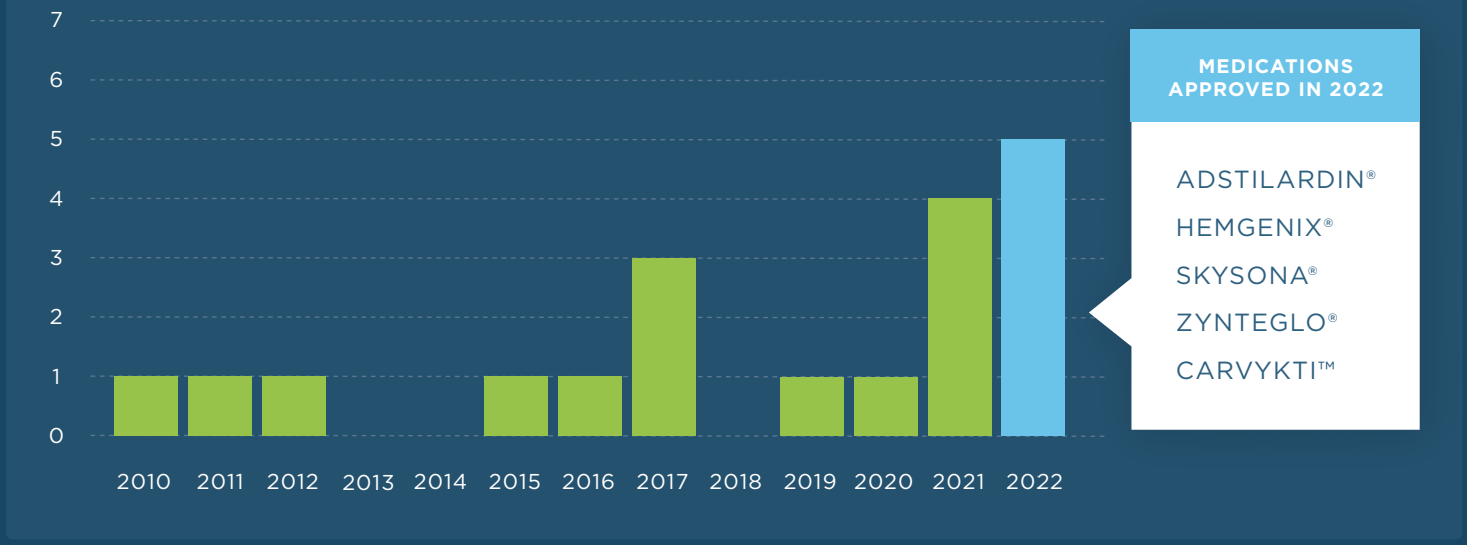
The Orphan Drug Act (ODA) was created to support the development of treatments for rare diseases. Prior to the passage of the ODA, treatments for rare diseases were not a focus for drug manufacturers because of the higher financial risk of investment into the research and treatment development for a small number of patients.

This legislation created much-needed financial incentives to motivate the development of lifesaving or life-changing treatments for rare diseases that affect comparatively small populations. Subsequently, the number of orphan status designations granted have increased dramatically over the last four decades.[2] The three largest categories of orphan drug designations are oncology, neurology, and infectious diseases.[2]

There has been remarkable progress not only with small molecule medications but also with gene and cell therapies,[2] which means more focus on personalized medicine. Personalized or precision medicine is a disease prevention and treatment method based on individual characteristics at the genetic level.[3]

Shields monitors the orphan drug pipeline on behalf of its health system partners and in conjunction with drug manufacturers. The year 2022 set a record for new rare disease gene therapy approvals.[4] The graph below outlines all FDA approved gene and cell therapy products over the years since 2010, and highlights approved drugs in 2022.[5]

### CELL AND GENE THERAPY APPROVALS




Source: Approved Cellular and Gene Therapy Products, FDA.gov


**Rare diseases that have no FDA-approved treatment.**

On the clinical side at Shields, the Rare Disease and Complex Therapies Team collaborates with our health system partners to develop and implement innovative, data-driven protocols to treat, monitor, and assess patients with rare diseases. Unfortunately, despite more than 5,000 drugs and biologics receiving orphan status since 1983,[2] most rare diseases do not yet have FDA-approved therapies. In fact, according to the National Organization for Rare Disorders (NORD), 95% of rare diseases have no FDA-approved treatment.[4] Patients with rare diseases face issues not only obtaining the correct diagnosis—which may take years—but also in facing limited or zero treatment options once the diagnosis is made.[4]

## RARE DISEASE: POLICY LANDSCAPE

The Orphan Drug Act continues to be the backbone of federal policy for the rare disease space. Given the relatively small number of patients and high costs of treatments, policy efforts are generally focused on improving patient access to care and supporting innovation for the development of new treatments. Advocacy organizations have focused efforts on challenges related to access to drugs (LDD access), payer coverage (value-based pricing and value-based contracts) and reduction of out-of-pocket costs (e.g., availability of financial assistance such as copay coupons).

Innovation policy efforts are often focused on incentivizing manufacturers to continue to develop highly specialized treatments through tax, patent, and pricing exemptions (e.g., exemptions from drug price negotiation policies in the Inflation Reduction Act). Also, such small patient populations limit the available data sets for clinical trials. The FDA's accelerated approvals pathway has offered manufacturers a way to advance treatment availability, although recent changes to the program in the 2022 Omnibus gives the FDA more authority to withdraw such drugs from the market if post-approval efficacy data is concluded.

## COORDINATION OF CARE FOR PATIENTS WITH RARE DISEASES

When treatments are available for rare diseases, they can be difficult for patients to access and navigate, due to the high cost of many therapies and lack of local provider expertise, especially for those living in rural locations. A Shields health system partner, whose children's hospital has been designated a Center of Excellence for Rare Diseases by NORD, assign a rare disease coordinator to each patient and their family to help navigate the complexities of treatment. These coordinators also assist the health care team by streamlining patient communication.

Patient-centered, collaborative care is necessary to achieve the best outcomes, particularly since many rare diseases impact multiple systems of the body. Involvement by a rare disease coordinator early in the diagnostic odyssey is ideal, as a centralized way to communicate with patients and their families so they

complete the diagnostic process, obtain treatment, and adhere to it. Social determinants of health (SDOH) certainly come into play as well, especially in the diagnosis of rare genetic disorders in minority populations.[6] A systematic review of the literature also suggests that SDOH may affect the clinical progression of hemophilia and other inherited bleeding disorders and are associated with inferior health outcomes.[7]

## INTEGRATED SPECIALTY PHARMACY CAN OVERCOME BARRIERS TO CARE

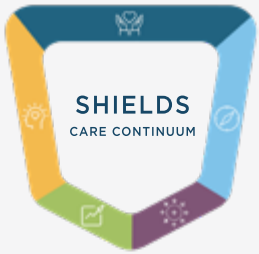
While the primary indication for most specialty drugs is not for the treatment of rare diseases, many, if not most therapies for rare diseases are considered specialty drugs. The high-touch, whole-patient model of HSSP can help patients overcome the considerable challenges and barriers to treating and managing a rare disease.

However, medication access can be a hurdle for HSSPs, since most specialty drugs are limited distribution (LDD) or are not available to patients whose insurance coverage is constrained by payer carve-outs and other administrative or financial barriers. When access to specialty drugs remains within the health system, the care team has access to and can create touchpoints along the entire patient journey, from genetic testing and precision medicine to connections with community resources.

In terms of clinical trials, the participation of academic medical centers is often independent of specialty pharmacy access to the medication; being a clinical trial site can create a pathway to access but does not guarantee it. Ideally, after the end of the clinical trial, if the medication is approved, patients can continue to receive the medication through the health system pharmacy.

By eliminating or reducing the likelihood of gaps in the medical record and in communication, integrated HSSP is better able to address medication affordability, adherence challenges, and the sheer stress and complexity of navigating the day-to-day challenges and long-term consequences of a rare disease.


The high-touch model of integrated health system specialty pharmacy (HSSP) can help patients overcome the considerable challenges and barriers to treating and managing a rare disease.




By simplifying navigation and coordination of care, the Shields Care Continuum provides a single point of contact for patients.

## BENEFITS OF PARTNERSHIP WITH SHIELDS

A partnership with Shields benefits health systems (including their providers and patients), manufacturers, and payers/plan sponsors. For health systems, providers, and patients, the benefits are clinical, financial, and administrative.

The Shields Care Continuum provides a single point of contact for patients to simplify care coordination. Because patients with rare diseases often have multiple co-morbidities, a higher level of care management is necessary. This high-touch patient management and application of best practices maximize outcomes for patients with rare diseases and those who are prescribed orphan drugs. Assistance with prior authorization (PA) also reduces the administrative burden for providers, while helping patients navigate possible avenues for financial assistance.

The Shields Trade Relations Team monitors the drug pipeline alongside its health system partners to help access therapies that would benefit their patients, and the team has the expertise to access ultra-expensive drugs at scale for health systems and to make sure patients who need them can obtain them.

For manufacturers, Shields aggregates data and insights across patient populations. While these populations may be very small within any given health system, the scope across the country may reach a meaningful size from which to draw conclusions. Similarly, Shields' access to data and insights can lead payers to greater understanding of rare diseases and orphan drugs.

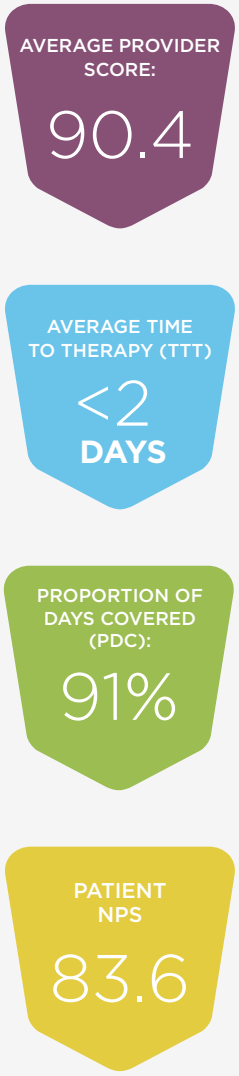
Shields benefits payers and plan sponsors through our care model, aggregation of health system data, and insights about medication utilization. Rare and orphan drugs have significant upfront costs that require health systems to implement additional infrastructure to support the necessary clinical management and training programs (including Elements to Assure Safe Use (ETASU) Risk Mitigation Evaluation

Strategy (REMS programs) as well as data collection and reporting. But this infrastructure also allows health systems to seamlessly report on critical data points required by payers, such as time to therapy, medication adherence and utilization. Use of standardized assessments and data can be used to help payers understand the value of care provided to these patients. An HSSP with high touch points places the patient at the center of a multi-disciplinary, coordinated care team, which best positions them to deliver and improve the care and clinical outcomes of patients.

## SHIELDS CLINICAL PROGRAMS FOR RARE DISEASES

With its health system partners, Shields has developed several programs specific to rare disease states, including PAH, hemophilia, and HAE. In the PAH program, patient liaisons, clinical pharmacists, and nurses all play integral roles in onboarding patients with PAH and monitoring their progress.

Characterized by high blood pressure in the pulmonary arteries, PAH is a rare, progressive, and incurable disease that affects about 50,000 people in the U.S.[8] Using standardized, validated assessment tools such as EmPHasis-10, clinical pharmacists and nurses review patient reported outcomes specific to PAH and assess patient quality of life. Clinicians perform a risk stratification for each patient and adjust the cadence of follow-up assessments based on disease severity. For patients who report the most severe symptoms, clinicians work directly with the provider and the care team to adjust medications and address potential medication non-adherence concerns.




***Shields Outcomes, Calendar year 2022**

## CASE STUDY:
## IMPLEMENTING AN INNOVATIVE PAH CARE MODEL

### THE CHALLENGE

In December 2020, Shields partnered with an integrated HSSP to implement a clinical care model for patients with PAH receiving ambrisentan, a specialty medication with a required REMS protocol with ETASU. Since ambrisentan was the first PAH medication to be clinically followed at a Shields specialty pharmacy partner, the patient management system required customization to support accreditation and payer requirements for PAH, REMS regulatory requirements, and clinical outcomes to measure the program's impact.

### THE APPROACH

At the operational level, a workflow process was designed and implemented for PAH-trained nurses and pharmacists to safely and efficiently onboard, counsel and clinically monitor PAH patients with coordination support from in-clinic pharmacy liaisons to comply with restrictive shipping guidelines for ambrisentan. A training curriculum was developed, incorporating ETASU REMS and adverse event reporting requirements, policies and procedures, and knowledge assessment.

### THE RESULTS

Within two years, Shields collaborated with a total of four health system partners to develop and implement this innovative PAH clinical care model with full REMS audit compliance and strict adherence to adverse event and data reporting requirements, as demonstrated by six successful ambrisentan REMS desktop audits to date with no reported REMS infractions.

A more detailed case study is available from Shields. A preliminary review of patient-reported outcomes suggests stability or improvement in PAH symptoms across the patient population serviced with this care model.

## CONCLUSION

**A variety of factors, including legislative incentives, timely regulatory review, medical and scientific breakthroughs, patient advocacy, and opportunity in therapeutic areas with little competition, suggest increased future investment in rare disease treatments.[9] The expertise of the Shields Rare and Complex Disease Team will help patients, providers, manufacturers, and payers make sense of the evolving landscape.**

## REFERENCES


[1] Genetic and Rare Diseases Information Center. https://rarediseases.info.nih.gov/about. Accessed November 9, 2022.

[2] Miller KL, Fermaglich LJ, Maynard J. Using four decades of FDA orphan drug designations to describe trends in rare disease drug development: Substantial growth seen in development of drugs for rare oncologic, neurologic, and pediatric-onset diseases. Orphanet Journal of Rare Diseases. 2021;16(1). doi:10.1186/s13023-021-01901-6.

[3] Center for Devices and Radiological Health. Precision medicine. U.S. Food and Drug Administration. https://www.fda.gov/medical-devices/in-vitro-diagnostics/precision-medicine. Accessed January 24, 2023.

[4] Regenerative medicine: 2022 the Pipeline Momentum Builds. http://alliancerm.org/wp-content/uploads/2022/09/ARM-H1-2022-R12.pdf. Accessed November 9, 2022.

[5] Center for Biologics Evaluation and Research. Approved cellular and gene therapy products. U.S. Food and Drug Administration. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products. Accessed January 24, 2023.

[6] Fraiman YS, Wojcik MH. The influence of social determinants of health on the genetic diagnostic odyssey: who remains undiagnosed, why, and to what effect? Pediatr Res. 2021 Jan;89(2):295-300. doi: 10.1038/s41390-020-01151-5. Epub 2020 Sep 15. PMID: 32932427; PMCID: PMC7897209. Accessed November 22, 2022.

[7] Lopez K, Norris K, Hardy M, Valentino LA. Defining the Impact of Social Drivers on Health Outcomes for People with Inherited Bleeding Disorders. Journal of Clinical Medicine. 2022; 11(15):4443. https://doi.org/10.3390/jcm11154443.

[8] Deborah Jo Levine MD. Pulmonary arterial hypertension: Updates in epidemiology and evaluation of patients. AJMC. https://www.ajmc.com/view/pulmonary-arterial-hypertension-updates-in-epidemiology-and-evaluation-of-patients. Accessed November 9, 2022.

[9] Crean DH. Why Invest in Rare Diseases & Orphan Drugs? Pharma Boardroom. Published February 19, 2019. Accessed November 21, 2022. https://pharmaboardroom.com/articles/investments-and-deal-activity-in-orphan-drug-products/


### ABOUT SHIELDS HEALTH SOLUTIONS

Shields Health Solutions (Shields) is the premier specialty pharmacy accelerator in the country. The Shields Performance Platform, an integrated set of solutions, services and technology, is intentionally designed to elevate payer and drug access for specialty pharmacies, elevate health outcomes for complex patients, and elevate growth throughout the entire health system. As the foremost experts in the health system specialty pharmacy industry, Shields has a proven track record of success including access to over 80 percent of all limited distribution drugs (LDDs) and most (health insurance) payers in the nation; and a clinical model proven to lower total cost of care by 13%. In partnership with more than 75 health systems across the country through national-scale collaboration, Shields has a vested interest in delivering measurable clinical and financial results for health systems.

**To learn more visit Shieldsrx.com or email us at info@shieldsrx.com**

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