Nonprofit Pharma, Advancing a New Model for Equitable Access to Medicines

Lessons Learned from Bringing a Product to Market in the U.S.

By Medicines360

Acknowledgements:

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Executive Summary

In 2009, before the Affordable Care Act was law, one of the most effective and reversible methods of birth control was unaffordable for most women. The hormonal intrauterine device (IUD) was approved by the U.S. Food and Drug Administration in 2000, yet, was not covered by most private insurance. One large private foundation recognized this equity gap and decided to invest significant philanthropic capital to make hormonal IUDs available to more women. Their solution: partner with pharmaceutical pioneer Victoria Hale to develop a hormonal IUD and make it available in the U.S. market at an affordable price.

Hale decided to create the new entity that would develop the product as a nonprofit pharmaceutical organization. A mission-driven nonprofit pharmaceutical organization—freed from the primary corporate objective to show strong financial returns and instead focused on generating public health benefits—could address this market gap. Supported by a six-year, $82.2M grant from the private foundation, Medicines360 was born.

Hale and a small team of pharmaceutical industry veterans shared a vision for a nonprofit pharmaceutical organization that would merge "public-sector mission with commercial marketing vigor" to reduce cost as a barrier to health by developing and providing affordable women's health products. In early 2015, after years of extensive research and development, Medicines360 launched our hormonal IUD. In doing so, Medicines360 demonstrated what a mission-led, commercially minded, nonprofit pharmaceutical organization can achieve for the public's benefit.

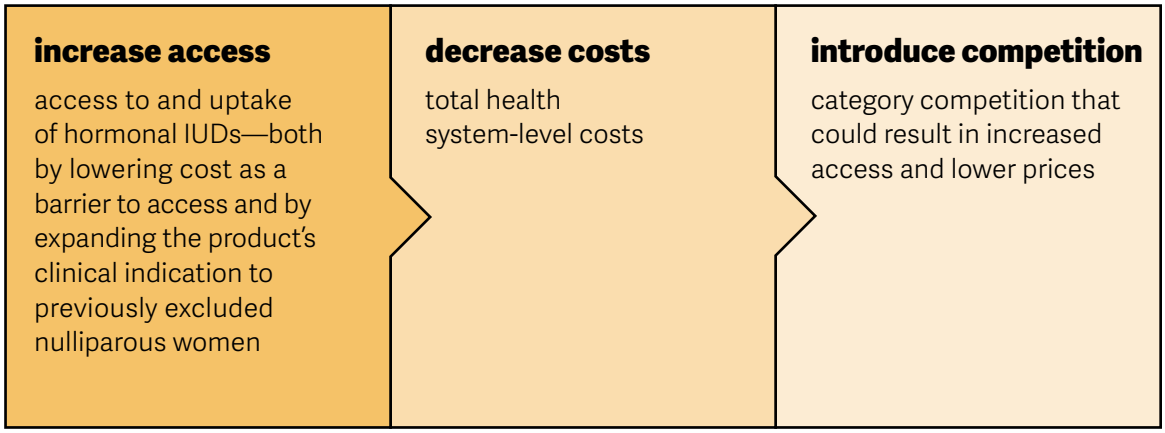
The following is a case study of Medicines360's journey bringing a branded product to market. The case study is based on a mixed method analysis including a review of Medicines360 business plans and market analyses, clinical trial and regulatory records, interviews with past and current key staff members, and a cost and impact analysis.

To bring a drug or device to market in the United States, a pharmaceutical company must decide what product to develop, mobilize sufficient funding for research and development, demonstrate product safety and efficacy to obtain FDA approval, and then work with distributors and purchasers to get the product to patients. To navigate this exceptionally complex process without losing sight of Medicine360's mission and vision, we acquired a hormonal IUD already in development, tested it in a U.S. clinical trial to earn FDA approval, and forged a commercial partnership with a traditional pharmaceutical company to bring the product to market. Medicines360 also decided to maintain ownership of the regulatory filing information and the New Drug Application (NDA), which turned out to be key to Medicines360's strategy in maintaining leverage in a commercial partnership and prioritizing the public health mission.

KEY LEARNING: Existing systems are not structured to support nonprofit pharmaceutical organizations, who must instead rely on innovation, drive, and creativity. Bringing a branded drug to market in the United States is incredibly time-, labor-, and capital-intensive, and current funding, regulatory, and healthcare policy practices do little to ease the burden on nonprofits attempting to achieve a public benefit within a market of well-funded, for-profit counterparts. Though Medicines360 managed around these challenges with a thoughtful organizational structure, careful new-drug application, and an innovative commercial partnership with a unique pricing strategy, we, at every phase, had to navigate the complexities and challenges of a public health system that does not currently incentivize equitable access.

To reduce cost as a barrier to hormonal IUD access for women who get care in publicly funded clinics and hospitals in the U.S., we made our product available to these "safety net"[1] clinics at a deeply discounted price through the federal 340B program.

In bringing a low-cost hormonal IUD to market, Medicines360 aspired to:



Medicines360 made strong progress against these goals. Our organization's research greatly broadened the sector's understanding of who can safely use hormonal IUDs, and as of January 2022, more than 369,000 units of our product had been distributed at a deeply discounted price to approximately 2,500 safety net clinics and hospitals in the U.S.[2]

KEY LEARNING: A mission-based nonprofit pharmaceutical organization can fill gaps in the U.S. public health system. A profit-driven pharmaceutical company with an obligation to earn the highest possible return for shareholders is not incentivized to take on costly clinical trial and regulatory processes to service niche or low-margin markets or to offer discounted pricing and reduce access barriers to safety net clinics and hospitals. By contrast, without the requirement to maximize financial returns for shareholders, a mission-driven nonprofit can invest in drug development to benefit the greater public good and the health of lower-income and uninsured people. Not only did Medicines360 run a complex and inclusive clinical trial to expand hormonal IUD indications for previously underserved women, but we also made our approved product available to public clinics and hospitals at a deeply discounted price to reduce cost as a barrier to hormonal IUD access.

Our economic analyses indicate that the low-cost of Medicines360's hormonal IUD for public clinics and hospitals resulted in health system savings of an estimated $82 million for the 340B segment in the first seven years after the product's launch.[3] These savings were particularly notable for self-pay patients, who are typically unable to access any market discounts; we estimate these patients each saved over $200 when prescribed Medicines360's hormonal IUD, assuming they were only charged the product's acquisition cost.

Additionally, in the years following our product's 2015 launch, the only other hormonal IUD manufacturer announced a partnership to make its products "available with greater access and affordability to all public health providers."[4] We believe that Medicines360's presence in the marketplace introduced this catalytic competitive pressure.

KEY LEARNING: Nonprofit pharmaceutical organizations can serve as a catalyst and ignite a virtuous cycle within a for-profit healthcare system. By introducing a safe, effective, and low-cost alternative before the entry of generics, we were not only able to increase access to a critical product, but we also created marketplace competition which may have influenced the only other pharmaceutical company marketing a hormonal IUD to expand their drug indications and/or to increase the accessibility and affordability of their products.

However, these victories were hard-fought. A for-profit healthcare system presents fundamental challenges to the idea of developing products to "benefit the public good", and at every step along the journey to market, Medicines360 faced

system-level barriers to advancing the primary mission of the organization. Market dynamics that favor maximizing profit—as well as policies that fail to incentivize the use of lower-priced drugs— were contrary to our original hypothesis that simply lowering a product's price would be enough to drive uptake and system savings.

KEY LEARNING: A low price does not necessarily increase product demand and uptake, as the U.S. healthcare system is not structured to incentivize equitable access to affordable drugs. Medicines360's experience bringing a branded product to market revealed with greater clarity the market forces that limit access and inflate drug prices in the U.S. Offering our hormonal IUD at a deeply discounted price did not prompt as immediate or widespread product uptake as we originally hypothesized.

None of the barriers Medicines360 faced are inherently insurmountable; to the contrary, they present opportunities for policy interventions. Government partnership with nonprofit pharmaceutical entities can help address access and public health gaps, while policies that support or incentivize nonprofit innovators can spark the reimagining of how therapies are brought to market, priced, and made more accessible. As such, this case study will present five federal administrative and legislative policy recommendations that—at each step in the process—could mitigate or eliminate barriers to market entry and allow future nonprofit pharmaceutical organizations to advance health equity and reduce overall costs to the healthcare system. If implemented, these changes have the potential to spur innovation, lower costs, and achieve important public health goals.

Introduction

In 2009, before the Affordable Care Act was law, one of the most effective and reversible methods of birth control was unaffordable for most women. The hormonal intrauterine device (IUD) had been approved by the U.S. Food and Drug Administration (FDA) in 2000 yet was not covered by most private insurance; even women who did have insurance faced copays of upwards of $1,000 to access this method. One large private foundation recognized this equity gap and decided to invest significant philanthropic capital to make hormonal IUDs available to more women. Their solution: partner with pharmaceutical pioneer Victoria Hale to develop a hormonal IUD and make it available in the U.S. market at an affordable price.

Hale made a decision that would be pivotal to offering the hormonal IUD at an affordable price. She decided to establish the new entity that would develop the product as a nonprofit pharmaceutical organization. For a myriad of reasons, traditional pharmaceutical companies were not incentivized to improve the affordability nor accessibility of hormonal IUDs. However, a mission-driven nonprofit pharmaceutical organization—freed from the primary corporate objective to show strong financial returns and instead focused on generating public health benefits—could address equity gaps in the market. Supported by a six-year, $82.2M grant from the private foundation, Medicines360 was born.

Bringing a branded drug to market in the United States is an incredibly time-, labor-, and capital-intensive endeavor. It requires deciding what product to develop (a decision often driven by potential financial return on investment but, in Medicines360's case, by the potential public health impact), mobilizing sufficient funding for research and development, demonstrating product safety and efficacy to obtain FDA approval, and then working with distributors and purchasers to get the product to patients.

At the outset of this endeavor, the Medicines360 team hypothesized that affordability, access, and uptake were interdependent, such that simply increasing the product's affordability would in turn increase its access and uptake. The premise was that by introducing a low-cost option, public safety net clinics and hospitals would be able to afford to stock the product and offer it to their patients, creating greater health equity by removing cost as an obstacle to access for low-income women and ultimately driving down overall healthcare costs and reducing barriers in the marketplace.

In bringing a low-cost hormonal IUD to market, Medicines360 aspired to:

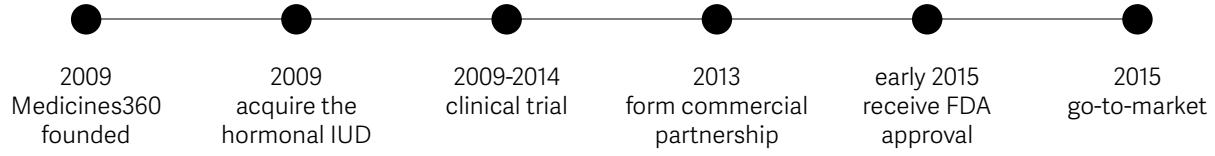
01 increase access to and uptake of hormonal IUDs—both by lowering cost as a barrier to access and by expanding the product's clinical indication to previously excluded nulliparous women

02 decrease total health system-level costs

03 introduce category competition that could result in increased access and lower prices

In retrospect, the pursuit and achievement of these goals for a low-cost product proved to be far more challenging than hypothesized.

GO-TO-MARKET TIMELINE



The following case study of Medicines360's journey in bringing a branded product to market is based on a mixed method analysis including review of Medicines360 business plans and market analyses, clinical trial and regulatory records, interviews with past and current key staff members, and a cost and impact analysis.

The goals of this case study are to:

1. Describe each phase of Medicines360's process—from responding to a market need through product development—to better understand the strategy, effort, and cost required to bring a branded drug to market in the United States.
2. Examine major barriers encountered in the drug development and approval process and identify if/how those barriers are unique to nonprofits.
3. Present policy recommendations to address identified issues in the current U.S. drug development system that would allow nonprofit pharmaceutical organizations to better fulfill their missions to both increase access to drugs and lower drug prices.

Filling a Public Health Need

The IUD is one of the most effective forms of reversible contraception.[5] Effectiveness is not dependent on user adherence, there are non-contraceptive health benefits women experience, with a rapid return to fertility once women discontinue use.[6,7] At the time of Medicines360's founding in 2009, there was just one hormonal IUD on the market in the U.S. and despite these advantages, usage of IUDs (copper or hormonal) in the United States was low compared to other forms of contraception and compared to IUD adoption in other developed countries. A survey of contraceptive use in 2002 found that 1.3 percent of American women had an IUD, rising to 3.5 percent by the end of the decade, and to 6.8 percent by 2015.[8] By comparison, among women using a method of contraception between 2006 and 2008, 17.3 percent reported using the oral contraceptive pill. Between 2006 and 2008, the percentage of women in France and Norway who used an IUD was over 20 percent, multiples greater than among American women.[9]

Low IUD uptake in the United States can be attributed to multiple factors. The first was safety concerns, stemming from problems with an earlier version of the IUD. The Dalkon Shield, an IUD popular in the 1970s and 80s, had design flaws that were associated with serious complications including increased risk of infections, septic abortions, and death which led to concerns about IUDs that endured for decades.[10] Media accounts and high-profile legal actions cemented negative impressions of the devices among the public and clinicians, causing IUD usage to drop. Though other IUD brands did not carry the risks of the flawed Dalkon Shield, manufacturers pulled other products from the market due to fears of litigation, insurance costs, and weakening demand for the method.[11]

The second factor contributing to low IUD uptake was availability. By 2009, there were two IUDs commercially available in the U.S.: a copper IUD approved in 1984 and a hormonal IUD approved in 2000. Concerns over IUD risks and lack of familiarity created a challenging market environment for IUDs, while the regulatory environment, and high research and development costs heightened the barrier to market entry. Limited competition, in turn, led to high pricing and limited accessibility, keeping this highly effective form of contraception out of reach for low-income and uninsured women, who are also disproportionately women of color.[12]

A 2008 unpublished study assessing the impact of higher prices on purchasing behavior amongst publicly funded family planning clinics

found that 36 percent offered only one type of IUD (copper or hormonal) or did not offer either product. Clinic staff cited the cost of purchasing and stocking the IUD as the number one reason, followed by low demand and lack of clinician training. Among clinic patients, only 56 percent of women reported a clinic staff person discussing an IUD in conversations about contraception, even though clinicians reported that when an IUD is clinically appropriate for a patient, they are highly likely to recommend it. Of the 43 percent of patients receiving a recommendation for an IUD, only 9 percent decided to accept the method.[13]

Cost was unmistakably a barrier to IUD use for some women. The first hormonal IUD entered the U.S. market in 2000 with a list price of $316, which rose to $470 in 2007 and to $730 in 2010.[14,15] At that time, for uninsured patients, choosing to use a hormonal IUD could cost upwards of $1,000 for the product plus the medical procedure required to insert it.[16] Even for insured patients, it was unreliable whether a health insurance plan would cover contraception, and out-of-pocket costs could be high. In one 2011 study, 43 percent of women had no insurance coverage for IUDs, and women who faced out-of-pocket expenses greater than $50 were

Affordable Care Act

The Affordable Care Act (ACA) is the most significant regulatory overhaul of the U.S. healthcare system since the enactment of Medicare and Medicaid in 1965. Signed into law in 2010, the ACA expanded health insurance coverage to millions of uninsured Americans and implemented reforms to the health insurance market intended to constrain healthcare costs and improve quality of care. Not only did the ACA expand coverage through private insurance reforms,[19] premium tax credits and subsidies, and Medicaid expansion, but the law also expanded essential benefits for women and healthcare infrastructure to support women's care.

With respect to women's health, the ACA required most private insurance plans and expanded Medicaid to cover a wide range of recommended preventive services without cost-sharing, including well woman visits, contraceptive counseling, and all 18 FDA-approved contraceptive methods. ACA Medicaid expansions increased insurance coverage among all women by 3.4 percentage points, and more than 55 million women now have timely access to family planning services because of the ACA's private insurance reforms. The ACA also created a process for states through State Plan Amendments to permanently expand Medicaid eligibility for reproductive health and family planning services to low-income women who did not otherwise qualify for the Medicaid program.

The ACA did more than expand coverage. It also made investments that supported community health centers, the nation's largest source of comprehensive primary care for medically underserved communities and populations. Increased patient revenues due to the expansion of insurance coverage, along with substantially increased direct federal investment in community health centers infrastructure, have led to growth in the number of health centers and their capacity to provide services.[20]

significantly less likely to have an IUD inserted.[17] The findings from this study heavily informed Medicines360's business case.

It is important to note that at the time of Medicines360's founding in 2009—prior to the passage of the ACA—the landscape for women's health with respect to both access and costs was radically different. It wasn't until 2013 that provisions of the ACA took effect and classified contraception as preventive care, requiring individual health plans and small- and large-group health insurance to cover contraceptives with no cost-sharing. The ACA applies to most (but not all) health plans, though women with insurance can still incur out-of-pocket costs for contraception, including IUDs, depending on network rules and other plan specifics. Analysis from the first year after the ACA contraceptive coverage mandate took effect shows that the average insured patient's out-of-pocket expense for an IUD dropped from $262.38 to $84.30.[18] For women who were uninsured or on health plans not regulated by the ACA's rules on contraception, costs remain high.

The barriers to entry discussed above made the IUD market a less attractive area for research and development among for-profit companies. Nonprofit pharmaceutical companies, however, are organizations with a charitable purpose that prioritize public benefit over maximizing profits. This enables them to create solutions and serve public health needs that might otherwise be overlooked as too small or unprofitable. Medicines360 was able to do just that: the organization prioritized the potential impact of a new, more affordable hormonal IUD on women's health and remained committed to filling this public health need.

Securing Funding

Bringing a branded drug to market in the United States is an expensive proposition. The original commitment from the private foundation to Medicines360 to develop the product and bring it through the regulatory process was $82.2 million. Between 2009 and first product approval in 2015, Medicines360 spent $73.4 million on establishing the organization, research and development, regulatory and legal fees, operations, staffing, and insurance.[21]

Though nonprofit pharmaceutical organizations have similar functions, funding needs, and organizational processes as for-profit companies, typically they are not able to obtain private capital from investors who are seeking strong financial returns. Securing sufficient funding to develop and launch a product is a major barrier for current and future nonprofit pharmaceutical organizations.

Medicines360 was able to successfully bring a low-cost hormonal IUD to market because of the vision and commitment of a philanthropic funder. In providing the capital required to create our organization and to bring a new, low-cost hormonal IUD to market, the foundation demonstrated that philanthropy has the power to catalyze meaningful change in the American healthcare system, filling gaps in the market that the private sector does not have the incentive to serve.

While nonprofit pharmaceutical organizations are freed from the pressures to demonstrate strong financial returns for their shareholders, they are still subject to the same economic and business realities as their for-profit counterparts and must therefore find ways to financially support and sustain their research and operations. Having more funding options in addition to philanthropic capital would expand opportunities for mission-driven organizations to develop or market pharmaceutical products. These funding solutions would need to address funding requirements for both starting a nonprofit pharmaceutical organization and ongoing assistance at different stages of the drug development process.

POLICY RECOMMENDATION:

Congress should create a federal funding stream for nonprofit organizations tied to developing products which achieve discrete public health goals.

Congressionally authorized federal funding for nonprofit organizations developing therapies which meet targeted public health objectives could be beneficial to both the government's objectives and the nonprofit pharmaceutical industry. Such funding would encourage competition in drug manufacturing, while also making it feasible to bring drugs to the market that are unattractive to for-profit companies to develop.

Creating a dedicated funding stream for nonprofit pharmaceutical organizations might focus on "high need" drugs or "public health objective" drugs, such as insulin. The funds might also focus on widely used drugs, generics, or devices that have extremely slim profit margins or only one manufacturer. Federal investment could also be particularly impactful for high utilization products for chronic illnesses, where the current options are prohibitively expensive. Federal investment that supports nonprofit development of pharmaceuticals could create competition to lower drug prices or alternatively could create financial incentives to develop drugs that would otherwise be unattractive to for-profit companies.

The funding agency would have to establish standards for nonprofit organizations to meet—requirements that would likely result in increased transparency for both parties. Especially as interest in nonprofit pharmaceutical organizations grows, this increased transparency will be an asset for new stakeholders to understand the missions and legitimacy of the nonprofit pharmaceutical industry.

Note: *The Expanding Access to Affordable Prescription Drugs and Medical Devices Act (S.2257) was introduced by Senator Jacky Rosen (D – NV) in early 2021. This bill, referred to in this case study as the "Rosen Bill", was the result of several months of member outreach, education, and drafting that included Medicines360 and other partners. The Rosen Bill includes language that would authorize cooperative agreements and low interest revolving loans up to $5 million to nonprofit pharma entities meeting a range of strict requirements and making products expected to achieve discrete public health goals. The government would be entitled to buy products from nonprofit pharmaceutical companies at a discount for the strategic national stockpile. The intent of this policy in the Rosen Bill is to help fill out an organization's funding, not to fund its entire work. Currently, the Rosen Bill is still active, and Senator Rosen remains a strong supporter. Additional policies around this topic, such as the one detailed above, would aim to expand the amount and scope of the government's funding commitment.*

Acquiring the Product

An early cornerstone in Medicines360's plans for developing a hormonal IUD was the decision to acquire a product already in clinical trials in Europe, rather than developing a novel IUD.

Shortly after forming the organization, Medicines360 identified a Belgian women's health company that had developed a hormonal IUD and was completing a Phase 3 clinical trial in Europe for the treatment of menorrhagia, a serious form of heavy menstrual bleeding. We chose this partner for several reasons, including the company's university affiliation; reputation for scientific research; technology; probability and potential speed of a successful market launch; and favorable relationship, business terms, and costs to Medicines360.

Medicines360 finalized a collaborative agreement with the Belgian company in October of 2009, and while the IUD inserter—an important component of the product—needed a redesign to meet U.S. market expectations, this partnership armed Medicines360 with a Phase 3 clinical trial-ready product for the U.S. that would save both time and costs. As part of this agreement, the Belgian firm assumed responsibility for designing and manufacturing the IUD, while Medicines360 was responsible for conducting a Phase 3 contraceptive clinical trial in the U.S. and designing and developing the new inserter. [22]

Conducting a Phase 3 Clinical Trial

Clinical Trial Design

Achieving FDA regulatory approval to market a new drug in the United States requires a Phase 3 U.S. clinical trial of safety and efficacy with testing in human volunteers. The design of a clinical trial also lays the groundwork for a drug's FDA application and label, defining who may use the product and how.

Conversely, no clinical trial, or only limited clinical trial data, is required by the FDA for approval of generics. The only requirement for this less costly option is to demonstrate that the generic and the already-approved brand name drug are bioequivalent.[23] Though Medicines360's product shared the same hormone load as the branded hormonal IUD already on the market, there was no FDA approval pathway for a generic hormonal IUD at that time, primarily due to the product's complexity. It wasn't until January 2020 that the FDA published draft guidance for reviewing and approving a generic hormonal IUD product that includes levonorgestrel.[24]

Medicines360's hormonal IUD was developed under the 505(B)(2) pathway, requiring a Phase 3 clinical trial and extensive product characterization data. This expense was a barrier to entry in the marketplace for other manufacturers.

As future nonprofit pharmaceutical organizations and philanthropists explore where and how to create the greatest public health benefits, having regular and predictable FDA processes for issuing guidance for generic approval pathways on complex generics would empower them to make the most of their funding and time.

POLICY RECOMMENDATION:

Congress should establish a timelier process for the FDA to issue guidance to support approval pathways for complex generic products.

While FDA has taken actions in the past year to support a process for complex generics,[25] timely access to affordable generic products can help to lower costs for patients, providers, and payers. A nonprofit pharmaceutical organization, given its mission, may be interested in developing complex generics for products where public health is a priority, and price remains a barrier to access, such as auto-injectable epinephrine.[26] Having the FDA issue draft guidance within five years of when the first brand-name product is approved would provide a regulatory starting point for nonprofit organizations to develop products where there is a significant public health need.

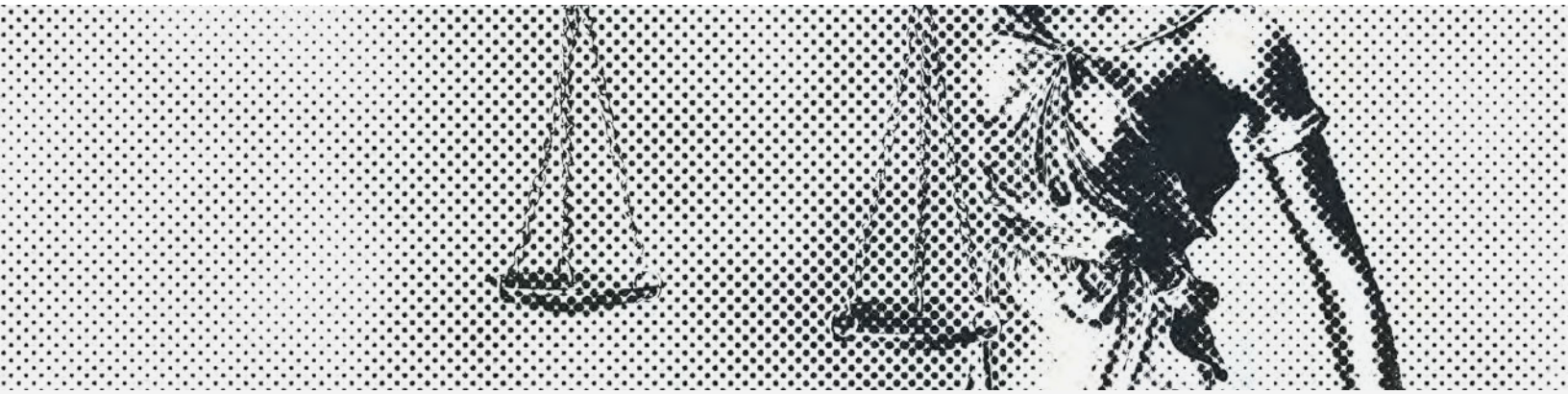
Even if a generic pathway had been feasible, it is unlikely that Medicines360 would have pursued it for this product. The generic label would have been too restrictive to meet our organization's goal of increasing access, as generics bear the same labeling as the brand-name version, and the only U.S. hormonal IUD already on the market had a label limiting its recommended use to women who had already given birth. Instead, to meet our mission of expanded access, Medicines360 pursued a large Phase 3 clinical trial and a new drug application.

In designing the clinical trial, Medicines360 considered patient preferences, knowledge, and historical coercion in contraception as influential factors that had contributed to the hormonal IUD's low utilization. To address these factors, Medicines360 sought to generate clinical data on the safety and efficacy across a broad range of populations to provide data that would encourage providers to make the product available to a diversity of women. Medicines360 set out to demonstrate that the hormonal IUD is safe and effective for more women than previously recognized. The clinical trial included participants from groups historically underrepresented in hormonal IUD research: women who had never given birth (nulliparous women), women of color, and women who are obese. Bolstered by the immediate engagement of family planning physician leaders eager to assist Medicines360 in the research and development of our product, we produced the largest Phase 3 clinical trial ever conducted in the U.S. on a hormonal IUD.

The costs to conduct such an extensive clinical trial were significant. Clinical research costs leading to initial product approval in 2015 totaled $20.3 million. A traditional profit-driven pharmaceutical company, backed by private capital or public stockholders, might

not have been incentivized to conduct such an inclusive clinical trial. For a pharmaceutical company that needs to earn a profit for investors, it is not necessarily advantageous to include an expansive number of endpoints in a clinical trial. While a narrower approach to proving a drug's safety and efficacy may result in a faster time to market and less costly, a less inclusive label often limits product uptake and is less likely to contribute to a body of public health knowledge or serve a public health purpose.

Medicines360's trial design was driven by a public health mission to widen access to the hormonal IUD. This intentional investment in more inclusive clinical trial design yielded new insights about hormonal IUDs and served as an important example of how nonprofits can drive innovation and set new standards for the pharmaceutical in-



POLICY RECOMMENDATION:

Congress should authorize grants for nonprofit manufacturers that commit to conducting clinical trials in diverse populations representative of all potential users.

Historically, clinical trials have been over-representative of certain populations, such as men, white-identifying people, and people without medical comorbidities.[29,30] As a result, data from trials can lead to insufficient guidance or subpar products for underrepresented clinical populations such as women, people of color, or individuals with comorbidities such as diabetes or high blood pressure.[31,32] Diverse clinical trials that include representative population samples provide better scientific data that is more generalizable to the general population and allows for all people to receive the highest standard of care regardless of their identity.[33]

In November of 2020, the FDA released non-binding guidelines and recommendations for enhancing the diversity of clinical trials, including eligibility guidelines, enrollment practices, and study design.[34] The guidance document details research practices that encourage diverse participants to enroll and remain in studies. However, as nonbinding guidance, companies are not legally obligated to follow it. Nonprofit pharmaceuticals, however, are uniquely situated to help the administration commit to more diverse clinical trials by making public health and diversity a priority in their programs.

Congress has an opportunity to help foster equitable, effective, and more affordable public-health advances by authorizing investments in nonprofit pharmaceuticals that commit to conducting clinical trials in diverse populations. Where for-profit companies may have to justify the added expense of recruiting and retaining a representative trial population to shareholders, inclusive and transparent clinical trials are central to mission-driven nonprofits' goals of benefiting the public health needs of underserved communities.

dustry. We recently witnessed the importance of inclusive and diverse clinical trials, with renewed government and public interest in the wake of the COVID-19 pandemic.[27,28]

Within months of forming the organization in 2009, Medicines360 began enrolling patients in the landmark clinical trial, ACCESS IUS (A Comprehensive Contraceptive Efficacy and Safety Study of an Intrauterine System). The study included subjects ages 16 to 45 years old, whose races mirrored U.S. census data, and who had (43.3 percent) and had not (57.7 percent) ever given birth. The study included no limit on weight and Body Mass Index (BMI); more than 50 percent of subjects were overweight or obese and 5.3 percent were morbidly obese.[35] We enrolled women from a wide variety of clinical trial sites, including large teaching hospitals, safety net clinics/hospitals, and Planned Parenthood locations, many of which served low-income communities and uninsured women. Finally, like other clinical trial protocols, women participating were tested for STIs; however, test results were not required before IUD insertion. Women with positive results were treated and the IUD was left in place. This allowed Medicines360 to demonstrate the safety of obtaining a hormonal IUD in a single clinic/hospital visit, instead of requiring a second appointment for IUD insertion after STI treatment, thereby reducing the burden of obtaining contraception.

Medicines360's clinical trial opened the door to IUD access for women:

AGES 16 TO 45	OF ALL RACES
OF ALL BODY WEIGHTS	AT ANY POINT IN THEIR MENSTRUAL CYCLE
WHETHER OR NOT THEY'VE GIVEN BIRTH	TO RECEIVE SAME DAY INSERTION WITH STI TESTING

In addition to product safety and efficacy, the study evaluated the hormonal IUD's impact on menstrual bleeding, fertility after discontinuing use, and insertion timing. This research provided a wealth of clinical knowledge for practitioners, bringing down what one researcher called "knowledge and myth barriers."

Clinical Trial Results

The ACCESS IUS study generated data supporting the use of hormonal IUDs for nulliparous women (women who have never given birth), which resulted in a meaningful expansion of the use of the product.[36] The study further provided important clinical and pharmacokinetic information on the use of the product in non-white races and differing body weights, which gave clinicians the data they need to counsel non-white and heavier women about hormonal IUD use.

Medicines360's research also generated data on the return to fertility for women after the product's removal: 86% women who discontinued use of Medicines360's hormonal IUD with a desire to get pregnant did so within 12 months, with a median time to conception of 92 days.[37]

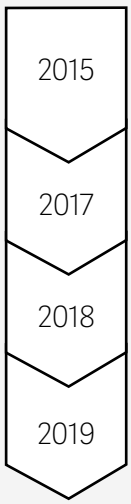
Medicines360's hormonal IUD expanded the timing window of insertion for all patients, removing the need for multiple office visits. The product was allowed to be inserted at any time during the menstrual cycle rather than just in the first seven days.

We continued clinical research of the product after its initial launch, with investigators studying safety and efficacy over additional years to demonstrate that the product could be used for longer time periods. This would translate to fewer procedures (IUD insertion and removal), fewer clinic/hospital visits, and reduced costs for patients over time.

Earning FDA Approval

Medicines360's product received initial FDA approval for three-year duration of use in February of 2015. The FDA then granted approval for an indication of four-year duration of use in 2017, five years in 2018, and a landmark six-year approval in 2019. We have currently filed with the FDA for an eight-year duration of use.

DURATION OF USE EXTENSIONS



3-year approval

4-year approval

5-year approval

6-year approval*

*First hormonal IUD in the world to earn a six-year indication

The hormonal IUD is considered a complex drug-device combination product and as referenced earlier no generic pathway existed for Medicines360 to pursue FDA approval. FDA approval came at the end of a regulatory process known as 505(b)(2), an application category that allows drug developers to apply for FDA approval leveraging some evidence of safety and effectiveness "from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference."[38] This evidence may include the FDA's previous findings of safety and efficacy on similar products or information found in published literature for clinical and non-clinical aspects of the product. The 505(b)(2) pathway is not a generic or interchangeable product approval, but rather allows a drug the ability to rely on some existing data from the active pharmaceutical ingredients and other similar products to enable a shortened development pathway, reducing the time and money required for product development.[39] While Medicines360's hormonal IUD approval requirement from FDA still included a large Phase 3 clinical trial and substantial manufacturing characterization data, less evidence was required than in the traditional 505(b)(1) approval pathway.

In an attempt to further expedite FDA approval, we sought but did not receive priority review of our application, which would have resulted in FDA action within six months instead of the standard 10 months.[40] The priority review process is meant to speed the approval of drugs that, if approved, exhibit significant improvements in the safety or effectiveness of a treatment.[41] Medicines360 made a case that a low-cost hormonal IUD addressed an unmet need in public health. The FDA did not grant the priority review, responding, "The Division is unable to take pricing information into consideration in determining whether a product addresses an unmet need," as the FDA's jurisdictional limitations preclude the analysis of cost in a patient's access to medicines.[42]

Note: *While there is not a policy recommendation on this key issue in this case study, there is potential legislation that would address this: S.2257, "Expanding Access to Affordable Prescription Drugs and Medical Devices Act". Led by Senator Rosen it includes language that would give the Department of Health and Human Services (HHS) the authority to deem a medical device or drug "essential" for priority review based on some measures of cost. For medical devices, the Secretary could deem them essential if similar goods' prices have increased at rates greater than inflation or if there are two or fewer alternate manufacturers for comparable products. For drugs, the Secretary could deem them essential if the alternate treatment's public list price is more than $50 for a one-month supply, or if there are two or fewer alternate manufacturers for comparable products.*

Although Medicines360 did not qualify for priority review of our application, as a small business, we did qualify for a one-time waiver of the FDA's substantial new drug application filing fee ($2,169,100 in 2014). The FDA waives the fee for the first new drug application when the applicant:

- Has fewer than 500 employees, including employees of affiliates
- Has not had a prior drug approved and marketed
- Is submitting its first application[43]

Note: *When a company applies for a drug approval, it pays the FDA a "user fee" for the agency to review the application. In 2022, the user fee for applications requiring clinical data was $3,117,218. The Rosen Bill currently includes policy reform to waive these user fees for nonprofit pharmaceutical drug applications to reduce the financial burden of getting a product approved.*

Despite qualifying for the one-time waiver from the FDA, Medicines360's spent nearly $3.8 million between 2009 and 2015, including regulatory submission and consulting expenses. Obtaining FDA approval required additional evaluations because our product combines both a drug (the hormone levonorgestrel) and two devices (the t-shaped frame of the IUD, and inserter). Because combination products are regulated under different types of FDA regulatory authorities and/or Centers, they raise additional review challenges.

Earning FDA approval was a major milestone both for Medicines360 and for women's health more broadly. Thanks to the robust body of clinical evidence in our application, its approval meant more women were eligible for hormonal IUD use than ever before and doctors were now armed with the data they needed to make informed and confident recommendations to their patients.[44]

On February 27, 2015, our hormonal IUD was approved by the FDA.

Bringing the Product to Market

Founding as a 501(C)(3)

Medicines360's founders chose to establish as a nonprofit public benefit corporation that is tax exempt under Section 501(c)(3) of the Internal Revenue Code to protect the assets as a public benefit in perpetuity, allowing for the mission and decision making to be free of shareholder return requirements. Following past experiences Medicines360 applied to the Internal Revenue Service to be recognized as a 501(c)(3) public charity, which made our organization both tax-exempt and eligible to receive tax-deductible donor funding in the form of charitable contributions and foundation grants. Public charity and tax exempt status, however, comes with two important constraints.

First, in order to qualify as a public charity, regulations require that most charitable organizations demonstrate "public support," or diverse sources of funding.[45] Medicines360, however, did not have the diversified funding sources to pass the "public support" test, so, once our clinical trials were underway, we applied to the Internal Revenue Service to change our public charity status to a medical research organization (MRO), which—along with academic institutions, hospitals, churches, and few other categories—does not have to demonstrate broad-based or "public" financial support.[46] However, the MRO category requires the nonprofit to be continuously involved in medical research—such as a clinical study—conducted in conjunction with a U.S.-based nonprofit or government hospital. If clinical research does not remain the designated share of the organization's activities as required by the MRO tax regulations, then MRO tax status may no longer be a feasible means of maintaining Medicines360's public charity status. In that case, Medicines360 would still be a tax-exempt

organization, but it would be classified as a private foundation rather than as a public charity. Private foundations are subject to greater operating restrictions than a public charity and are required to pay a 2% excise tax on their investment income. Because substantial levels of medical research expenditures are required to maintain MRO status, an MRO is not an ideal means of maintaining public charity status for a nonprofit entrant into the pharmaceutical market.

Second, revenues from drug sales may be considered "unrelated business income," which will be subject to taxation and also jeopardize tax-exempt status. Selling drugs in the U.S. healthcare system—even at low cost, to public clinics and hospitals, for public benefit—may be considered "unrelated business income" under the IRS's poorly defined "commerciality" doctrine. Under that doctrine, if an exempt organization operates in a manner that is like a for-profit commercial enterprise, e.g., selling goods like those sold by for-profit commercial enterprises, then the exempt organization's revenues and income from that commercial activity will be treated as unrelated business income. The parameters of the commerciality doctrine are based on rulings and court decisions that are in many cases inconsistent. We know from the experience of other organizations that the IRS has under this doctrine required a nonprofit pharmaceutical organization to give away most of its products and sell a substantial portion of its remaining products at more than 50% below cost as a condition of attaining exempt status. The lack of regulations or other IRS guidance to support nonprofit organizations selling low-cost, high-quality drugs and devices for the public benefit is a shortcoming in the tax code. Nonprofit pharmaceutical organizations, which aim to sell drugs on a cost-plus basis, are consequently forced to seek out alternative commercial strategies to comply with current guidance and the IRS's views on the commerciality doctrine.

Note: *The Rosen Bill S.2257 currently includes policy reform that would clarify the status of these organizations to enable them to sell pharmaceutical products on a nontaxable basis within certain cost-plus parameters.*

Creating a Commercial Partnership

Prescription drug and medical device distribution in the United States is exceptionally complex. As a small organization, Medicines360 expected to partner with a for-profit pharmaceutical company to commercialize the product. In both publicly financed healthcare settings and in private clinics and hospitals, drugs and devices are distributed through wholesalers, benefit managers, and purchasing organizations, and are subject to a variety of reimbursement programs. Navigating these systems—and individual clinic/hospital purchasing preferences—would require an experienced commercial partner. This would be accomplished by licensing the commercial rights (and commercial market product control) to a for-profit pharmaceutical company, so it was critical to identify the right fit in a commercial partner.

In our search for the right partner, Medicines360 prioritized a relationship that would preserve our nonprofit status while helping us pursue financial sustainability of the organization and reflect our mission and values. Particularly, Medicines360 sought to maintain ownership of the new drug application (NDA)-- a critical lesson learned from Hale's past experiences. This would allow Medicines360 to have control of the product and continue the clinical trial work beyond the initial approval to obtain additional product indications. Another non-negotiable requirement was that hormonal IUDs sold to public clinics or hospitals carry a deeply discounted price set by us. To secure a beneficial agreement that prioritized both affordable access for the public sector and financial sustainability for Medicines360, the team agreed on "must haves" for any potential commercial partner.

"Must have" partner criteria included:

- Commitment to prioritize the new hormonal IUD among its other products
- Reputation of trust in the women's healthcare sector and demonstrated long-term commitment to the field
- Resources and capacity to market and distribute the product
- Large, efficient sales and marketing operation
- A financial deal structure supportive of Medicines360's longer-term sustainability

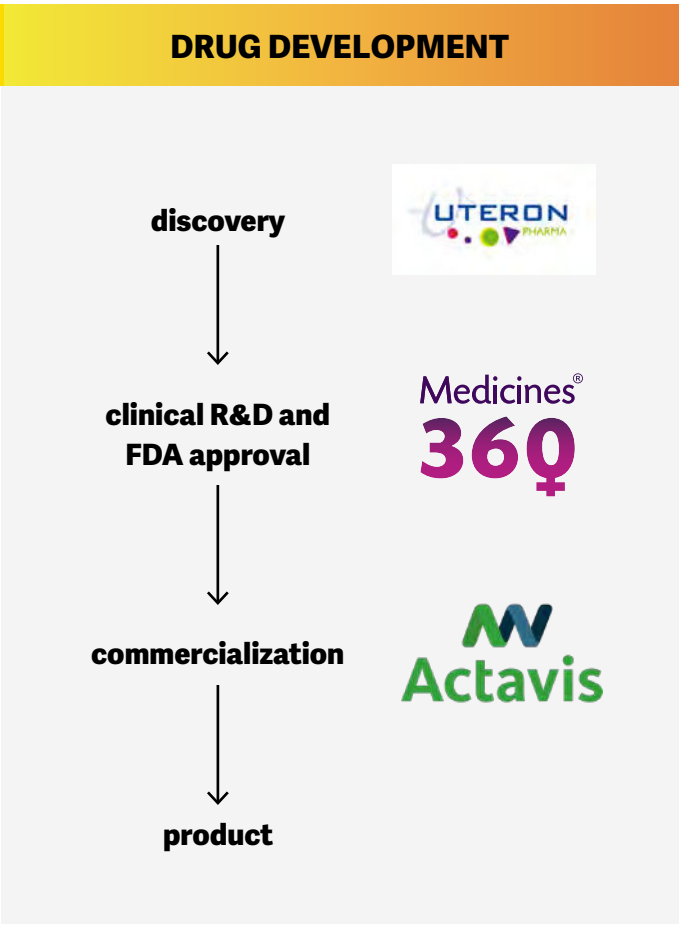
In return, Medicines360 offered our for-profit partner:

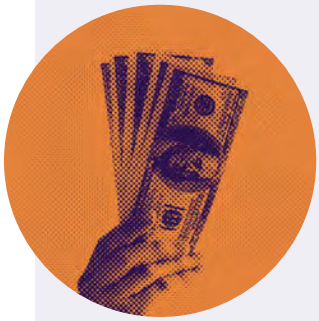
- A product with enough committed financial support to fund it through FDA approval
- Strong clinical data supporting the product's safety and efficacy
- Product entry into an underdeveloped market with a single competitor, ripe for growth
- Ability to price and profit from units sold in the private sector
- Use of U.S. contraceptive clinical trial data to support regulatory submissions in other countries

To evaluate potential partners, Medicines360 hired a team of highly credentialed bankers and lawyers with experience structuring complex transactions, a record in healthcare, relationships throughout the industry, and experience with nonprofits. We intentionally timed our search for a commercial partner to coincide with the evaluation of the first results of our clinical trial to reduce risk for any potential commercial partner and bolster Medicines360's negotiating position. With the help of our advisors, we considered six different pharmaceutical companies as potential partners. After an extensive evaluation process, Medicines360 selected Actavis (formerly Watson Women's Health, then Allergan, and now AbbVie) as our commercial partner.

In June of 2013, Medicines360 announced a global partnership with Actavis that included making the product available in the U.S. private sector and at a deeply discounted price for public clinics and hospitals. As part of this agreement, Medicines360 retained the new drug application (NDA) and the rights to sell the product in low- and middle-income countries and to market to public clinics and hospitals throughout the U.S., including family planning clinics that service low-income women.

Per our agreement, Actavis licensed M360's intellectual property, and in exchange, Actavis made both an upfront payment and milestone payments and continues to pay Medicines360 royalties for the intellectual property on units sold. This revenue is defined in the tax code as "passive income" rather than "unrelated business income," allowing Medicines360 to generate revenue without jeopardizing our nonprofit status.[47]





340B Drug Pricing Program

The Medicaid Drug Rebate Program was established in 1990 and requires drug manufacturers to enter into a national rebate agreement with the Secretary of Health and Human Services (HHS) in exchange for state Medicaid coverage of most of the manufacturer's drugs. The Medicaid Drug Rebate Program ensures that the Medicaid program receives the lowest or "best price" at which manufacturers sold the drug.

As part of the Medicaid Drug Rebate Agreement, manufacturers must also participate in the 340B Drug Pricing Program, which requires manufacturers to provide discounts on covered outpatient drugs to qualifying providers and hospitals that serve a substantial portion of vulnerable and underserved patients. The intent of the 340B Program is to enable safety net hospitals and providers to stretch scarce federal resources as far as possible.

Product Pricing

An IUD is a physician-administered product that women must have inserted and removed in a clinic or hospital outpatient setting. The product is "buy-and-bill", meaning the clinic or hospital must buy, stock, and make the IUD available to patients who choose it, and then the clinic or hospital bills insurance to be reimbursed for that upfront product cost and a fee for the procedure. For public clinics and hospitals operating on razor thin margins, having to bear the upfront purchase cost reduces their ability to stock more expensive buy-and-bill products; it was therefore Medicines360's hope and hypothesis that a lower priced option would make it more likely that these public clinics and hospitals would stock and offer their patients a hormonal IUD.

Given our focus on making a hormonal IUD accessible and affordable for low-income and uninsured women, a key purchaser of our hormonal IUD was safety net clinics and hospitals, also referred to as "340B clinics/hospitals" as they receive access to a drug discount program outlined in a federal code of the same name.

In 2008, unpublished research completed by the anonymous funder set the discounted price of Medicines360's hormonal IUD at $50 when sold to safety net clinics and hospitals. We kept this price point until January 2020, when we received approval for six-year product usage, at which time we increased the price to $100 for sales made to these 340B clinics/hospitals.

The original $50 price point was based on findings in the unpublished research that showed a low price would enable safety net clinics and hospitals to purchase and stock a hormonal IUD. During this time, the primary market force preventing patient access was the high cost to clinics and hospitals to stock the product and have them available to offer to patients. The 2008 research showed a $50 price was a substantial reduction from what these clinics and hospitals were paying and would enable them to more readily stock and offer our hormonal IUD. Spending less to acquire the product means the clinic/hospital ties up less of its budget while the product is in stock and has not yet been reimbursed by the patient or their insurance. Indeed, when Medicines360 conducted a 2019 online survey of 340B clinics and hospitals offering at least one LARC method, 92 percent of sites offering our hormonal IUD agreed that the product was valu-

able because of its lower 340B acquisition cost compared to other hormonal IUD brands.

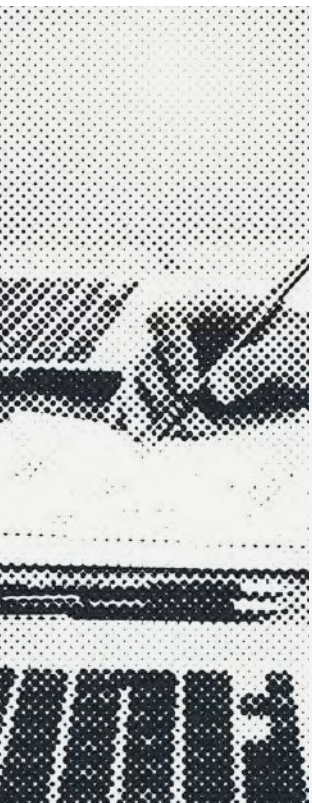
However, by the time the Medicines360 hormonal IUD entered the market in 2015 (post-ACA), the landscape had changed, and low price alone did not prove to be as strong a motivator for safety net clinics to purchase the product as anticipated. Though we forecasted that we would sell 100,000 units the first year in 340B clinics and hospitals, actual sales were less than half that.[48] Lower-than-expected uptake of Medicine360's hormonal IUD is thought to be largely due to idiosyncrasies in how drugs are priced, discounted, distributed, and reimbursed in the United States—especially post-ACA—all of which proved to weaken Medicines360's hormonal IUD's value proposition in a public health system designed around for-profit companies.

Though the ACA successfully increased family planning access and coverage, it also introduced policies that had the (unintended) consequence of incentivizing use of more expensive treatment options and, as a result, introduced unforeseen challenges for Medicines360. Low prices became less essential to safety net clinics and hospitals once the ACA was fully implemented in 2014. In a great advance for health equity, the ACA made more people eligible for subsidized private insurance or free coverage under Medicaid, and private insurance was now required to provide coverage for contraceptives. But, because clinics/hospitals now had greater certainty that they would be reimbursed for the products they stocked, there was less urgency to keep purchasing costs as low as possible.

To realize the full cost-saving potential of low-cost products, additional incentives may need to be created.

The Pharmaceutical Supply Chain

Though pharmaceutical manufacturers make drugs and devices, wholesalers, distributors, and other intermediaries in the pharmaceutical supply chain play an equally important role in healthcare: they move products from manufacturers to patients and can strongly influence which products are available to providers and patients and at what price. When setting a product's price, the pharmaceutical company must consider the fees they'll need to pay to these intermediaries at each point along the pharmaceutical supply chain.



POLICY RECOMMENDATION:

The administration should use government purchasers to incentivize the use of low-cost products developed by nonprofit pharmaceutical organizations.

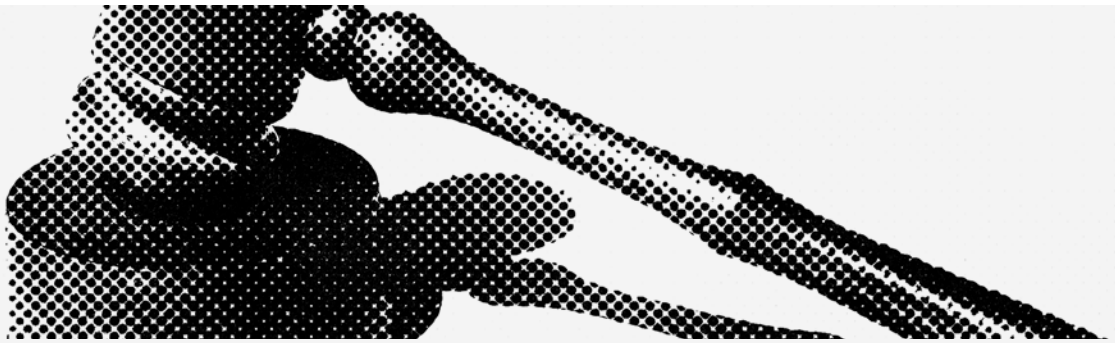
Incentivizing the use of products developed by nonprofit pharmaceutical organizations would create a predictable purchaser for those nonprofits, allowing them to remain focused on increasing access and affordability for underserved populations and enabling a way for nonprofits to gain market pull through for their low-priced products. For organizations tied to mission rather than financial return, having a reliable government purchaser could also incentivize additional funding from foundations or others looking to fill access or affordability gaps. It would also provide federal purchasers with opportunities to partner with organizations that have no obligations to investors and can bring products to market at a lower cost. For Medicines360, the knowledge of a reliable government purchaser of the product could have given our organization leverage to secure additional favorable agreements with commercial entities, increased the footprint of our product, and amplified our impact towards our mission.

Pharmaceutical companies contract with wholesalers to move products from their warehouses into the commercial marketplace. Wholesalers, in turn, move those products to either clinics/hospitals or to pharmacies, who then provide them to patients. Along the way, Group Purchasing Organizations (GPOs) and Pharmacy Benefit Managers (PBMs) work to negotiate better prices on behalf of clinics/hospitals and pharmacies, respectively. To offer these services, wholesalers, GPOs, and PBMs charge fees, form partnerships, and promote products in ways that create positive economics for themselves, not necessarily for the patient. As a result, in a for-profit marketplace the final price tag attached to a drug or device reflects value creation at each step along this pharmaceutical supply chain. This entire system in which several intermediaries in the supply chain seek a financial return, results in increased prices for patients and insurers.

For example, wholesalers earn fees for delivering drugs from pharmaceutical companies to clinics, hospitals, and pharmacies, and these fees are typically a percentage of the list prices of the drugs they wholesale. When drug prices are higher, the wholesaler makes more. Even when a clinic/hospital buys a drug or device from a wholesaler at a discount under the 340B program, the wholesaler earns its margin on the higher list price, not on the lower 340B price. This incentivizes the wholesaler to stock and promote more expensive drugs and devices over less expensive alternatives.

Sales of Medicines360's product under the 340B program remain subject to the traditional system of healthcare supply chain economics, even though our marketplace intervention was a deeply discounted 340B price. The post-ACA pricing, discount and reimbursement systems render our deeply discounted 340B price alone less effective at driving sales of the product.

As the supply chain operates today, intermediaries have little economic incentive to pull a low-priced product through to the end user. We believe the fee structures in the supply chain which incentivize sale of higher priced drugs need to be addressed.



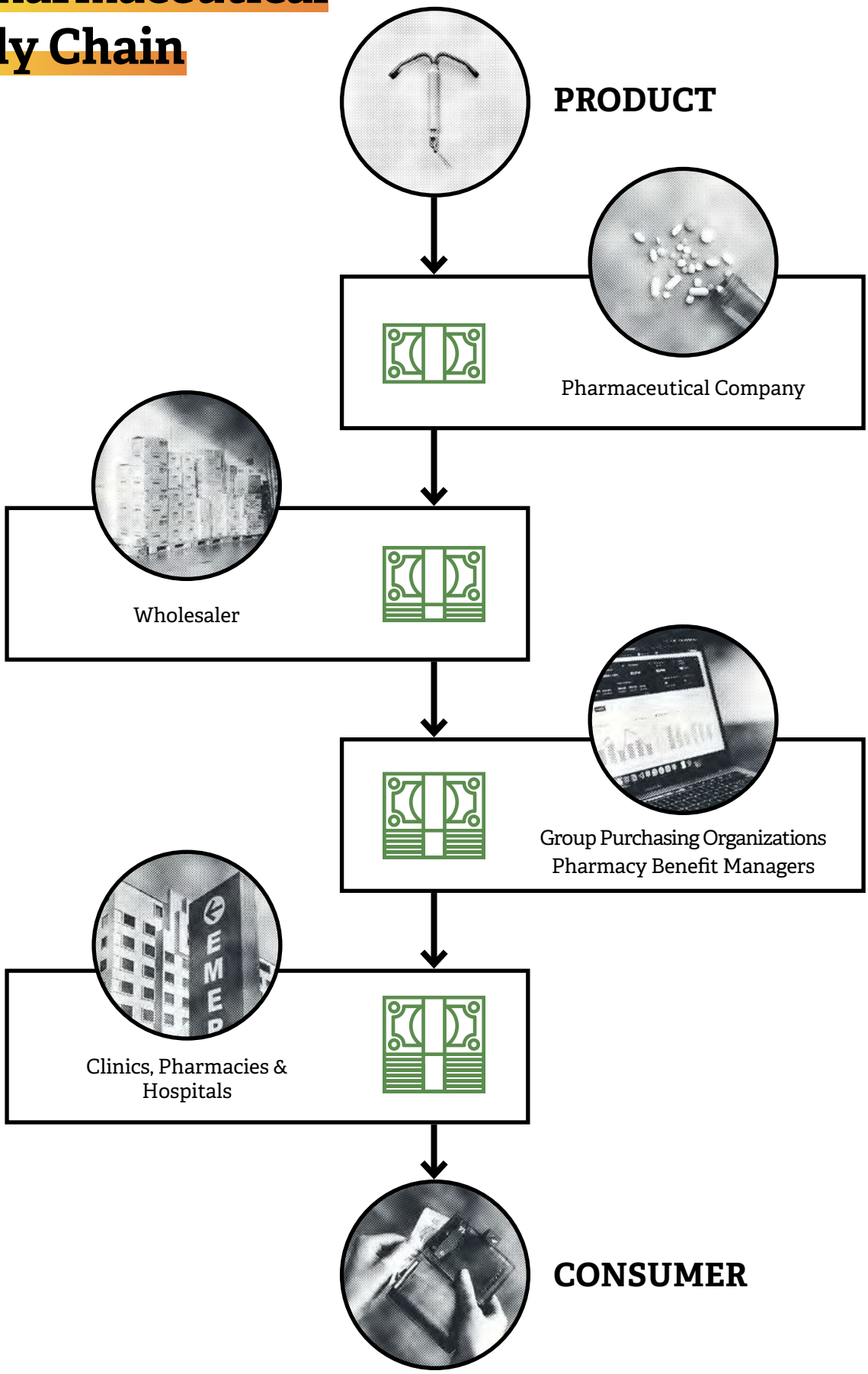
POLICY RECOMMENDATION:

Congress should initiate tax incentives for for-profit intermediaries who partner with and carry medications from nonprofit pharmaceutical organizations.

To relieve patients of the burden of high drug prices, it is important that companies throughout the pharmaceutical supply chain are economically incentivized to pull low-cost products into and through the system.

Lawmakers often use tax benefits as a method to advance public health goals, such as the orphan drug tax credit, which incentivizes companies to work on products which will benefit smaller patient populations and may not have tremendous reimbursement opportunities. Establishing a tax credit specifically for for-profit healthcare intermediaries interfacing with nonprofit pharmaceutical organizations offering low-priced products would increase the negotiating power of nonprofits in these conversations.

The Incremental Costs of the Pharmaceutical Supply Chain

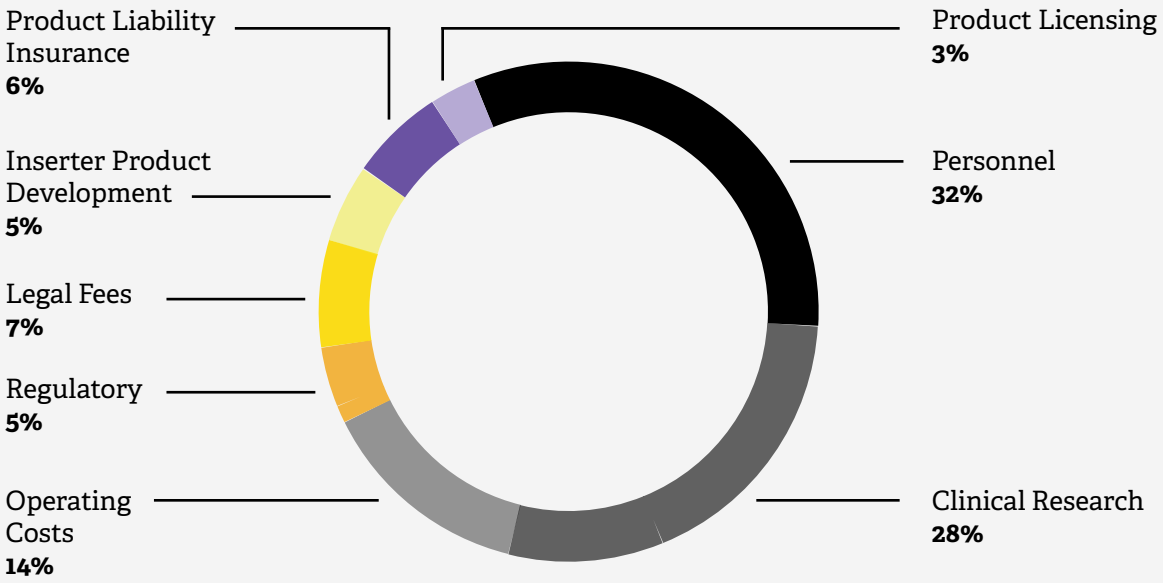


Total Cost of Bringing the Product to Market

The total cost of bringing our hormonal IUD to market was $73.4 million. This included $23.7 million in salary and benefits for employees, $20.3 million in clinical trial costs, an estimated $4.0 million in product liability insurance, $4.0 million for product and inserter development, $3.8 million in regulatory submission and consulting expenses, $2.0 million in product licensing fees to our Belgian partner for the exclusive rights to the product, $5.0 million in legal fees, and operating overhead such as rent, IT, communications, and travel at $10.6 million.

TOTAL COSTS

Bringing Medicines360's product to market in 2015 took six years and cost a total of $73.4 million, spread across the following activities:



Measuring Impact

Over our short history, Medicines360 has taken on challenges that traditional, for-profit pharmaceutical companies had little financial incentive to tackle. Our central effort was to make a safe and effective hormonal IUD accessible for underserved women in the United States. Along the way, we brought transparency to the drug development and commercialization process; significantly expanded hormonal IUD access via the largest and most inclusive clinical trial in category history; provided hundreds of thousands of American women with an affordable and effective form of contraception; and cut millions of dollars of unnecessary spending from the U.S. healthcare system. Most importantly, Medicines360 created a new playing field for product access.

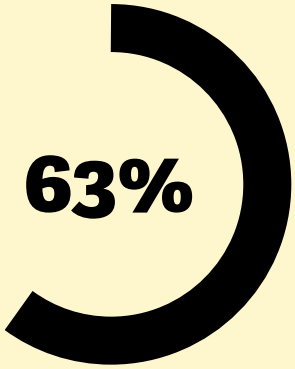
Though market forces, regulatory barriers, and incentive structures reduced the product's reach compared to expectations, Medicines360 was able to make progress against each of its goals:

01 Increasing access to and uptake of hormonal IUDs—both by lowering cost as a barrier to access and by expanding the product's clinical indication to previously excluded nulliparous women.

Thanks to the introduction of Medicines360's hormonal IUD into the market, women across the country encountered greater LARC access, choice, and affordability. As of January 2022, more than 369,000 discounted units had been distributed to ~2,500 safety net clinics and hospitals. In 2019, Medicines360 administered a national survey of more than 200 safety net clinics and hospitals offering family planning services; 63 percent reported that stocking the Medicines360 product had increased access to contraception at their locations. One clinic's medical director went on to say, "In this moment of defunding, we would not be able to offer as much free care as we are if it weren't for [Medicines360's hormonal IUD's] low pricing," while another said in 2020, "[Medicines360's hormonal IUD] offered an opportunity for patients to receive a hormonal IUD who would not otherwise be able to afford one."

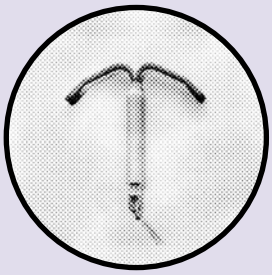
IMPROVED ACCESS

63% of surveyed safety net clinics and hospitals say the Medicines360 hormonal IUD increased access to contraception at their locations.



PUBLIC HEALTH DISTRIBUTION

As of January 2022, more than 369,000 discounted units have been distributed to ~2,500 safety net clinics and hospitals.



369,000 units

2,500 clinics

02 Decreasing total health system-level costs.

To better understand the impact of our product on total costs to the healthcare system, we commissioned a thorough evaluation of both costs and savings across several market segments. This assessment was completed by healthcare economics experts, using publicly available data for 2015-2019 (and extrapolated for 2020 and 2021, for which this data was not available).

This analysis estimates that our hormonal IUD saved approximately $82 million for the 340B segment of the healthcare system in its first seven years (2015 through 2021). Additional modeling estimates that Medicines360's hormonal IUD generated total healthcare system savings of $166 million during that same timeframe, mostly benefitting commercial payers and self-pay customers—the latter of whom are estimated to have saved over $200 each because of Medicines360's product.[49]

03 Introducing category competition that could result in increased access and lower prices.

Medicines360's extensive clinical trial research opened the door for current and future hormonal IUD manufacturers to expand their own indications in terms of both demographics and timeline. Further, Medicines360's presence

in the marketplace introduced competitive pressure that encouraged the market's only other hormonal IUD manufacturer to announce a partnership to make their products "available with greater access and affordability to all public health providers."[50]

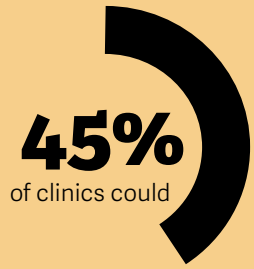
Our organization demonstrated that a nonprofit pharmaceutical organization can prioritize a public benefit, insist on high quality, and provide an innovative medical solution. Medicines360 provides ongoing support and product education through clinic engagement to public health providers. This investment—together with Medicines360's clinical data and continuing commitment to making a low-cost hormonal IUD available to 340B safety net clinics and hospitals—has resulted in increased product awareness, and use among both providers and patients across the U.S.

Impact measurement has been a critical component of Medicines360's work since our hormonal IUD first entered the market, and while our approach to impact research has evolved over time—from a singular investigative study about product uptake to directly surveying safety net clinics—these studies will continue to guide our organization's understanding of both impacts to date and opportunities for increased impact moving forward.

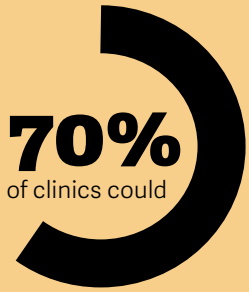
SURVEY OF 200 CLINICS

Among sites that were already offering hormonal IUD, Medicines360's hormonal IUD enabled clinics to:

Increase hormonal IUD insertions among self-pay patients



Offer hormonal IUDs to new groups of patients



Lower hormonal IUD out-of-pocket costs for self-pay patients

Increase the total number of hormonal IUD insertions

Conclusion: The Potential of Nonprofit Pharma

Medicines360's journey to bring a hormonal IUD to market reveals much about the drug development process, the healthcare system more broadly, and the potentially broadened role for nonprofit pharmaceutical organizations within the system. Although they maintain a relatively small presence in today's pharmaceutical ecosystem, nonprofits have the potential to address incentives in the U.S. drug supply chain that result in unequal access to drugs and bring transparency to otherwise opaque pricing and procurement processes. By prioritizing public health, they could both reduce costs in an inflated healthcare system and expand access to affordable, quality care for millions of Americans. Further, in their pursuit of public health priorities, nonprofits can fill market gaps that may be unappealing for for-profit companies—such as niche medical needs or high-risk research—and can advance the science of drug discovery by prioritizing thorough, diverse clinical trials with representative clinical samples.

Our journey also highlights the unique barriers that—without policy intervention—future nonprofits are certain to encounter, from securing capital for start-up costs to market economics that incentivize higher pricing. Our experience suggests that left unchanged, certain tax policies, regulatory processes, and healthcare payment arrangements may constrain the success or impact of future nonprofit pharmaceutical companies.

The opportunities for policy changes are robust. As detailed in this case study, greater federal funding for nonprofit pharmaceutical product development would encourage more organizations to enter the market with the primary goal of improving public health and would enable diverse and inclusive clinical research. Clearer guidance around generic pathways would help nonprofit organizations identify opportunities to fulfill significant public health needs with lower development costs. And government incentives for partnering with nonprofit pharmaceutical organizations and/or using their products would promote the use of low-cost drugs and reduce total system costs. Given the tremendous potential at stake, it is imperative that policymakers contemplate opportunities to create a sustainable model for these types of organizations looking to fill public health gaps and increase affordable access for patients.

Endnotes

1 Medicines360 defines safety net clinics as public health departments, disproportionate share hospitals, Planned Parenthood affiliates, and federally qualified health centers.

2 Internal M360 data on file.

3 Internal M360 data on file.

4 https://www.prnewswire.com/news-releases/afaxys-and-bayer-healthcare-form-alliance-to-expand-access-to-contraception-in-the-public-health-sector-300094950.html

5 Trussell J., et al. "Efficacy, Safety, and Personal Considerations." In: Hatcher R.A., et al. Contraceptive Technology. 21st ed. New York: Ayer Company Publishers, 2018.

6 "Long-acting reversible contraception: implants and intrauterine devices." Practice Bulletin No. 186. American College of Obstetricians and Gynecologists. 2017; 130: e251–69.

7 "Noncontraceptive uses of hormonal contraceptives." Practice Bulletin No. 110. American College of Obstetricians and Gynecologists. 2010; 115(1), 206–218.

8 Key Statistics from the National Survey of Family Growth. Center for Disease Control and Prevention. https://www.cdc.gov/nchs/nsfg/key_statistics/c.htm#contraception

9 Use of Contraception in the United States: 1982-2008

10 https://www.guttmacher.org/journals/psrh/2002/03/checkered-history-and-bright-future-intrauterine-contraception-united-states

11 https://www.kff.org/womens-health-policy/fact-sheet/intrauterine-devices-iuds-access-for-women-in-the-u-s/

12 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3412526/

13 Internal M360 data on file.

14 Red Book, accessed 2022.

15 "Price increase for IUD proves problematic for family planners." Contraceptive Technology Update. July 1, 2010. Accessed at https://www.reliasmedia.com/articles/19378-price-increase-for-iud-proves-problematic-for-family-planners

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