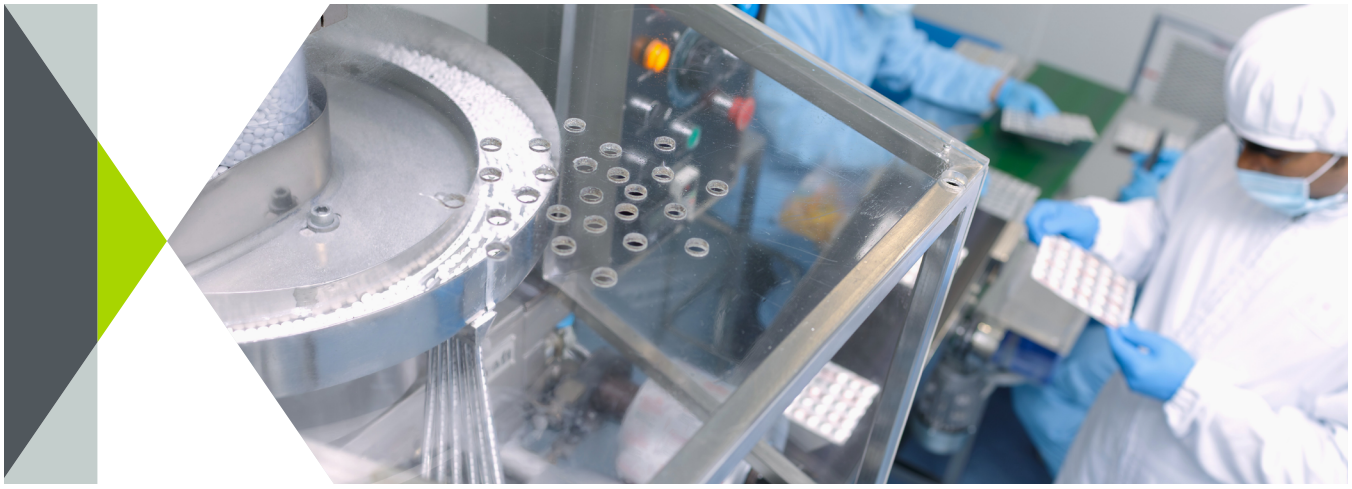


EXECUTIVE INSIGHTS

Work in Progress: Enhancing Drug Product Factors for Capturing and Sustaining Value

- In addition to data generation, biopharmas can maximize long-term value through ongoing product or franchise improvement.
- Major archetypes of such enhancements include updating the route of administration, dosing frequency, delivery device, administration time and formulation; oftentimes, these product enhancements touch on multiple archetypes.
- Biopharmas should plan ahead, striving to bring the product to market rapidly while designing postlaunch product improvements in parallel.
- The value and impact of product enhancements are often nuanced; it is paramount that biopharmas optimize these decisions across patient, physician and payer dynamics and motivate cross-product migration while acting in accordance with the evolving policy landscape.

Bringing a drug to approval is only the beginning. Continued R&D investment is a critical lever for maximizing long-term value — and one of the most effective levers is ongoing product improvement. Beyond evidence generation, pharmaceutical companies can sustain growth in core markets through formulation and delivery enhancements, whether by refining an established product or introducing a next-generation agent within the same franchise.

In this edition of *Executive Insights*, L.E.K. Consulting examines key formulation and delivery enhancement archetypes, offering key considerations and guiding principles for drug developers.

Investing in product/franchise improvements may have several benefits

Formulation and delivery improvements can strengthen the value proposition for prescribers, patients and payers — driving uptake, compliance and coverage. They can help a product remain competitive as new entrants emerge and create new stock-keeping units (SKUs) that enable differential pricing across indications. A broad portfolio within a given market also allows biopharmas to appeal to distinct stakeholder subsets and realize commercial synergies, such as a shared sales force and patient services infrastructure.

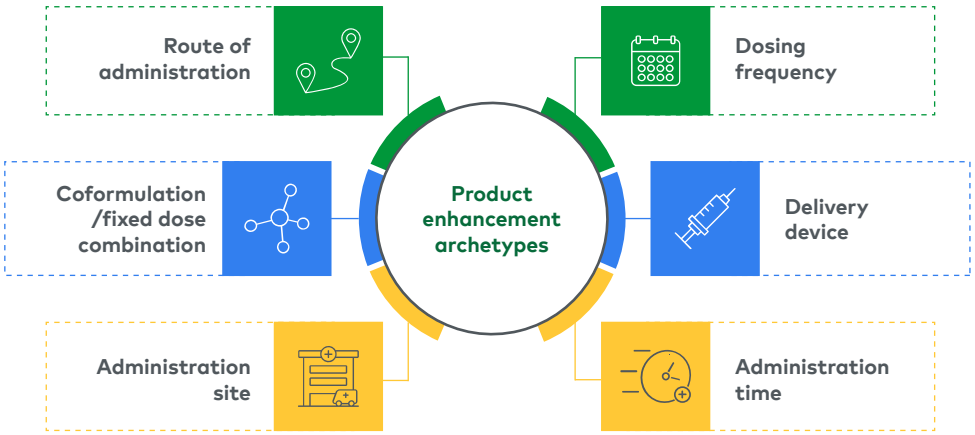
It may also help extend the product/franchise life cycle. New product versions or next-generation molecules can extend patent exclusivity and allow for product/patent hopping[1] — converting patients from a product losing exclusivity to one with additional time on patent. A variety of SKUs act as part of a "patent thicket,"[2] dissuading generic/biosimilar entry or uptake (e.g., Humira's citrate-free formulation and delivery device improvements[3]). Additionally, formulation changes have at times been used to navigate the Inflation Reduction Act's Medicare Drug Price Negotiation Program, for example, by introducing a fixed-dose combination with another "active" agent or a next-generation agent intended to constitute a distinct qualifying single source drug. This pathway is narrowing, however. In its final guidance for initial price applicability year 2028, the Centers for Medicare & Medicaid Services (CMS) revised which fixed-combination products qualify as distinct qualifying single source drugs,[4] and in a proposed rule issued in June 2026, CMS moved to codify the program permanently and further modify the fixed-combination policy to limit product modifications used to avoid selection, with comments open through August 2026.[5] Biopharmas should therefore treat formulation-driven exclusivity strategies as subject to active and tightening regulatory scrutiny rather than as a reliable lever.

There are multiple ways to improve drug formulation and delivery

With numerous methods of improving on a drug's formulation and delivery, biopharmas can draw on a range of improvement archetypes, each with distinct considerations (see Figure 1).

Figure 1

Major product enhancement archetypes

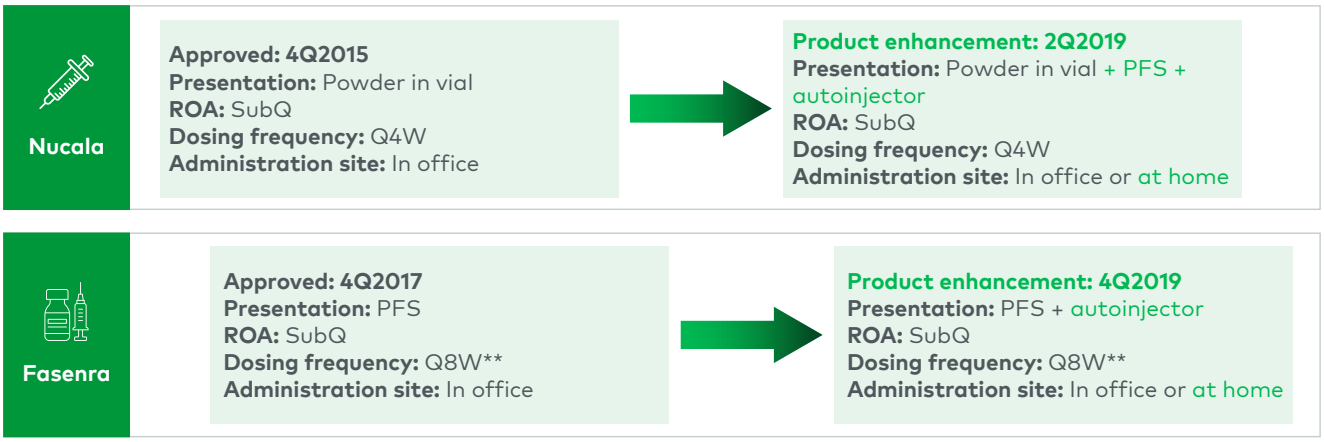


Source: L.E.K. research and analysis

In practice, a new product version or next-generation agent will often encompass multiple factors simultaneously (see Figure 2). The examples below are illustrative, not exhaustive.

Figure 2

Severe asthma anti-interleukin-5 drug timeline, US*



*Specific to severe asthma – parameters may vary for other indications; excludes Cinqair, which launched in 2016 as an IV (Q4W, in office) and failed to successfully convert to SubQ
**After Q4W dosing for the first three doses
Note: ROA=route of administration; SubQ=subcutaneous; Q4W=every four weeks; Q8W=every eight weeks; PFS=prefilled syringe; IV=intravenous
Source: Drugs@FDA

Route of administration

A new route of administration (ROA) for a given product may improve convenience and efficiency (administration time, administration site), provide optionality and potentially enhance compliance. While there are many permutations, common conversions include intravenous to subcutaneous (IV to SubQ), oral to long-acting injectable (LAI) and SubQ to oral. Many recent IV-to-SubQ conversions have been enabled by hyaluronidase-based coformulation technology, such as Halozyme[6] (e.g., Darzalex, Herceptin, Ocrevus) and Alteogen (e.g., Keytruda),[7] though they are not required (e.g., Benlysta, Entyvio, Orencia). Oral to LAI is best exemplified by franchises in schizophrenia (e.g., Abilify, Invega) and human immunodeficiency virus treatment/PrEP (Gilead, ViiV). The shift toward oral options has been featured prominently in the news with two distinct strategies in anti-obesity care. Oral Wegovy is a true reformulation: a novel oral presentation of the same semaglutide molecule that Novo Nordisk markets as a subcutaneous injection.[8] Eli Lilly's Foundayo (orforglipron) is a different play: rather than converting an existing injectable, it is a de novo oral small-molecule GLP-1 receptor agonist (Lilly's second anti-obesity product) that competes directly with injectable incumbents. The former illustrates a route-of-administration conversion within a franchise; the latter illustrates how a new oral molecule can reshape a category without an injectable predecessor. Updating the ROA typically comes with other changes to the product profile, which are covered in more detail below. Key questions when changing the ROA include:

- Does this change alter the person or location administering the drug?
- If so, is the drug delivery device conducive for such delivery?
- What are the benefits and limitations for drug administrators?

Dosing frequency

Less frequent dosing may benefit convenience and/or compliance, improve operational efficiency and make dosing more discreet and private (i.e., avoiding any disease-associated stigma). The oral-to-LAI conversions fit this category. The Abilify and Invega franchises evolved from once daily to once monthly (Abilify Maintena, Invega Sustenna) and then spaced out further: every two months (Abilify Asimtufii), every three months (Invega Trinza) and every six months (Invega Hafyera) (see Figure 3). Other examples include high-dose formulations (e.g., Eylea/Eylea HD), extended-release formulations (e.g., Keppra/Keppra XR) or different molecules (e.g., Advair/Breo).

Figure 3

Atypical antipsychotic brands by ROA, dosing frequency and FDA approval year

Decreasing dosing frequency*

	Oral	Injectable			
	Every day	Every month	Every two months	Every three months	Every six months
Abilify franchise**	Abilify (2002)	Abilify Maintena (2013)	Abilify Asimtufii (2023)		
Invega franchise	Invega (2006)	Invega Sustenna (2009)		Invega Trinza (2015)	Invega Hafyera (2021)

Brand (FDA approval)

*Typical maintenance dosing shown; indications may vary across brands
**Excludes the short-acting Abilify intramuscular pro re nata injection introduced in 2006 and Abilify MyCite (approved in 2017 as a daily oral with ingestion tracking)
Note: ROA=route of administration; SubQ=subcutaneous; Q4W=every four weeks; Q8W=every eight weeks; PFS=prefilled syringe; IV=intravenous
Source: Drugs@FDA

Altering the dosing frequency can have implications across stakeholders, making it critical to ensure the value proposition is optimized. Key questions include:

- Is dosing frequency a burden impacting patient compliance or persistence?
- How does the dosing schedule align with physician check-ins?
- Is dosing standardized in practice or do physicians opt to titrate?
- Is there a chance a patient will need to switch medications during the dosing window?
- How can a seamless transition be enabled?
- How do the dosing frequency and pricing impact physician economics and operations (e.g., inventory management, patient throughput)?

Delivery device

Ideally, delivery devices ease administration, minimizing human error and/or improving process flows. These improvements can help enable at-home administration for drugs that might otherwise require an in-office visit while allowing administration that accommodates the patient's schedule. To illustrate the concept simply, a prefilled syringe removes a process step and potential error associated with vial transfer. An autoinjector may further improve the process, allowing a patient to self-inject with a hidden needle and improved ergonomics. The Auvi-Q autoinjector provides voice-guided instructions, aiding emergency epinephrine

administration. A manufacturer can also offer dosing optionality through a variety of delivery devices. Improving on drug delivery may provide additional benefits as well. Having multiple device options provides optionality; for example, Empaveli is a large-volume SubQ drug that can be administered with a commercially available pump (e.g., Koru[9]) or an on-body delivery system (e.g., Enable's enFuse[10]).

Sometimes a device can change a process flow more radically — Neulasta OnPro provides a delayed dose, obviating the need for a next-day clinic visit and addressing a market pain point in a way that poses a strong defense against biosimilar competition.[11] Drug delivery may also incorporate digital features and mobile connectivity. For example, the Omnipod automated insulin delivery system captures disease management insights and integrates with continuous glucose monitoring devices (e.g., Dexcom, FreeStyle Libre). For additional perspectives on drug delivery devices, please see other recent L.E.K. Executive Insights.[12, 13]

When opting for a delivery device, biopharmas need to understand the range of administrators (patient, caregiver, healthcare provider [HCP]), the strength of the value proposition for each and any potential risks. Human factor studies are critical. Key questions include:

- Is the device essential or a nice-to-have?
- How would the device improve drug delivery?
- How valuable is this improvement to different user archetypes?
- What are the risks of misuse or mechanical failure?

Administration time

Delivery devices and IV-to-SubQ conversions — both discussed above — are among the most impactful levers for reducing administration time and improving patient convenience. For HCP-administered drugs, this can help improve throughput, allowing centers to dose more patients given the constraints on infusion chairs and/or support staff. Such benefits need to be kept in the context of real-world drug usage and administration to ensure the value proposition is not diluted. Key questions include:

- Is the drug dosed in combination with other IVs?
- What does the HCP need to do to administer the drug?
- Will new process flows be required?

Administration site

Shifting the site of administration may drive benefits but requires navigating a more complex web of reimbursement economics and stakeholder incentives.

Moving from outpatient HCP administration to self-/caregiver administration improves convenience — patients no longer must travel to receive their medication. It also shifts a product from the medical benefit to the pharmacy benefit. This provides payers with greater utilization management control and financial incentives (as such, sometimes payers push toward "white bagging" to circumvent the medical benefit). For HCPs, the impact is more mixed. It frees up HCP time and resources (e.g., inventory, administration); however, it removes the buy-and-bill financial incentives, it may remove a desired patient check-in and it may introduce dosing errors. Examples include Nucala and Fasenra (initially HCP-administered SubQs) and Entyvio (IV to SubQ). Neulasta OnPro's delayed dose allowed it to remain HCP-administered and reimbursed under medical benefit, retaining buy-and-bill economics while still enabling at-home dosing. Conversely, Cosentyx launched in 2015 as a self-administered SubQ and added an IV option in 2023, which allowed it to address patients who preferred not to self-administer and physicians/centers that preferred buy-and-bill.

Biopharmas can also help shift clinical practice to move HCP-administered inpatient (i.e., hospital benefit) drugs to outpatient. Chimeric antigen receptor T (CAR-T) therapies are a prime example, with studies supporting outpatient dosing, with inpatient admission as needed.[14] This frees up hospital resources while making the billing/reimbursement simpler and more financially viable.

Key questions when altering administration site include: **How does in-office administration impact patient compliance and fit into disease management? How do prescribers value the buy-and-bill option? What is the expected impact on utilization management?**

Coformulation/fixed-dose combination

Drugs may be coformulated or combined with other agents commonly dosed together individually (e.g., Janumet is Januvia plus metformin) or to enable a new dosing option (e.g., hyaluronidase-based formulations enabling IV-to-SubQ conversion). Phesgo is an example that does both — a combination of Roche/Genentech's Herceptin, Perjeta and hyaluronidase for SubQ use. A manufacturer can also opt to introduce a new product in fixed-dose combination with an older one it owns (e.g., Opdualag), providing life cycle benefits for the older product. A fixed-dose combination acts as a new branded product and comes with exclusivity benefits. For a manufacturer, the cost of a fixed-dose combination varies and may become

operationally complex if spanning multiple branded owners. Key questions when developing a fixed-dose combination include:

- **Are the components' dosing and schedules conducive to coformulation?**
- **Are there any other combination agents that need to be added on top?**
- **What is the risk of circumventing the fixed-dose combination with individual components?**

Others

The categories above are not exhaustive. A few additional examples illustrate how product improvements often span multiple factors simultaneously. Humira removed citrate, lowered dosing volume and altered needle gauge to reduce injection-site pain. Daybue was originally launched as an oral solution that required refrigeration and discarding 14 days after opening the bottle; Daybue Stix, an oral powder, was introduced to offer flexibility and choice in dose volume and taste (by mixing with different water-based liquids) while allowing for room-temperature storage.[15]

Biopharmas should carefully plan for optimized product improvements across the drug life cycle

Investment in life cycle management behind a strong product is a critical lever, allowing products to reach new patients, enhance benefits to users and protect share from branded and generic competition. Given the breadth of formulation and delivery options available, biopharmas should consider the following guiding principles:

- **Do not sacrifice time to market:** Biopharmas should maintain their focus on bringing viable products to market in a timely fashion, accelerating patient benefit and generating revenues to support operations. Unless the initial product presentation is a significant detraction, product improvements should be made after the initial approval and launch.
- **Plan product improvements in parallel with development:** Given pressures on product life cycle (e.g., Medicare Price Negotiation, competition), biopharmas should plan ahead. Sequential development may sacrifice time on market and the ability to convert patients from one product to another.
- **Enable switching:** Generate data (e.g., switch studies, noninferiority/head-to-head, human factors), create protocols (e.g., Invega's[16]) and offer support services to motivate switching to the next-gen drug while alleviating any concerns or frictions from physicians, patients or payers. An ideal strategy migrates ahead of loss of exclusivity.

- **Optimize product improvements to address stakeholder preferences and unmet needs:** It is critical to understand the implications of planned product improvements across stakeholder types, optimizing the improvement and its commercial support. Often the theoretical benefit is more nuanced in the real world. Value proposition testing should be coupled with a detailed understanding of practice economics, which should be incorporated in the go-to-market strategy.
- **Ensure regulatory and legal integrity and distinguish genuine value from evasion:** The policy environment around life cycle management is tightening, not stabilizing. CMS is moving to codify the Medicare Drug Price Negotiation Program permanently and to narrow the fixed-combination and new-formulation pathways that have been used to defer selection, and the Federal Trade Commission has signaled continued scrutiny of product/patent hopping and patent thickets. Enhancements that deliver real, demonstrable benefit to patients, physicians or payers (e.g., improved adherence, reduced administration burden, lower total cost of care) sit on durable ground and are unlikely to draw the same scrutiny. Enhancements pursued primarily to reset exclusivity or evade negotiation carry escalating regulatory, legal and reputational risk, and biopharmas should pressure-test each planned improvement against that distinction, not merely confirm technical compliance.

L.E.K. has extensive experience optimizing product value propositions and supporting life cycle development planning across the biopharma sector. For more information, please **contact us.**

Endnotes

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