



Article

A Decade of Innovation: Medicinal Products with New Active Substances Centrally Authorized Within the EU Between 2011 and 2020

Robert Ancuceanu ¹ , Doina Drăgănescu ^{2,*}, Beatrice Elena Lascu ¹ and Mihaela Dinu ¹

¹ Department of Pharmaceutical Botany and Cell Biology, Faculty of Pharmacy, Carol Davila University of Medicine and Pharmacy, 050474 București, Romania; robert.ancuceanu@umfcd.ro (R.A.); beatrice-elena.lascu@drd.umfcd.ro (B.E.L.); mihaela.dinu@umfcd.ro (M.D.)

² Department of Pharmaceutical Physics and Informatics, Faculty of Pharmacy, Carol Davila University of Medicine and Pharmacy, 050474 București, Romania

* Correspondence: doina.draganescu@umfcd.ro

Abstract

Background: Pharmaceutical innovation plays a vital role in advancing global health. This study evaluates the landscape of pharmaceutical innovation in the European Union (EU) over the 2011–2020 decade. **Methods:** A retrospective analysis was performed on new medicinal products containing new active substances (NAS) authorized between 2011 and 2020 through the centralized procedure. Products were categorized into first-in-class, advance-in-class, and addition-to-class. Trends in therapeutic areas (ATC codes), orphan designation, technology platforms, administration routes, and dosage forms were analyzed. **Results:** Across the decade, 357 new medicinal products received authorization. Of these, 56% were designated as first-in-class and 28% as advance-in-class, indicating that 84% of new products contributed substantive therapeutic innovation. Small molecules remained the predominant technology (63.5%), yet the decade also witnessed a pronounced expansion in monoclonal antibodies and the introduction of cell and gene therapies (Advanced Therapy Medicinal Products, ATMPs). The increased use of subcutaneous delivery systems, particularly for monoclonal antibodies, suggests a broader shift toward patient-centered administration routes. **Conclusions:** Between 2011 and 2020, pharmaceutical innovation in the European Union (EU) was characterized by a high rate of breakthrough innovations and a transition to more sophisticated biologic therapies. The EU could boost innovation further by refining expedited approval pathways (e.g., PRIME).

Keywords: pharmaceutical innovation; innovation metrics; EMA; first-in-class; advance-in-class; addition-to-class; marketing authorizations



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1. Introduction

Pharmaceutical innovation plays a key role in enhancing population health outcomes by extending life expectancy, improving quality of life, expanding the range of available treatments, reducing costs, and elevating the overall efficiency of healthcare systems [1]. Pharmaceutical innovation plays a partial yet meaningful role in shaping population health over the long term. The health of pharmaceutical companies is more directly tied to their ability to bring new drugs to market [2].

Definitions of innovation are diverse, often highlighting aspects such as economic growth, job creation, and profit for the innovators [3]. From both medical and patient

perspectives, value primarily stems from meeting therapeutic needs and achieving health outcomes, rather than from intrinsic novelty or macroeconomic impacts [4]. It has therefore been argued that neither novelty alone nor effectiveness on its own are sufficient to define pharmaceutical innovation, and combining the two does not necessarily result in its definition [4]. Significant progress often stems from a series of small advancements rather than isolated breakthroughs. Historical examples demonstrate this: Orville Wright's initial 37-m (120 feet) flight in a heavier-than-air machine [5] paved the way, through many incremental improvements, for routine transatlantic flights today. The journey to modern high-fidelity sound began with the Edison phonograph, a basic device whose initial recordings were dismal (with considerable background noise) and very short-lived; it was only through a series of gradual, cumulative enhancements that today's sophisticated instruments were achieved. The first human kidney transplant was performed by Dr. Yurii Voronoy in Ukraine on April 3, 1933, with the patient surviving for just two days; similar pioneering attempts in Boston, Chicago, and Paris also ended in failure [6]. In the field of pharmaceuticals, compounds that initially exhibit limited efficacy or effectiveness can nonetheless introduce innovative characteristics that, through refinement, may lead to the development of approved therapies. Consequently, iterative research efforts are preferable to stagnation. Particularly from the pharmaceutical perspective, innovation has been defined as "the technological progress that leads to the creation of an entirely new product or a reduction in the cost of producing or an increase in the therapeutic value of an existing product" [7,8].

Pharmaceutical innovation can be assessed through four interconnected dimensions: (1) novelty, which refers to the degree of newness in the active ingredient, mechanism of action, or technological platform, such as distinguishing between first-in-class and follow-on drugs [1]; (2) therapeutic value, which includes enhancements in efficacy, safety, tolerability, quality of life, or addressing unmet needs [1,9]; (3) the nature or degree of innovation, whether incremental or radical, ranging from minor iterative improvements to significant breakthroughs, with cumulative advancements often resulting in substantial long-term progress [10]; and (4) practical impact, which encompasses benefits like improved adherence, convenience, reduced treatment burden, lower costs, or broader accessibility [11]. These dimensions are interrelated, and a comprehensive evaluation requires balancing all four rather than concentrating on a single criterion.

In the mid-2000s, concerns were expressed that the pharmaceutical sector prioritized "me-too" products over true novelty [12], while in 2011, two United States (U.S.) researchers stated that few new drugs were reaching the market amid rising research and development (R&D) costs [13]. A 2009 analysis spanning 60 years showed dramatic increases in annual R&D investment (reaching \$50 billion), yet stagnant new medicine approvals (only 21 (new molecular entities (NMEs) in the US in 2008), and noted that just 6% of over 4300 companies had registered an NME since 1950 [14]. These patterns prompted inquiries into the sustainability of the industry and its capacity for long-term innovation.

The decade from 2011 to 2020 was a crucial period to evaluate whether these concerns persisted or improved, particularly in the wake of the Human Genome Project's completion. This project had promised more targeted, personalized drug development and raised expectations for incremental progress leading to significant advances in the following decades (although it was accepted that improvements in healthcare effectiveness would still be limited and only bloom during the 2021–2030 decade) [15].

While quantifying innovation (e.g., via NME counts) is straightforward [16,17], measuring its quality with appropriate metrics remains challenging. To address this, industry critics have invented systems that categorize innovations into labeled tiers (e.g., "highly innovative," "moderately innovative"), sometimes basing these labels on the assessment

of a drug's value at the time of its initial approval by the relevant regulatory authority. In the literature, however, this approach has been evaluated as follows: "But this approach is far from reliable and is just as subjective and selective as anecdotal descriptions of innovations." [12]. Conventional distinctions between "radical" (typically NMEs) and "incremental" (me-too drugs, reformulations) innovations are muddled, as many me-too products are NMEs while non-NMEs (e.g., enantiomers, new dosage forms) may also qualify as incremental.

More nuanced frameworks include a four-tier general model (incremental, market breakthroughs, technology breakthroughs, and radical) [18] and a pharmaceutical-specific tripartite approach by Lanthier et al. (2013), categorizing NMEs as first-in-class (novel mechanisms establishing new pathways), advance-in-class (follow-ons with priority review for major clinical improvements), or addition-to-class (functional similarity without substantial gains) [17]. Alternative scaffold-based distinctions (pioneers, settlers, and colonists) have also been proposed [19]. These highlight that not all NMEs or blockbusters are equally innovative [20].

The European Medicines Agency (EMA) is a decentralized EU agency based in Amsterdam that evaluates, supervises, and monitors medicines for use in the EU. It protects public and animal health by ensuring that medicines in the EU market are safe and effective. The EMA assesses applications for new medicines, recommends marketing authorizations, and monitors approved medicines through pharmacovigilance. It provides scientific guidance to companies, supports research, and evaluates vaccines during health emergencies. While the EMA makes recommendations, the European Commission makes final, binding decisions for EU member states [21–24].

Robust, objective measurement of pharmaceutical innovation remains limited, especially outside the US. This paper aims to explore how medical progress can be quantified using the methodological framework proposed by Lanthier et al. [17], applying it to European centralized regulatory data from the EMA, and analyzing patterns of pharmaceutical innovation from 2011 to 2020. Specifically, the paper addresses three research questions: (1) What was the overall scale and magnitude of therapeutic innovation introduced to the EU market during 2011–2020? (2) What were the principal characteristics and distinctive features of new medicines approved by the European Commission based on EMA recommendations over this period? (3) How can the assessment of pharmaceutical innovation be refined to capture more nuanced dimensions?

This approach allows for a comprehensive evaluation of the decade's contributions, bridging earlier concerns about stagnation with evidence on whether (and how) innovation evolved in response to scientific, regulatory, and therapeutic drivers.

2. Materials and Methods

2.1. Data Set Compilation and Data Extraction

A dataset on marketing authorizations (MAs) granted by the EMA for medicinal products containing new active substances (NMEs) between 2011 and 2020 was compiled through manual extraction and synthesis of publicly available regulatory information from the EMA. The decade 2011–2020 was selected for three main methodological and substantive reasons:

- (a) The period ends in 2020 to maintain a ten-year window unaffected by COVID-19 disruptions (which impacted regulatory pathways and approvals through 2024), providing an undistorted comparator for 2021–2030.
- (b) Using the complete 2011–2020 decade creates a stable benchmark for analyzing 2021–2030 using identical methodology. Including post-2020 data would introduce

- pandemic-related effects from emergency authorizations and shifted priorities, compromising comparability across decades.
- (c) The 2011–2020 period, following the Human Genome Project, coincides with the expansion of targeted therapies, biologics, ATMPs, and new regulatory tools. This window evaluates how these advances influenced pharmaceutical innovation under the European centralized procedure.

This study is a retrospective, census-based descriptive analysis of all medicinal products authorized through the European centralized procedure between 1 January 2011 and 31 December 2020. The primary source was Annex 9 or 10 of the EMA’s Annual Reports (2011–2020) [25], which provided structured summaries of newly authorized medicinal products, including therapeutic class, innovation status, and regulatory milestones. Additional data, particularly for defining the innovation class for each product, were retrieved from the European Public Assessment Reports (EPARs) [26] and the Union Register of medicinal products [27], and relevant scientific literature was identified through searches in PubMed and Google Scholar. The year of authorization reflects the date of initial EU marketing approval. Inclusion in the PRIME scheme was assessed based on the relevant list published by the EMA [28]. Food and Drug Administration (FDA) breakthrough therapy designations were evaluated based on the chart made publicly available by Friends of Cancer Research [29]. FDA priority review status was assessed based on two sources: the compilation of Center for Drug Evaluation and Research (CDER) NME and New Biologic Approvals 1985–2024, prepared by the FDA [30] and information made publicly available by the FDA for each authorized drug (retrieved through a manual search for each product) [31]. The main sources of information, including the key variables extracted, weblinks, and dates of access, are summarized in Table 1.

Two researchers (RA and BEL) independently carried out the tasks of data extraction and classification. They utilized a standardized electronic data extraction form to gather the following details for each centrally authorized medicinal product: brand name, international non-proprietary name (INN), dosage form, route of administration, technology class, whether it was a first-in-class product (with a brief explanation), year, classification if not first-in-class, ATC code, EMA orphan status (at the time of the CHMP opinion), and EMA product number. Discrepancies between the two researchers were identified through both automated comparison and manual review. Any disagreements were resolved through consensus discussions among the four authors.

Table 1. Overview of the data collection framework, including primary information sources, key variables, URLs, and retrieval dates.

Source	Key Variables Extracted	Weblink
EMA Annual Reports (2011–2020), Annex 9 or 10	Brand name, INN, therapeutic class/ATC code, year of authorization, orphan status	https://www.ema.europa.eu/en/about-us/annual-reports-work-programmes , accessed on 5 January 2026
European Public Assessment Reports (EPARs)	Detailed information for defining innovation class, first-in-class status, technology class, rationale, dosage form, route of administration, ATC code	https://www.ema.europa.eu/en/medicines/download-medicine-data , accessed on 5 January 2026
Relevant scientific literature (PubMed and Google Scholar)	Additional data for innovation classification, first-in-class explanations, and rationale	https://pubmed.ncbi.nlm.nih.gov/ and https://scholar.google.com/ , accessed on 5 January 2026

Table 1. *Cont.*

Source	Key Variables Extracted	Weblink
EMA PRIME scheme list	Inclusion in the PRIME scheme	https://www.ema.europa.eu/en/human-regulatory-overview/research-development/prime-priority-medicines (monthly updated list), accessed on 5 January 2026
Friends of Cancer Research—Breakthrough Therapy Designations chart	FDA breakthrough therapy designations	https://friendsofcancerresearch.org/breakthrough-therapies , accessed on 5 January 2026
FDA Compilation of CDER NME and New Biologic Approvals (1985–2024)	FDA priority review status and related approval details	https://www.fda.gov/drugs/drug-approvals-and-databases/compilation-cder-new-molecular-entity-nme-drug-and-new-biologic-approvals , accessed on 5 January 2026
FDA individual product information (manual search)	Additional confirmation of FDA priority review status (when not included in the compilation)	https://www.accessdata.fda.gov/scripts/cder/daf/ (Drugs@FDA), accessed on 5 January 2026

2.2. Inclusion and Exclusion Criteria

A list of the criteria used in collecting the data, as well as the inclusion and exclusion criteria, is shown in Table 2, and all main definitions for the purpose of this study are included in Table 3.

Table 2. Inclusion and exclusion criteria for medicinal products analyzed in this study.

Criterion	Inclusion	Exclusion
Study period	Marketing authorizations granted by the European Commission via the centralized procedure between 1 January 2011 and 31 December 2020	Authorizations granted before 1 January 2011 or after 31 December 2020
Type of authorization	All initial marketing authorizations	Marketing authorizations for active substances previously authorized within the EU, as well as line extensions and variations
New active substance (NAS) status	Products containing a new active substance at the time of the first marketing authorization in the EU	Products whose active substance had already received a previous EU marketing authorization (even under a different brand or combination)
Fixed-dose combinations	Included if at least one component qualifies as a new active substance at the time of authorization	Combinations in which all active substances had been previously authorized in the EU
Duplicate/subsequent authorizations of the same active substance	Only the first marketing authorization of a given active substance was retained	Subsequent authorizations of the identical active substance (e.g., a standalone product after an initial combination, or a later brand under a different MAH)
Biosimilar or generic products	Not applicable (excluded by definition)	All biosimilars and generics

Table 2. Cont.

Criterion	Inclusion	Exclusion
Special cases: same substance, different manufacturing/formulation	Treated as the same active substance unless the applicant successfully demonstrates that the new version differs significantly in safety and/or efficacy (case-by-case assessment based on the EPAR)	Products considered by the EMA/CHMP to be essentially the same active substance
Withdrawn products	Products that received marketing authorization within the study period are included, even if later withdrawn (e.g., Unituxin)	-
Distinct but related substances	Different active substances are counted separately when the applicant provides evidence of meaningful differences in manufacturing process, safety, or efficacy (e.g., dinutuximab vs. dinutuximab beta)	Products not accepted by the EMA as distinct active substances

Table 3. Main definitions used in the study, including source, legal status, and rationale for selection.

Term	Definition Used in This Study	Source	Legally Binding?
New active substance (NAS)/New molecular entity (NME)	An active substance that has not been previously authorized as a medicinal product in the European Union. In the case of biologics, a biological substance previously authorized but differing significantly in molecular structure, source material, or manufacturing process with regard to safety and/or efficacy.	EMA (Annex I to Directive 2001/83/EC and related reflection papers)	Yes (EU pharmaceutical legislation)
First-in-class	A medicinal product drug that works through a new biological mechanism of action (targeting a pathway, receptor, enzyme, or process that no previously approved drug has targeted).	Scientific literature and standard pharmacotherapeutic classification (e.g., new ATC 4th level or novel target); applied after review of EPAR and primary literature	No (scientific/consensus-based classification)
Advanced therapy medicinal product (ATMP)	Briefly, any of the following medicinal products for human use: a gene therapy medicinal product, a somatic cell therapy medicinal product, or a tissue-engineered product (as defined in EU legislation, i.e., Regulation 1394/2007)	Regulation (EC) No 1394/2007 and Directive 2009/120/EC	Yes (EU legislation)

Table 3. Cont.

Term	Definition Used in This Study	Source	Legally Binding?
Orphan medicinal product	Briefly, a medicinal product intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition that affects not more than 5 in 10,000 persons in the EU (or would not be developed without incentives), and where no satisfactory authorized method exists or the product offers significant benefit (the full legal definition is provided in Regulation 141/2000)	Regulation (EC) No 141/2000	Yes (EU orphan legislation)
PRIME scheme	A “scheme run by the European Medicines Agency (EMA) to enhance support for the development of medicines targeting unmet medical needs. It is based on early dialogue with companies to optimize development plans and speed up evaluation.”	EMA PRIME guidance	No (voluntary regulatory scheme; eligibility is EMA decision-based)
FDA Breakthrough Therapy designation	“A process designed to expedite the development and review of drugs that are intended to treat a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).”	FDA (FDASIA, Section 902)	Yes (U.S. legislation)
FDA Priority Review designation	A system created by the FDA where the goal of the regulatory authority “is to take action on an application within 6 months (compared to 10 months under standard review).”	Prescription Drug User Act (PDUFA), FDA guidance	Yes (U.S. legislation)

Specific examples illustrating the applications of the inclusion and exclusion criteria and the specific challenges are included in the Supplementary File S1 document.

2.3. Innovation Classification

Each centrally authorized medicinal product was classified according to the tripartite framework proposed by Lanthier et al. (2013) [17], which distinguishes three levels of innovation: first-in-class (products introducing a novel mechanism of action), advance-in-class (products offering meaningful improvements in efficacy, safety, or tolerability within an established therapeutic class), and addition-to-class (products providing therapeutic benefits similar to existing agents without substantial added value). Regulatory designations such as FDA Priority Review or the EMA PRIME scheme were not used as primary criteria for innovation classification. These designations are influenced by multiple factors beyond

intrinsic novelty or therapeutic merit, including submission timing, sponsor engagement, and regulatory resource considerations. Moreover, significant differences exist in the use of expedited pathways across regulatory jurisdictions, with expedited designations being granted substantially more frequently by the FDA than by the EMA [32,33]. Consequently, reliance on such designations would risk systematic misclassification of innovative products. Classification into the advance-in-class category was therefore based on the authors' expert assessment, informed by peer-reviewed clinical and pharmacological literature. This assessment considered the product's pharmacodynamic mechanism, comparative efficacy and safety data from pivotal trials, and therapeutic positioning relative to existing treatments. All classifications were performed independently by two authors (RA and MD). Discrepancies were resolved through discussion among all four authors until consensus was reached. The classification was conducted exclusively from the European Union regulatory perspective, taking into account the date of marketing authorization by the European Commission and the therapeutic context at the time of approval. Following peer review, and at the suggestion of an anonymous reviewer, we conducted a sensitivity analysis to validate our initial classifications. This involved cross-referencing our dataset with the PRIME scheme (EMA), as well as FDA breakthrough therapy and priority review statuses to ensure consistency in our assessment of therapeutic innovation.

The complete dataset, including the innovation classification and a brief rationale for each product, is provided in Supplementary Table S1.

2.4. Statistical Analysis

All statistical analyses were performed using R, v. 4.5.2 [34], under Rstudio (2023.06.0 Build 421) [35]. Graphs were generated using the "ggplot2" R package [36]. Because the dataset represents the full population of medicines approved during the study period (a census), results are presented descriptively using counts and proportions rather than inferential statistical tests.

3. Results

3.1. Distribution by Innovation Degree

A total of 357 medicinal products containing new active substances were authorized by the European Commission via the centralized procedure between 2011 and 2020 (Figure 1). Of these, 204 were classified as first-in-class. The remaining 154, while based on new active ingredients, did not qualify as first-in-class and were therefore considered to represent a lower level of innovation. Within this group, 55 were categorized as additions-to-class and 98 as advances-in-class.

While inclusion in regulatory programs such as the EMA's PRIME scheme or the FDA's Breakthrough Therapy and Priority Review designations was not the primary metric for our innovation classification, we conducted a sensitivity analysis to assess the concordance of our framework with these external benchmarks. Within the dataset, 13 products were enrolled in the PRIME scheme, 92.31% ($n = 12$) of which were independently identified as first-in-class by our model. This high level of alignment suggests strong validity for our classification criteria. Analogous results were observed for products utilizing FDA pathways, including Breakthrough Therapy designation (Table 4) and Priority Review (Table 5).

Priority review vouchers (PRVs) can be bought or earned by a company and then redeemed to secure priority review, regardless of the product's inherent attributes. Using a PRV does not mean the product qualifies for priority review on its own; it simply shortens the review timeline [32]. The dataset contained only five products in this category, and they were predominantly used for less innovative products rather than first-in-class ones.

Upon aggregating the “advance-in-class” and “first-in-class” categories, breakthrough therapy designations exhibited 88.24% concordance with at least some degree of therapeutic innovation. Similarly, priority review status was associated with innovation in 90.86% of the analyzed cases. Such results provide empirical validation for the classification used in the framework of this paper.

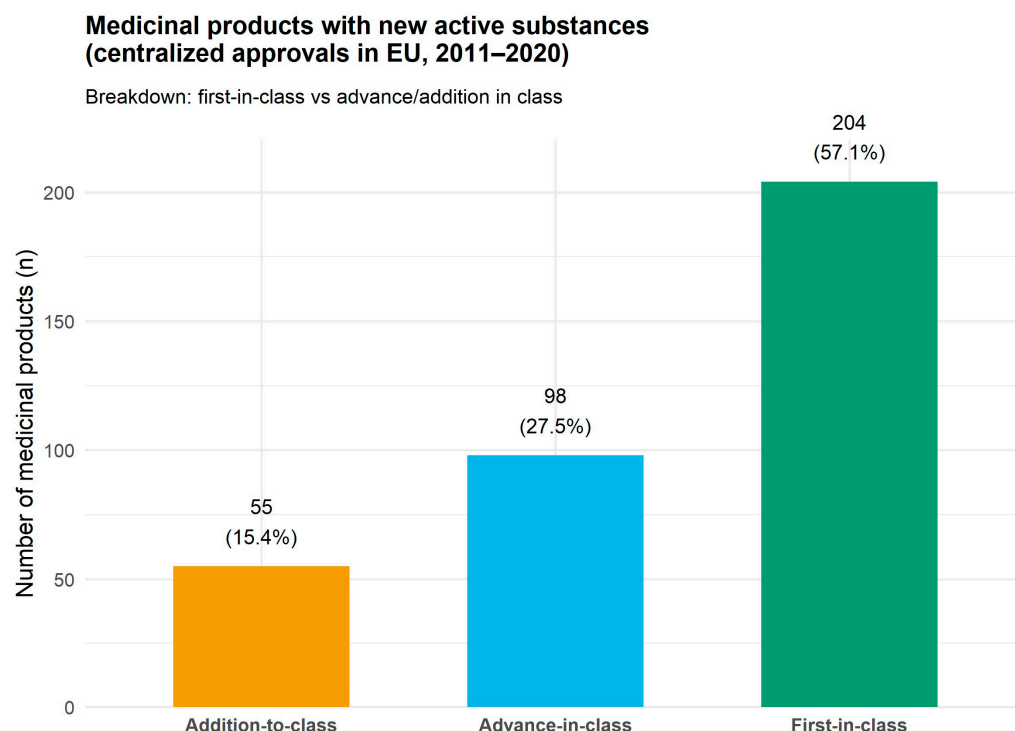


Figure 1. Distribution of the 357 medicinal products by their innovation status: first-in-class, advance-in-class, or addition to class.

Table 4. Relationship between novelty and Breakthrough Therapy status across the entire dataset of medicinal products.

Breakthrough Designation	Addition-to-Class (%) (N)	Advance-in-Class (%) (N)	First-in-Class (%) (N)	Total (%) (N)
Yes	11.76 (12)	21.57 (22)	66.67 (68)	100.00 (102)
No	17.98 (41)	30.26 (69)	51.75 (118)	100.00 (228)
Not FDA approved	7.41 (2)	25.93 (7)	66.67 (18)	100.00 (27)

Table 5. Relationship between novelty and Priority review status across the entire dataset of medicinal products.

Priority Review Status	Addition-to-Class (%) (N)	Advance-in-Class (%) (N)	First-in-Class (%) (N)	Total (%) (N)
Yes	9.14 (17)	23.66 (44)	67.20 (125)	100.00 (186)
No	24.64 (34)	32.61 (45)	42.75 (59)	100.00 (138)
Not FDA approved	7.14 (2)	25.00 (7)	67.86 (19)	100.00 (28)
Priority with voucher redemption	40.00 (2)	40.00 (2)	20.00 (1)	100.00 (5)

3.2. Time Evolution

The year-by-year pattern (Figure 2) of newly authorized products indicates a general upward tendency over the decade, but with intermittent variability marked by two pronounced drops in 2016 and 2019, each followed by substantial recovery in the subsequent year. The lowest number (30) of new MAs granted was in 2011, while the highest (41) was granted in 2018 and 2020. With the exception of 2013, first-in-class products outnumbered advance-in-class products in every year of the dataset.

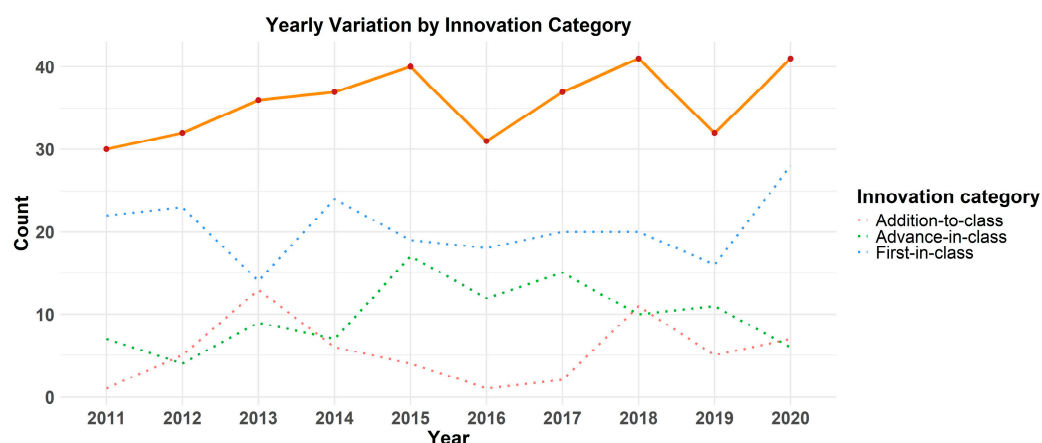


Figure 2. Number of new marketing authorizations (MAs) granted yearly by the European Commission between 2011 and 2020 within the European Union, showing year-to-year variation (the three interrupted lines) and an overall upward trend despite intermittent declines (the continuous line).

3.3. Variation by Therapeutic Class

The 357 medicines vary widely by therapeutic class, as shown in Table 6. The most widely represented class is that of antineoplastic and immunomodulating agents, which alone accounted for 36.1% of the total; in other words, on average, out of every three newly authorized medicinal products, one was an anticancer or immunomodulating agent. At the opposite pole, only three new medicines were part of the systemic hormonal preparations class.

Table 6. Distribution of the 357 new medicinal products by the ATC code.

ATC Code	Category	Drug Count
L	Antineoplastic and immunomodulating agents	129 (36.13%)
J	Anti-infectives for systemic use	64 (17.93%)
A	Alimentary tract and metabolism	36 (10.08%)
B	Blood and blood forming organs	34 (9.52%)
N	Nervous system	24 (6.72%)
V	Various	17 (4.76%)
C	Cardiovascular system	11 (3.08%)
M	Musculo-skeletal system	10 (2.80%)
R	Respiratory system	10 (2.80%)
D	Dermatologicals	7 (1.96%)
S	Sensory organs	7 (1.96%)
G	Genito-urinary system and sex hormones	5 (1.40%)
H	Systemic hormonal preparations	3 (0.84%)

The 130 antineoplastic and immunomodulating agents authorized over the last decade are distributed unevenly across the four major ATC classes. Antineoplastic agents (L01) dominate the landscape with 92 products, followed by 29 immunosuppressants (L04). In contrast, endocrine therapies (L02) and immunostimulants (L03) represent a much smaller share of the market, with only four approvals each. Among the 92 antineoplastic agents, 53 were first-in-class, 21 advance-in-class, and 18 addition-to-class.

Within the category of anti-infectives for systemic use (ATC code J), antivirals (J05) were the most prevalent, accounting for 27 products, followed by vaccines (J07, $n = 18$) and antibiotics (J01, $n = 13$). The J06 class (immune sera and immunoglobulins) was limited to two (first-in-class) monoclonal antibodies: Zinplava (bezlotoxumab) and Nyxthracis (obil-toxaximab). Innovation in other subclasses was also limited; only two antimycobacterials (Sirturo and Dovprela, bedaquiline and pretomanid, respectively) and a single systemic antimycotic (Cresemba-isavuconazole) were authorized during this period.

Among the products for the alimentary tract and metabolism (ATC code A), the most widely represented were those of subclass A10 (drugs used in diabetes, 12 products), and A16 (other alimentary tract and metabolism products, $n = 15$).

3.4. Variation by Technology Class

A synthetic presentation of the technology classes to which the 357 medicinal products belong is shown in Table 7.

Table 7. Distribution of the 357 medicinal products by the technology class used.

Technology Class	Number of Medicinal Products	First in Class (% Within Column)	Advance in Class (% Within Column)	Addition to Class (% Within Column)
Small molecules	157	80 (39.22%)	50 (51.02%)	27 (49.09%)
Monoclonal antibodies	64	45 (22.06%)	6 (6.12%)	13 (23.64%)
Proteins/polypeptides	52	33 (16.18%)	12 (12.24%)	7 (12.73%)
FDCs	26	5 (1.96%)	17 (17.35%)	4 (9.09%)
Vaccines	18	9 (4.41%)	9 (9.18%)	0 (0.00%)
Radiopharmaceuticals	9	7 (3.43%)	0 (0.00%)	2 (3.64%)
ATMP cell therapies	5	5 (2.45%)	0 (0.00%)	0 (0.00%)
Gene therapies (excluding CAR-T cells)	5	5 (2.45%)	0 (0.00%)	0 (0.00%)
siRNA	4	4 (1.96%)	0 (0.00%)	0 (0.00%)
Complex, non-herbal	5	2 (0.98%)	2 (2.04%)	1 (1.82%)
CAR-T cells	3	3 (1.47%)	0 (0.00%)	0 (0.00%)
Antisense oligonucleotides	3	3 (1.47%)	0 (0.00%)	0 (0.00%)
Complex, herbal	3	3 (1.47%)	0 (0.00%)	0 (0.00%)
Glycopeptides	3	1 (0.49%)	2 (2.04%)	0 (0.00%)
Total	357	204 (100.00%)	98 (100.00%)	55 (100.00%)

Bold type: Shows the total values.

We were also interested in whether these technology classes followed certain time trends across the analyzed decade. Between 2011 and 2020, the number of small-molecule medicine authorizations in the EU showed no sustained long-term trend, fluctuating

considerably from year to year. This moderate variability included peaks in 2013 and 2020 and a sharp dip in 2016 (Figure S1).

In contrast, monoclonal antibodies (mAbs) displayed a clear upward dynamic over the decade. Approvals were modest early on (two to three per year from 2011 to 2013) but began to expand rapidly starting in 2014–2015, driven by a sharp increase in 2015 (nine approvals). This sustained high output in the mid-2010s led to a plateau of consistently higher approval numbers in the latter part of the decade (Figure S2). The proportion of mAbs among the first-in-class medicinal products (22.06%) was almost equal to the proportion of mAbs among addition-to-class products (23.64%), but it was lower among those classified as advance-in-class (Table 7).

The number of proteins and polypeptides authorized in the EU between 2011 and 2020 exhibited substantial year-to-year variability, with no sustained directional trend. The general pattern for proteins and polypeptides was a fluctuating but generally stable landscape, marked by random increases and decreases rather than a consistent upward or downward trend. The number of proteins and peptides authorized each year across the decade was also relatively stable, fluctuating around an annual mean of 5.2 (Figure S3). Proteins and polypeptides represented a larger fraction of the first-in-class medicinal products compared to those classified as either advance-in-class or addition-to-class (Table 7).

The mean annual number of FDCs involving at least one new active substance was 2.89 (standard deviation (SD) 1.54), with variations between 1 and 5 (Figure S4). These data exclude FDCs based on previously authorized active ingredients (i.e., this was limited to authorizations under Article 8(3) of Directive 2001/83/EC, excluding those authorized under Article 10b of Directive 2001/83/EC). The fraction of fixed-dose combinations (FDCs) was the lowest among the first-in-class products, but this proportion was the highest among the advance-in-class products (Table 7). The annual number of authorized *vaccines* ranged from 1 to 4, with a mean of 2.0 (SD 1.1) (Figure S5).

Radiopharmaceuticals were authorized in only 5 out of 10 years considered here (2012–2014 and 2016–2017), and in each of those years, the number of approved radiopharmaceuticals was two, except for 2016, when only one was authorized. Out of the nine radiopharmaceuticals approved during this period, seven were first-in-class, while two were considered addition-to-class.

More innovative technologies were authorized in the analyzed decade than in the previous one. For instance, five cell-based Advanced Therapy Medicinal Products (ATMPs) were authorized between 2014 and 2019, whereas before this decade, a single somatic-cell therapy medicine (sCTMP) had been authorized within the EU, i.e., ChondroCelect (authorized in 2009). Four additional products are also based on somatic cells, for instance Zalmoxis (allogeneic T cells genetically modified with a retroviral vector encoding a truncated form of the human low affinity nerve growth factor receptor (-LNGFR) and the herpes simplex I virus thymidine kinase HSV-TK Mut2)) or the three CAR-T cell therapies, but they are legally classified (under EU Regulation (EC) No 1394/2007) as gene therapy medicinal products (GTMPs), because the T cells contained in those products are genetically modified. To those four gene therapies, a product based on an oncolytic virus (Imlygic, with the active ingredient talimogene laherparepvec, a genetically modified, oncolytic herpes simplex virus), two gene therapies using adeno-associated viruses (Luxturna, voretigene neparvovec, and Zolgensma, onasemnogene abeparvovec), as well as an ex vivo gene therapy (Libmeldy, atidarsagene autotemcel) should be added, increasing the total number of gene therapies authorized in this period to eight. Considering that only one such product had been authorized before the beginning of this decade, progress has been rather spectacular. Although not classified as gene therapies, but only as biologicals, three antisense oligonucleotide medicinal products were authorized in this period (whereas

before only one had reached regulatory approval and was withdrawn in 2002). Also, four siRNA (small interfering RNA) medicinal products were approved as medicines based on a new technology platform, for the first time in this decade, opening new ways of treating a variety of diseases. All such sophisticated products were categorized as first-in-class, zero were classified as advance-in-class or addition-to-class.

A small number of the new medicinal products had complex active ingredients, four of non-herbal origin and three of herbal origin. The active ingredient of Velphoro is sucroferriic oxyhydroxide, a complex made of polynuclear iron(III)-oxyhydroxide combined with sucrose and starches, which functions as a phosphate binder within the gastrointestinal tract, whereas ferumoxytol consists of superparamagnetic iron oxide nanoparticles enveloped by a carbohydrate coating made of polyglucose sorbitol carboxymethyl ether. Colestilan (the active ingredient of BindRen) and patiomer (Veltassa) are polymers with binding properties for phosphates and potassium ions, respectively. In the analyzed decade, only three new products were based on complex herbal extracts: a defatted powder of peanuts (*Arachis hypogaea* L.) used in the treatment of peanut allergies, a birch bark extract (Episalvan) authorized for the treatment of partial-thickness wounds (and withdrawn after several years for commercial reasons), and a bromelain-enriched proteolytic enzyme preparation from *Ananas comosus* (L.) Merr. (Nexobrid) authorized for the enzymatic debridement of deep burns. Defibrotide (the active substance of Defitelio) is a mixture of oligonucleotides derived from porcine intestinal mucosa.

3.5. Administration Routes

By far the most widely used administration route was oral (159 products), followed by intravenous (106 products); combined, these accounted for 73.82% of the dataset (however, as shown below, parenteral routes collectively outweighed the oral route). The pursuit of oral formulations remains a major driver of pharmaceutical innovation, with first-in-class drugs exemplifying this trend and reinforcing the historical preference for oral administration. The substantial number of first-in-class oral products indicates ongoing innovation in addressing key challenges in drug development, represented by bioavailability and first-pass metabolism. Intravenous (IV) administration has traditionally been reserved for drugs requiring rapid onset, high bioavailability, or instability in the gastrointestinal tract, particularly various proteins, including mAbs. Since peptides, proteins, and mAbs represent about one-third of all datasets, the high number of IV products (29.53%) should not be surprising. These two routes were followed by subcutaneous (44 products, including one subcutaneous implant) and intramuscular (13 products) routes. The high number of medicines administered subcutaneously, particularly the first-in-class products (28 out of 44 such medicines), indicates a shift towards subcutaneous (SC) delivery of biologics, as before 2010 the SC route tended to be used especially for vaccines and insulin; now both monoclonal antibodies and a variety of other biological products use SC as the main delivery route. Several products offered more flexible administration options, such as oral + IV (4 products), oral + intramuscular (IM), IV for the initial dose followed by SC for subsequent doses, and even intradermal (ID) + SC + intratumoral + peritumoral injection following radiolabelling (Lymphoseek/tilmanocept). Other parenteral routes (such as intra-articular, intracerebroventricular, and intralesional) were largely reserved for rare first-in-class products. Other administration routes included three nasal vaccines, one vaginal pessary (Intrarosa), and five topical (cutaneous) treatments. Ophthalmic innovations featured unique delivery methods, including the Holoclar ocular surface implant and Luxturna's subretinal injection (Table 8).

Table 8. Distribution of the 357 products by administration route and the innovation level.

Administration_Route	Addition-to-Class (% Within Column)	Advance-in-Class (% Within Column)	First-in-Class (% Within Column)
Oral	28 (50.91)	56 (57.14)	73 (35.78)
IV	14 (25.45)	17 (17.35)	75 (36.76)
SC	7 (12.73)	9 (9.18)	28 (13.73)
IM	1 (1.82)	7 (7.14)	5 (2.45)
Topical	0	0	5 (2.45)
Intralesional	0	0	3 (1.47)
Ophthalmic	0	0	2 (0.98)
Oral + IV	0	3 (3.06)	1 (0.49)
Nasal	0	2 (2.04)	1 (0.49)
Intravitreal	1 (1.82)	1 (1.02)	1 (0.49)
ID + SC + intratumoral + peritumoral injection (following radiolabeling)	0	0	1 (0.49)
In vitro radiolabeling of medicinal products, which are subsequently administered by the approved route	0	0	1 (0.49)
Intra-articular	0	0	1 (0.49)
Intracerebroventricular	0	0	1 (0.49)
Intrathecal	0	0	1 (0.49)
IV (first dose) + SC (subsequent doses)	0	0	1 (0.49)
Ocular (surgical implantation onto the corneal surface/under the conjunctiva)	0	0	1 (0.49)
SC (implant)	0	0	1 (0.49)
Subretinal	0	0	1 (0.49)
Vaginal	0	0	1 (0.49)
Inhalation	3 (5.45)	1 (1.02)	0
Oral + gastrointestinal	0	1 (1.02)	0
Oral + IM	0	1 (1.02)	0
Oral + enteral	1 (1.82)	0	0
Total	55 (100.00)	98 (100.00)	204 (100.00)

Bold type: Shows the total values.

To facilitate a structured analysis of drug delivery trends, we categorized administration routes into four distinct groups: those involving systemic injections, infusions, or localized internal delivery (e.g., intravenous, subcutaneous, and intrathecal) were grouped as Parenteral; treatments applied to external or mucosal surfaces, such as topical, intranasal, and ophthalmic routes, were consolidated under Topical/Local; and products involving multiple delivery methods were designated as Mixed. When the products are thus grouped, the distribution is as follows: 172 parenteral, 156 oral, 15 topical/local, 11 with mixed delivery routes, and 3 others (two implants and one sui generis, in vitro radiolabeling, followed by an approved route). This more synthetic distribution of medicinal products by administration route and innovation category is shown in Table 9.

As shown in Table 9, oral administration dominates the lower-innovation categories (addition-to-class and advance-in-class), while the higher-innovation first-in-class products favor the parenteral route.

Table 9. Distribution of medicinal products by grouped administration routes across innovation classes. Individual delivery methods were consolidated into four primary categories: Parenteral (injections, infusions, and implants), Oral, Mixed (two or more alternative or concomitant routes), and Topical/Local (ophthalmic, intranasal, inhalation, and vaginal routes).

Administration_Route	Addition-to-Class (% Within Column)	Advance-in-Class (% Within Column)	First-in-Class (% Within Column)
Mixed	1 (1.82)	7 (7.14)	3 (1.47)
Oral	28 (50.91)	55 (56.12)	73 (35.78)
Parenteral	23 (41.82)	33 (33.67)	116 (56.86)
Topical/Local	3 (5.45)	3 (3.06)	9 (4.41)
Other	0	0	3 (1.47)
Total	55 (100.00)	98 (100.00)	204 (100.00)

Bold type: Shows the total values.

3.6. Pharmaceutical Forms

Although pharmaceutical forms depend on the route of administration, multiple forms are frequently available for a single route. It is consequently of interest to analyze the patterns in their use for newly authorized drugs during the period under review. In a number of cases, MAHs later submitted one or more alternative dosage forms. Since our analysis was restricted to the date of first authorization, subsequent dosage forms were not included. A synthesis of the main dosage forms used in the products analyzed and their frequencies is shown in Table 10.

Table 10. Frequency distribution of pharmaceutical forms for the 357 medicinal products, sorted in descending order of occurrence. Pharmaceutical forms appearing a single time are consolidated under the “Others” category.

Dosage_Form	Count (%)
Film-coated tablet	97 (27.17)
Hard capsule	38 (10.64)
Solution for injection	36 (10.08)
Concentrate for solution for infusion	35 (9.80)
Others	35 (9.80)
Powder for concentrate for solution for infusion	24 (6.72)
Powder and solvent for a solution for injection	21 (5.88)
Dispersion for infusion	7 (1.96)
Powder for solution for injection	6 (1.68)
Solution for injection in pre-filled pen	6 (1.68)
Tablet	6 (1.68)
Solution for infusion	5 (1.40)
Suspension for injection	5 (1.40)
Prolonged-release tablet	4 (1.12)
Soft capsule	4 (1.12)
Gel	3 (0.84)
Powder for solution for infusion	3 (0.84)
Solution for injection in pre-filled syringe	3 (0.84)
Dispersion for injection	2 (0.56)
Eye drops, solution	2 (0.56)
Film-coated tablet + powder for concentrate for solution for infusion	2 (0.56)
Inhalation powder, pre-dispensed	2 (0.56)
Nasal spray, suspension	2 (0.56)
Powder for concentrate and solution for solution for infusion	2 (0.56)
Powder for concentrate for solution for injection/infusion	2 (0.56)

Table 10. Cont.

Dosage_Form	Count (%)
Powder for oral suspension	2 (0.56)
Radiopharmaceutical precursor, solution	2 (0.56)
Solution for injection (pre-filled pen/syringe)	2 (0.56)
Suspension for injection (pre-filled syringe)	2 (0.56)
Total	357 (100.00)

Bold type: Shows the total values.

Pharmaceutical forms generally align with their respective administration routes. Within the oral category, film-coated tablets were the predominant dosage form (97 products). In contrast, non-coated tablets and prolonged-release tablets were rare, each appearing in only six products for non-coated tablets and four products for prolonged-release tablets. Hard capsules were the second most common oral formulation (38 products), significantly outnumbering soft capsules (4 products). Liquid-reconstitution forms were minimal: two products were powders for oral suspension, and one offered both effervescent and suspension formulations. No new active substances were authorized as powders for oral solution during this decade.

Parenteral pharmaceutical forms exhibited greater diversity than oral forms. Solutions for injection were most prevalent (36 products), followed by concentrates for solution for infusion (35) and powder for concentrate for solution for infusion (23). Other common formulations included powder and solvent kits for solution for injection (21), dispersions for infusion (7), and powder for solution for injection and solution for injection (in pre-filled pens) (6 each).

Topical (cutaneous) formulations were limited to four products: three standard gels and one powder and gel for gel (where the powder is first mixed with the gel to obtain the final gel that will be applied to the wound area). Only two products were formulated as eye drops: Oxervate (cenegermin) and Rhokiinsa (netarsudil).

A small number of products occurred twice in the list, while 35 products belonged to a diverse range of formulations, each one occurring only once. They are described in the Supplementary File S1.

3.7. Orphan Versus Non-Orphan Products

The distribution of orphan innovation status among the study participants is shown in Figure 3. Of the total sample ($n = 357$), about one-third (32.21%, $n = 115$) had orphan status, while the remaining two-thirds (67.79%, $n = 242$) were non-orphan. Looking at the first-in-class products, the number of non-orphans was slightly higher than that of orphans (115 versus 89, 32.21% of the total versus 24.93% of the total). Among orphan products, first-in-class had the highest number, whereas among non-orphan medicines, the distribution was more even (although the first-in-class was still the largest subcategory). We would like to clarify that this analysis reflects the orphan status assigned at the time each marketing authorization was granted. A comparison with the current EU Register of Medicinal Products reveals a markedly different picture, as the orphan status of many products has since changed, either at the request of the MAH or following withdrawal of the marketing authorization. We are preparing a separate paper that examines these post-authorization changes for the products in this dataset.

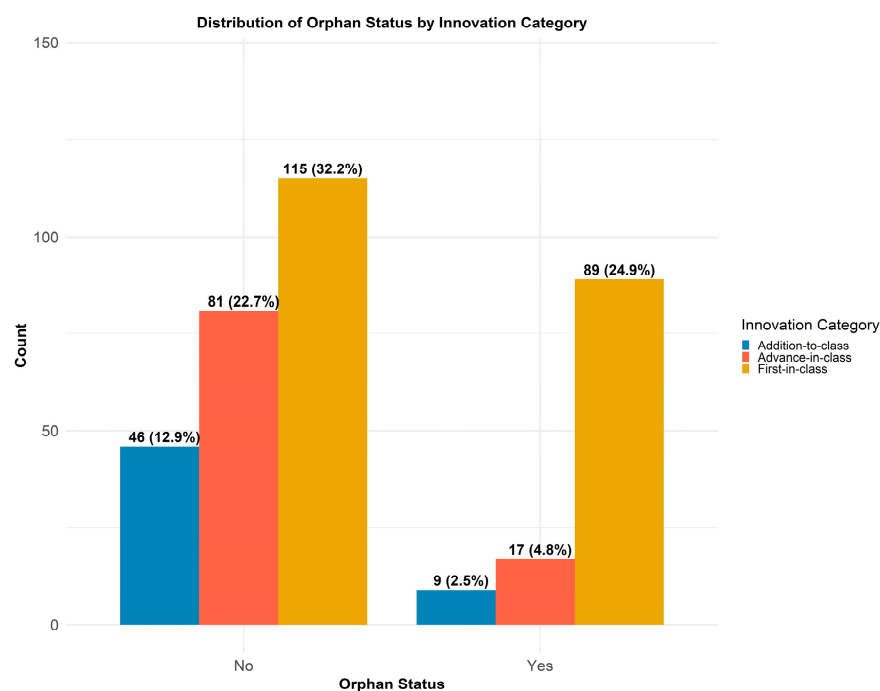


Figure 3. Distribution of innovation types by orphan drug status (counts and corresponding percentages).

4. Discussion

4.1. Innovation Levels and Competition Landscape

Our findings reveal a notable level of innovation among medicinal products containing new active substances (NAS) authorized through the European Commission’s centralized procedure from 2011 to 2020. Overall, these data indicate that roughly 57% of new drug approvals introduced groundbreaking therapeutic approaches, while the remaining 43% provided incremental advances or alternatives within existing classes. On the other hand, the same data can be interpreted as involving at least some form of advancement in about 85% of the cases, whereas they represented mere additions to existing classes in about 15% of cases. Such products introduce novel mechanisms of action and frequently address unmet medical needs or new therapeutic pathways [33]. These findings align with the EMA’s centralized procedure requirements. Because this pathway is compulsory for biotechnological and advanced therapy medicinal products (ATMPs), it serves as a primary pipeline for the most innovative therapeutic developments in Europe [37]. Although directly comparable statistics on first-in-class drug approvals at the EMA during this specific decade are not available, evidence from analyses covering an overlapping period of FDA–EMA approvals suggests a resilient European pipeline of novel mechanisms. However, the EMA seems to utilize expedited pathways for such innovations considerably less frequently than the FDA (30% versus 81% of first-in-class approvals receiving expedited status between 2013 and 2023) [38]. The high first-in-class share within the analyzed decade supports the idea that Europe’s regulatory systems prioritize innovative therapies, especially in oncology and rare diseases, where novel targets have increasingly proliferated [39]. The proportion of first-in-class is broadly in line with the tendency reported in the last two decades toward the domination of “pioneers” (at 60–80% in the 2010s) and a reduction in the share of “colonists” (to a 10–25% share) [19].

While groundbreaking therapies justifiably are drawing most of the attention, the distribution of approvals shows that the vast majority of NAS approvals (about 85%) offer at least some degree of therapeutic advancement over existing options. Among the advance-in-class products are those able to deliver meaningful improvements in efficacy, safety,

tolerability, pharmacokinetics, or patient convenience. New products within a specific therapeutic class can bring significant benefits even when they are only addition-to-class. Discrete clinical nuances, such as the different safety profiles of SSRIs or the selectivity properties of beta-blockers, can result in high adoption rates for what are called ‘me-too’ drugs. Limited evidence indicates that sometimes, even when priced above the first-in-class pioneer, these follow-on therapies command a large market share and are chosen by health professionals because they offer tailored options for patient-specific needs [40]. Moreover, among the Essential Medicines List developed by the World Health Organization (WHO), about 60% belong to “me-too” drugs (i.e., additions-to-class or at most advances-in-class). However, their availability can contribute to protection against shortages, as they allow professionals in the context of a shortage to substitute one product with another from the same class [41]. Our data show that most non-first-in-class drugs in Europe represent tangible progress rather than unnecessary alternatives, with only 16% being classified as additions without any advancement in care. This limited share of mere addition-to-class reflects the fact that the market appetite for drugs with minimal differences from reference products is dwindling, and the demand is increasing for products bringing superior safety or efficacy benefits over existing therapeutic options [42].

The balanced distribution of products with NAS among first-in-class and follow-on (advance-in-class or addition-to-class) products is likely to reflect intense development competition for the same target, rather than servile, low-risk imitation of a successful new product. Historically, the first drug to market in a class was often not the first to begin clinical testing [43]. Similarly, in about half of the cases, follow-on drugs were patented (in the U.S. or worldwide) before the pioneering first-in-class drug had secured any patent protection [44]. Therefore, regarding follow-on products as mere, low-quality imitators is overly simplistic and unfounded.

The observation that roughly one-third of the products carried an orphan designation is consistent with wider trends highlighting the increasing role of orphan medicines in contemporary pharmaceutical development. Orphan status is granted to treatments intended for rare diseases, which have traditionally benefited from limited treatment options due to small patient populations and reduced profitability. To address this, regulatory initiatives such as the U.S. Orphan Drug Act and the European Union’s Orphan Drug Regulation have introduced regulatory incentives, such as periods of market exclusivity, fiscal benefits, and regulatory stimuli [45–47]. The relatively small difference among the proportions of first-in-class products in orphan and non-orphan designations suggests that major therapeutic innovation occurs with similar frequency in both rare and common therapeutic areas, a finding similar to what was reported in the US in the same period [48]. This also reflects the commitment of the pharmaceutical industry to targeting previously unaddressed therapeutic needs, regardless of disease prevalence. This pattern likely stems from progress in fields such as multi-omics, precision medicine, and biomarker identification, which facilitate the development of more specific and novel treatment approaches [49,50].

While orphan drugs benefit from regulatory and financial incentives, their high costs and limited patient populations can pose challenges for healthcare systems and payers. Orphan drugs frequently deliver greater health benefits compared to non-orphan drugs, but their significantly higher prices often result in lower cost-effectiveness. This creates a dilemma for healthcare payers, who must balance ensuring patient access to these vital therapies with the need to maximize the value derived from pharmaceutical expenditures [51]. Traditional cost-effectiveness analysis (CEA), primarily based on quality-adjusted life year (QALY), is frequently devoid of the necessary sensitivity for evaluating such products. These standard frameworks are often ill-equipped to address the specific complexities of the rare disease landscape, particularly the interplay between high acquisition costs,

inherent limitations of small clinical datasets, and social equity goals such as prioritizing interventions for patients with the greatest medical need [52]. A significant gap between medical innovation and global access has been reported, as fewer than 5% of approximately 7000 rare conditions have authorized treatments, and prohibitive costs further restrict use in low- and middle-income countries (LMICs). These disparities are rooted in systemic challenges, including financial barriers, inadequate diagnostic infrastructure, and a lack of cohesive regulatory oversight [53]. The concentration of first-in-class innovation in the orphan category underscores the need for continued policy support to ensure that breakthrough therapies reach patients who need them, without compromising affordability or equitable access. Treatment costs rise sharply as disease prevalence falls, especially for ultra-orphan conditions. When generics exist, branded orphan drugs may cost up to 82,000 times more than their generic equivalents, underscoring generics' role in improving affordability [54]. However, this cost reduction offered by generics depends entirely on upstream innovation: reference products must first be developed and approved before generics can emerge. Although various frameworks, including global solidarity funds, regional pooled procurement, and equity-driven subsidies, have been proposed to harmonize orphan drug access across diverse economic landscapes, their operationalization is frequently stalled by localized legal, fiscal, and administrative limitations [53].

The temporal distribution of MAs for medicinal products containing NAS, submitted via the centralized procedure between 2011 and 2020, reveals a general upward trend in approvals. This general ascent reflects growing productivity in the European pipeline for cutting-edge medicines over this period, driven by greater R&D investments and breakthroughs in multiple therapeutic fields, particularly oncology and rare diseases, as well as in certain technology platforms, such as the now mature monoclonal antibody technology [55], but also newer ones, from siRNAs [56] to CAR-T cells [57] or progress in cell research and advanced therapies [58]. For instance, under the 7th Framework Programme (2007–2013) and Horizon 2020 (2014–2020), the EU allocated €3.2 billion to over 550 cross-border research collaborations dedicated to rare diseases [59]. Multiple EU initiatives and national projects within the EU have provided funding for cancer research, both at the basic and translational levels [60].

The significant declines observed in 2016 and 2019, followed by immediate recoveries, are in line with the known natural volatility of annual regulatory approvals, typically seen in both the EU and other regulatory regions [61,62]. Similarly low rates of approval in 2016 have also been reported in the US [61,63]. Time series analyses of US data have found cyclical patterns in FDA drug approvals, with regulatory, economic, and policy factors likely serving as the key influences [64]. The 2018 EU peak in approvals had an FDA counterpart, as the US agency approved 59 novel drugs in that year, marking a US record. This was fueled by widespread adoption of expedited procedures (namely Fast Track, Breakthrough Therapy, Priority Review, and Accelerated Approval) [65]. The 2020 peak is also consistent with one of the FDA's most productive years: 49 novel therapeutics were approved (nearly 23% above the 2011–2020 annual average of 40) [66].

Annual authorization rates in the EU during this decade are somewhat higher than those observed in the United States during the 1990s, yet remain below the peak levels seen in the U.S. in 2002 and 2003 [12]. Nevertheless, they exceed the total U.S. new molecular entity approvals from 2004 to 2009 [13]. For context, the number of new active substances (NAS) authorized annually in the EU between 2002 and 2010 ranged from 14 to 36, surpassing 35 only in 2007 and exceeding 25 in just two years (2007 and 2009) [67].

To conclude, the 2011–2020 data illustrate a robust and increasingly dynamic European regulatory environment for novel therapies, defined by long-term growth despite natural annual fluctuations. These findings align with international pharmaceutical trends,

indicating that European approval rates have kept pace with the accelerating rate of global scientific discovery in the field of drug development.

4.2. Therapeutic Classes

The dominance of antitumor therapies among newly approved products highlights the ongoing focus on oncology in global pharmaceutical innovation. Antineoplastic agents (ATC L01) accounted for the largest share of approvals over the last decade, reflecting both the high burden of cancer and the progress in developing a variety of new(er) antitumor approaches, from diverse targeted therapies such as small kinase inhibitors to a variety of immunotherapies, and monoclonal antibodies, including antibody-drug conjugates (ADCs). Antineoplastic drugs remain central to the therapeutic development efforts of pharmaceutical companies and public research, consistent with broader analyses showing their dominant role among oncologic approvals in recent years and in line with the perceived “strong unmet need” for both common and rare tumors [68]. This might also, to a certain extent, be driven by the perceived willingness of health systems to pay more for oncological products than for medicines intended for non-oncological diseases, even when the latter have relatively high DALY burdens [69]. Oncology has been a major focus of accelerated development pathways and regulatory incentives, such as access to expedited development procedures (Fast Track, Priority Review, etc.), and thus it is more appealing and may seem more rewarding and less risky than other therapeutic areas.

A paper based on USA’s data reported that even with 57 anticancer drug approvals occurring in a single year (2020), only 46 approvals with a new biological target were authorized over the 12-year period examined, implying that on average, the FDA authorized fewer than four novel targets each year [70]. A direct comparison is difficult to make because our focus was not on novel biological targets, but rather on first-in-class products (the two do not necessarily coincide); moreover, defining what constitutes a “novel biological target” is more complex than it would seem at first sight, as discussed in the introductory section.

It has been stated that “antibody development in oncology driven by collaborative work from academia and industry has surpassed the growth of other cancer-targeting agents such as kinase inhibitors, hormonal drugs, cancer vaccines, and chemotherapies by a wide margin” [71]. Within the 10-year period analyzed, our data do not corroborate this assertion. Among the 92 antineoplastic agents approved, 55 were small molecules compared with just 28 monoclonal antibodies, meaning that the latter represented only about half the number of the former. It remains possible that the subsequent decade (now partly completed) will align more closely with this statement.

The relatively lower approval volume in other L-class ATC level-2 subgroups, including endocrine therapies (L02), immunostimulants (L03), and immunosuppressants (L04), likely reflects both a combination of market demand and different R&D priorities. The progress in the field of immunosuppressants, while vital for transplant and autoimmune care, often centers on well-characterized targets and established therapeutic classes, and is less focused on novel breakthroughs, although “no immunosuppression regimen has proven to be without a potential pitfall” [72]. Endocrine therapies focus on hormone-driven malignancies or defined metabolic axes, implying a narrower field of application, and this probably explains the substantially lower number of products from this subclass. The development of immunosuppressive agents for oncology continues to be difficult, largely due to the immunosuppressive nature of the tumor microenvironment and the complexity of immune-evasion mechanisms [73]. There have been multiple obstacles in the pathway of developing new immunostimulants, but with recent progress, this might

change in the future, as indicated by the progress with the CAR-T therapies and checkpoint inhibitors [74].

Within ATC code J (anti-infectives for systemic use), antivirals (J05) were the most prevalent, followed by vaccines and antibacterials. The 28 antiviral agents cover a broad spectrum of viral targets, including HIV, HCV, influenza, and SARS-CoV-2, highlighting both persistent unmet needs and pandemic-driven momentum in antiviral development. A detailed presentation of the antivirals authorized within the analyzed decade is included in the Supplementary File S1.

Three lipoglycopeptide antibiotics (a subgroup of the larger glycopeptide class) were authorized in this period. The rise of vancomycin-non-susceptible strains spurred the development of lipoglycopeptides, which are semisynthetic glycopeptides with an added lipid tail that prolongs their half-lives and increases their efficacy against Gram-positive cocci. All three are bactericidal agents administered intravenously, despite having distinct dosing schedules and sharing a common bactericidal mechanism (interfering with cell wall synthesis via binding to the terminal D-Ala-D-Ala residues of precursors). Their efficacy is targeted primarily against susceptible Gram-positive bacteria, such as *S. aureus* (including MRSA) and streptococci, making them ineffective for most Gram-negative infections [75].

In the ATC A category, new drug development is heavily concentrated in two areas: type 2 diabetes (A10) and rare metabolic diseases (A16). This pattern highlights the two biggest drivers of recent innovation in this field, the (r)evolution of diabetes care [76] and progress in targeted medicines for ultra-rare conditions [45]. The inclusion of 14 agents in subclass A10 reflects a period of rapid transformation in diabetes pharmacotherapy during the analyzed period, particularly for type 2 diabetes. The list of subclass A16 is primarily composed of enzyme replacement therapies (ERTs), small-molecule substrate-reduction or chaperone therapies, and siRNA molecules targeting specific enzymes in the heme and oxalate biosynthesis pathways for acute hepatic porphyria and primary hyperoxaluria type 1 (givosiran and lumasiran).

4.3. Administration Routes and Dosage Forms

The examination of administration routes makes evident the tight linkage between delivery routes and the level of pharmaceutical innovation. Across the dataset, oral and intravenous formulations predominate, representing nearly three-quarters of all products and reaffirming their longstanding prominence in drug development. The oral route persists as the predominant mode of administration industry-wide [77], preferred for its established profile in patient compliance, convenience, and appropriateness for extended treatment regimens [78]. Its dominance among both addition-to-class and advance-in-class agents suggests that much of the incremental innovation is built on existing pharmacological and pharmaceutical foundations, in which the obstacles to effective oral delivery have been previously resolved or are reasonably manageable. The substantial number of first-in-class products intended for oral administration indicates that this delivery approach is not limited to incremental developments. Instead, it continues to be a major driver of innovation, with new molecular entities successfully overcoming classical barriers such as poor solubility, limited permeability, and extensive first-pass metabolism [79]. This finding reinforces the notion that advances in medicinal chemistry, formulation technologies, and enabling approaches (e.g., prodrugs and absorption enhancers) have expanded the scope of what can be achieved via the oral route, even for novel mechanisms of action.

Although oral dosing is the predominant route in general, parenteral administration, especially IV delivery, is widely used for first-in-class drugs. This is consistent with the fact that numerous novel and complex biologic agents, such as therapeutic proteins, monoclonal antibodies, and even some small molecules, are administered parenterally because they are

poorly absorbed and unstable in the gastrointestinal environment when taken orally [80–82]. By bypassing first-pass metabolism and entering systemic circulation directly, parenteral routes offer predictable pharmacokinetic profiles and consistent systemic drug levels (i.e., high bioavailability levels), both essential for medicines with novel pharmacological mechanisms [83,84].

Small molecules like opioids have been administered subcutaneously since the 1800s, but this route only became common for monoclonal antibodies with adalimumab's introduction, gaining widespread adoption after 2009. Within our dataset, among the 42 products for which the administration route was subcutaneous, half (21) were monoclonal antibodies. Today, subcutaneous delivery is preferred for managing chronic conditions like rheumatoid arthritis because patients can administer the medication themselves, improving adherence to treatment [85]. Compared to IV delivery, the SC route offers a less invasive alternative with significantly shorter administration times. Transitioning monoclonal antibodies to SC formats is a strategic priority aimed at alleviating pressure on healthcare systems, lowering costs, and enhancing the quality of life for both patients and their families [86]. The substantial share of SC products within the first-in-class subgroup (27 out of 42) in our dataset is consistent with this shift, in line with the move toward more patient-centric delivery formats for biologics.

Beyond standard oral and parenteral routes, the innovative products include 15 products that employ mixed administration strategies (e.g., oral plus IV, IV plus SC, IM plus SC,,), reflecting adaptable delivery designs that aim to pair rapid therapeutic onset with convenient long-term dosing (e.g., Sivextro, administered by the IV route for a rapid effect, and by the oral route otherwise) or simply alternative ways of administration (for instance Lymphoseek, in the meantime withdrawn from the market for commercial reasons, could be administered by intradermal, subcutaneous, intratumoural, or peritumoural injection) [87]. These hybrid approaches are commonly selected when clinical needs call for an immediate effect, followed by sustained management suitable for outpatient care [88,89]. Such flexible paradigms are gaining prominence in clinical development and formulation science as part of broader efforts to enhance both therapeutic performance and patient adherence [89].

Specialized administration routes (such as intralesional or subretinal) are predominantly utilized for high-innovation therapies or orphan drugs [90,91]; intranasal delivery has been adopted for the live attenuated influenza vaccine, offering distinct advantages compared with traditional inactivated, split-virion formulations [92]. This aligns with established research indicating that local delivery is the preferred strategy for novel targets or approaches requiring site-specific access [93]. Such precision is particularly critical for gene therapies and localized biologics, where therapeutic success depends on direct entry into specific tissue compartments.

Although cutaneous and other local routes represent a smaller share of products, they encompass some of the most distinctive delivery innovations. Examples like ocular surface implants (which have clear benefits over traditional techniques for ocular drug administration) and retinal injections for ophthalmic therapies indicate that, at least in some cases, the administration route can itself be a critical component of pharmaceutical innovation for certain therapeutic fields [94–96].

The range of pharmaceutical forms for the analyzed new products spans various administration routes, indicating both traditional drug delivery methods and newer solutions designed to enhance bioavailability, safety, and patient convenience. Oral solid and parenteral formulations dominate the list, serving as the foundation of pharmaceutical development. Moreover, a smaller segment corresponds to incremental technological improvements rather than groundbreaking innovations.

Film-coated tablets are the most popular oral dosage form, with 98 products, a finding that highlights their advantages in both production and patient preference. The coating offers multiple benefits: it facilitates swallowing and compliance, improves taste by creating a physical barrier between the taste buds and the active ingredient, shields the active substance from biological degradation or environmental damage, and allows for distinctive branding [97]. With only four non-coated tablets identified in the dataset, it is obvious that the vast majority of newly approved drugs, when in tablet form, use tablet coatings for the aforementioned advantages.

The low number of prolonged-release tablets (only four products) is worth noting. It probably reflects the intricate relationship between the pharmacokinetic profiles of novel molecular entities and the difficulties inherent in their formulation. On one hand, certain modern drug candidates, especially in oncology and immunology but not only, feature narrow therapeutic indices, wide inter-patient pharmacokinetic variability, or particular absorption patterns [98–101] that are less suited to controlled-release approaches, as inadequate control of drug release from such formulations may lead to diminished therapeutic efficacy or an increased risk of toxicity [102], and such risks are considerably higher for drugs with a narrow therapeutic index. On the other hand, creating modified-release dosage forms requires significant additional resources for formulation development and clinical testing, resources that developers may choose not to allocate during initial approval when standard immediate-release versions are sufficient to prove efficacy (and coming later with a prolonged-delivery solution provides an additional market advantage). For instance, a recent study estimated that in Thailand, the R&D costs associated with developing an incrementally modified sustained-release drug range between USD 1.5 and 3.0 million when development is limited to Phase I studies, and between USD 18.6 and 20.2 million for a full clinical development program [103]. Besides, the development of extended-release formulations from initially authorized immediate-release products is a widely used strategy in the pharmaceutical industry to prolong the commercial life cycle of medicines [104].

The predominance of hard capsules (36 products) over soft capsules (4 products) among the new products is consistent with the typical physicochemical profiles of the active pharmaceutical ingredients. Hard capsules come with strong manufacturing advantages (i.e., simplicity and flexibility) [105] and are compatible with a broad spectrum of enabling technologies for poorly soluble active ingredients, allowing incorporation of multiparticulate systems, liquid and semi-solid fills, interactive inhalation blends, and mini-tablet units in a single dosage form [106]. Soft capsules are well-suited to deliver lipid-based formulations due to their ability to hold liquids or semi-solids, flexible excipient choices, protective sealing, and quick dissolution in the body [107].

Parenteral administration presented significantly more varied formulations than the oral route, reflecting the key therapeutic areas that have driven recent regulatory approvals. Solutions for injection (35 products) remain widely used when chemical stability is achievable, benefiting from ease of manufacturing and administration. Yet, the high count of formulations requiring reconstitution, including concentrates for solution for infusion (33), powder for concentrate for solution for infusion (23), and powder and solvent kits (19), indicate stability challenges associated with many new biopharmaceuticals. Many protein therapies, including monoclonal antibodies, face challenges in maintaining stability in aqueous media over time [108,109]. The instability of proteins in solutions, coupled with their general sensitivity, necessitates lyophilization to create stable therapeutic products. Freeze-drying (lyophilization) remains the dominant strategy to ensure their long-term storage stability, despite additional complexities in manufacturing, distribution, and final use [110,111], although similar technologies with anticipatedly better results are being

explored [112]. The continued dominance of lyophilized products suggests that emerging alternatives such as liquid formulations with novel stabilizers (i.e., different families of excipients), those obtained by liquid-liquid phase separation, or other buffer-free and high concentration formulations [113–115], have not yet overcome these stability hurdles for the majority of therapeutic proteins.

The emergence of pre-filled pens and syringes (generally limited to two or three variants per device type in our data set) reflects a shift toward more patient-focused drug delivery. These integrated formulations improve adherence, minimize dosing errors, and empower patients to self-administer treatments for chronic diseases. Their limited adoption, however, indicates that they are primarily used for therapies intended for long-term outpatient care, where higher development costs are offset by improved health outcomes and competitive advantage.

Pre-filled pens and syringes (integrated formulations that include a drug plus an injection device) are more user-centric and can easily overcome the key challenges associated with drug delivery using parenteral routes: convenience issues, costs and logistics, measurement accuracy, sterility, risks associated with the breaking of the skin barrier, etc. They provide advantages such as ease of use, precise dosing, and reduced medication waste, as well as enhancing patient safety. By eliminating the overfill required with vials, they improve efficiency and are particularly valuable for high-cost or low-volume biologicals [116,117].

The paucity of topical (cutaneous) formulations (four products) and eye drops (two products) reflects partly the pharmaceutical industry's strategic prioritization of high-value therapeutic areas such as oncology, immunology, and rare diseases, where systemic therapies command premium pricing and address unmet medical needs. It has been recently stated that the widespread belief that dermatological drug products offer limited commercial viability has hampered innovation and fostered a cautious development strategy. For instance, efforts have largely centered on repurposing or reformulating established active pharmaceutical ingredients (APIs) to optimize them specifically for topical administration [118]. However, topical and ophthalmic drug delivery routes encounter unique physiological obstacles, which may also account for their limited representation. For example, eye drops typically achieve very low ocular bioavailability (less than 5%) because of rapid tear clearance and drainage through the nasolacrimal duct, resulting in a short residence time for the active ingredient, as well as corneal resistance, which restricts their effectiveness, especially in reaching deeper eye tissues [119]. While innovative delivery systems are being explored to address these barriers, the inherent pharmacokinetic challenges reduce the likelihood of new active substances being successfully developed for topical or ophthalmic use, regardless of therapeutic priorities. However, there remains a continuous interest in topical formulations, and in the last few years, new such therapies have been developed in major markets for atopic dermatitis [120], psoriasis [121], and other diseases. It should also be kept in mind that although topical/local routes are of interest for EMA when sufficiently innovative, there is a high likelihood that such products are authorized mostly through national regulatory routes [122].

Many of the products occur only twice, and the 33 products with unique formulations that appear only once in the dataset ("Others" in Table 10) exemplify the forefront of pharmaceutical innovation and address highly specialized therapeutic needs. Several patterns could be identified among this heterogeneous group:

- Pediatric-oriented formulations, such as chewable tablets and granules for oral suspension in sachets, remain underrepresented despite regulatory incentives for pediatric drug development [123]. The limited presence of gastro-resistant dosage forms suggests that few new active substances need shielding from gastric acid, or that

acceptable bioavailability can generally be achieved without enteric protection. This could be a consequence of current discovery efforts emphasizing compounds with robust absorption profiles or the deployment of alternative tools like acid-resistant prodrug designs. On the other hand, while enteric coating can optimize a drug's stability and release profile, its actual impact on oral bioavailability remains debatable, as its effectiveness often fluctuates based on a complex interplay between the drug's chemical properties and physiological factors such as gastric transit speed and pH fluctuations [124].

- Innovative delivery systems, including implants (e.g., Scenese/alfamelanotide [125]) and tissue-engineered therapies (e.g., Spherox, Holoclar) [125,126], are the result of the fusion of pharmaceutical innovation and regenerative medicine. While such products are still relatively rare, they reflect the rise of personalized [127] and long-acting therapies [128]. Scenese's implant, which achieves two months of continuous drug release, illustrates how such advanced technologies can redefine treatment approaches by minimizing the frequency of administration.
- While most radiopharmaceuticals approved during this period were formulated as conventional forms (such as solutions for injection, included in the products discussed earlier), three products were formulated as radiopharmaceutical precursor solutions (two) and a kit for radiopharmaceutical preparation. They reflect the unique requirements of nuclear medicine, where the radiopharmaceutical precursor must undergo radiolabeling at the clinical site, and kits must enable rapid, reliable preparation while maintaining radiochemical purity, labeling efficiency, and overall quality of the final radiopharmaceutical [129,130]. The predominance of ready-to-use solutions among radiopharmaceuticals indicates progress in developing stable formulations that can be centrally manufactured and distributed, as well as improved cold-chain logistics and generator-based radionuclides (e.g., ^{68}Ga , $^{99\text{m}}\text{Tc}$) [131–133], though the persistence of precursors and kits highlights situations where on-site preparation remains necessary, particularly due to the short physical half-lives of certain radionuclides or the complexity of the associated radiolabeling chemistry.

4.4. Limitations

Although our analysis maps EU pharmaceutical innovation from 2011 to 2020 in detail, a number of limitations should be acknowledged. First, the scope of the analysis was limited to medicinal products with NAS approved through the centralized procedure, handled by the EMA. Because of this limitation, non-orphan and orphan medicinal products based on “old” active substances, despite their potential for meaningful therapeutic innovation (e.g., mercaptamine, which was first authorized in the EU in 1997), were excluded. Additionally, innovative therapies authorized through national procedures in EU Member States were not included in our dataset. Products that involve reformulations or new delivery forms of previously approved active substances fall into a distinct category, necessitating a separate identification strategy, data sources, and evaluative framework. Including these would not only significantly expand the scope but also introduce methodological heterogeneity, potentially undermining the consistency and interpretability of our findings.

A second limitation refers to a certain extent of subjectivity in classification. Classifying innovation as “first-in-class,” “advance-in-class,” or “addition-to-class” carries inherent subjectivity, especially in assessing clinical advancements or mechanism novelty. Whereas FDA's Priority Review is often used as a proxy for innovation assessment, and the EU PRIME scheme could be used similarly for this purpose, neither is sufficient in itself for the classification of innovation, as shown above. Therefore, the categories here were based on the authors' expert assessment, informed by scientific literature and EPARs.

To prevent artificial overcounting, we clustered products based on a common active substance (authorized simultaneously), including fixed-dose combinations co-authorized with the parent NAS in the same month and year as a single product. This mitigates overcounting but might not fully capture the pharmaceutical innovation and development resources dedicated to fixed-dose combinations.

A further limitation stems from our geopolitical perspective: innovation status (e.g., “first-in-class”) was assessed solely from a European regulatory viewpoint. Since global approval dates differ, a drug deemed “first-in-class” in the EU may have been a follow-on product elsewhere, as illustrated by nivolumab and pembrolizumab, whose innovative status differs between the EU and the USA.

Finally, the decision to focus strictly on the decade 2011–2020 is deliberate and methodological. By establishing a clean, pre-2021 baseline decade, we create a robust comparator for evaluating trends in the subsequent decade (2021–2030). Integrating incomplete data from 2021 to 2024 would risk contaminating this benchmark with the profound, pandemic-induced disruptions that skewed pharmaceutical R&D and regulatory cycles. By maintaining this clean decade-to-decade boundary, we avoid confounding temporal variables and can more accurately determine whether shifts in advanced therapies or expedited approvals are permanent structural changes or merely transient, crisis-driven reactions. This framework ensures a rigorous “apples-to-apples” comparison once the current decade concludes, prioritizing long-term analytical integrity over premature updates. Current developments are already reshaping the trends observed in our study; however, we intend to evaluate these evolving dynamics in a follow-up paper once a full decade of new data becomes available.

4.5. Future Perspectives and Conclusions

The trends observed over the evaluated decade, together with early evidence from the current one, point to several directions for future research and industry development. Notably, technology platforms are expected to continue evolving and improving. The remarkable advances seen in gene therapies, siRNA, and ATMPs toward the end of the previous decade are likely to persist. Future research is expected to examine whether, and to what extent, these advanced platforms can extend beyond rare diseases into broader therapeutic areas. Artificial intelligence (AI) is expected to substantially reshape pharmaceutical innovation over the next decade, revolutionizing every phase of drug discovery, development, and delivery. Areas such as target identification and validation, de novo drug design, clinical trial optimization, drug repurposing, manufacturing and supply chain management, personalized medicine, real-world evidence and pharmacovigilance, collaboration and knowledge sharing, and regulatory compliance could all see major improvements or accelerations through AI integration.

As the boundary between “pioneers” and “followers” becomes increasingly nuanced, there is a growing need for robust, objective measures of innovation at both the authorization stage and during post-marketing use. We are currently developing a structured metric for initial innovation assessment. Post-marketing evaluation is expected to integrate long-term health outcomes, cost-effectiveness, and other relevant dimensions, moving beyond initial regulatory status or mechanism of action.

Subcutaneous (SC) administration of biologics and the growing popularity of pre-filled devices indicate a transition toward increased patient-centered care approaches. It is likely that in the future, gradually, pharmaceutical innovation will increasingly focus on developing treatments that lessen the load on healthcare systems while improving convenience in administration and adherence for patients managing chronic disease.

With approved treatments available for less than 5% of the over 7000 rare conditions, future policy and R&D initiatives must overcome systemic hurdles, such as exorbitant costs and limited access to appropriate diagnostic equipment, to ensure pioneering therapies are accessible to all patients, including those in low- and middle-income nations.

Our analysis of 364 new medicinal products authorized in the EU from 2011 to 2020 reveals a robust and growing innovation pipeline. The EU regulatory landscape stands to benefit from adopting efficiencies observed in other jurisdictions; modernizing the regulatory framework to facilitate easier access to accelerated approval tracks could create a more robust innovation ecosystem, providing the necessary incentives for companies to prioritize the European market for new drug launches. In the decade examined, a mere 14 products have used the PRIME scheme, in stark contrast to the 186 that were granted priority review and the 103 that were awarded breakthrough therapy status by the FDA. This is at least partially explained by the relatively late introduction of the PRIME scheme within the regulatory framework (2016, i.e., in the second half of the analyzed interval). Moreover, a number of significant and groundbreaking drugs that were being developed in the first years of the program were expected by the EMA not to benefit from PRIME, either because their development processes were already well advanced or because the companies sponsoring them had enough expertise and confidence to plan their studies independently without extra assistance [134]. We believe that the application of this regulatory framework (PRIME) will expand in the coming years and will have a positive impact on innovation and patient access to better medicines. This optimism is related to the fact that the scheme lowers the time from regulatory submission to market access, offers support to small and medium enterprises (SMEs) and academia, and makes the regulatory process more efficient, assisting developers in preparing high-quality evidence authorization files [134,135].

Over half (56%) were first-in-class, with breakthroughs concentrated on oncology and immunomodulation, anti-infectives for systemic use, the alimentary tract and metabolism, and rare diseases across different therapeutic areas. Although small molecules are still the most common technology, the surge in monoclonal antibodies and the emergence of gene and cell therapies reflect a transformative change in the pharmaceutical landscape.

Moreover, the analysis confirms that innovation extends beyond radical novelty and varies in degree; most (84%) new active substances provided at least some therapeutic advancement or clinical convenience over current options. While the industry meets therapeutic needs via novel chemical structures or biological approaches, mechanisms of action and delivery systems, a critical future challenge lies in reconciling the costs of such innovation with healthcare affordability and global distributive justice in access to new products.

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Abbreviations

The following abbreviations are used in this manuscript:

ADC	Antibody-drug conjugates
AI	Artificial intelligence
API	Active pharmaceutical ingredients
ATMP	Advanced Therapy Medicinal Product
CEA	Cost-effectiveness analysis
DALY	Disability-Adjusted Life Year
EMA	European Medicines Agency
EPAR	European Public Assessment Report
ERT	Enzyme replacement therapies
EU	European Union
FDA	Food and Drug Administration
FDC	Fixed-dose combination
GTMP	Gene therapy medicinal product
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
ID	Intradermal
IM	Intramuscular
IV	Intravenous
LAL	Lysosomal acid lipase
LMIC	Low- and middle-income countries
mAb	Monoclonal antibody
MAH	Marketing Authorization Holder
MPS IVA	Mucopolysaccharidosis type IVA
NAS	New active substance
NDA	New Drug Application
NME	New Molecular Entity
QALY	Quality-adjusted life year
R&D	Research and Development
SC	Subcutaneous
sCTMP	Somatic-cell therapy medicines
SGLT2	Sodium/glucose cotransporter 2
siRNA	Small interference RNA
WHO	World Health Organization

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