NATIONAL BANK OF GREECE

SECTORAL REPORT

April 2022

Greek pharma industry: In position to capitalize on EU shift towards more self-reliance

- Greece's pharmaceutical sector has been growing at a fast pace during the past five years (with sales up by 80%, vs 43% in the EU and 7% for other Greek manufacturing) – with exports being the main growth engine (with its extroversion increasing to 50% of sales in 2021 vs 30% in 2016). Noteworthy is the fact that the sector's investment appetite is gradually recovering, with the gross fixed capital formation-to-sales ratio reaching c. 10% (up from 7% five years ago and c. 15% in the EU).

- Looking ahead, the vigorous performance of Greek pharma is expected to be further boosted by a powerful combination of favourable factors:

  - ✓ Driven by technological advances and increased health concerns (due to the covid pandemic), global pharma sales could almost double by 2030 (reaching $3 tr, from $1.4 tr. currently), following a two-decade period of healthy sales growth (c. 6% per year).

  - ✓ Against this expansionary background, the recent introduction of the «European Common Pharmaceutical Strategy», presents new opportunities. The new strategy was triggered by concerns of high inter-regional dependencies (e.g. China provides 23% of EU pharma raw materials in 2019, up from 12% in 2010) and product shortages due to global supply chain disruptions (related with the shocks of covid pandemic and recent geopolitical turmoil). With its new strategy, the EU primarily aims i) to promote R&D towards both innovator and generic drugs, ii) establish a favourable institutional framework for manufacturers and iii) reinforce diversification of supply chains.

  - ✓ Amid an environment of advantageously changing conditions, Greece has also two unique circumstances working in its favour: (i) an imminent institutional reform mainly regarding clawback, and (ii) the reversal of past decade's tight financing conditions, being further boosted by the freshly available RRF funds.

  Despite a generally favorable environment, a word of caution is appropriate concerning rising energy and transport costs, affecting competitiveness in a highly regulated sector (especially for low-priced medicines).

- Leveraging on these prospects, Greek pharma manufacturers have already announced investment plans of c. €1bn for the period 2022-2026 – providing clear signs of their ongoing growth strategy. Based on our estimates, the sector has the potential to almost double its sales by 2026, mainly through higher extroversion. More importantly, the production boom could be coupled with increased R&D activity by cashing in on the significant pool of specialized human capital – therefore, turning Greece to a comprehensive hub for the pharma industry across the board, from research to production.

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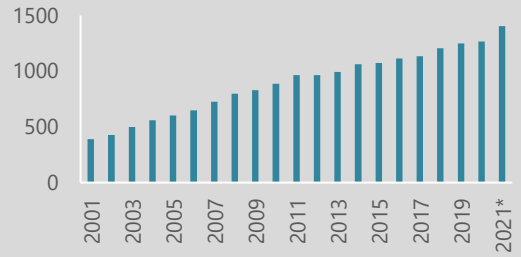
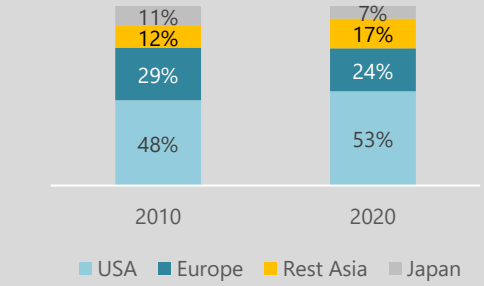
Global Pharma Revenues
(billion dollars)



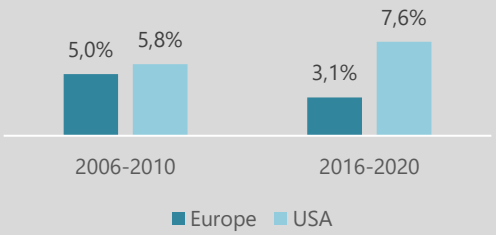
**estimate*
Sources: Statista, NBG estimates

Global pharma revenues by region
(% sales)



Sources: EFPIA, NBG estimates

Pharmaceutical R&D expenditure
(annual growth rate)(average annual growth rate)



Sources: EFPIA, NBG estimates

The global pharmaceutical sector is experiencing a wave of tremendous changes, with rapidly advancing technologies as well unimaginable shocks calling for novel strategies. In particular, pharmaceutical and biotech investments more than tripled during the past decade (to almost $30 billion)[1], while the outburst of the Covid pandemic has pushed global pharma expenditure by c. 10%. Note that the three main producers of Covid vaccines achieved net profits of about $35 billion in 2021 (up from $20 billion in 2020).

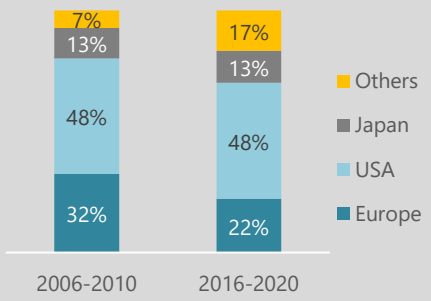
In this context, Greek pharma manufacturers could leverage on the positive momentum both on global and national levels, aiming to materialize the untapped potential of the sector. In this report, we present the challenges and opportunities of the global and European environment, the positioning of the Greek sector and our estimates for its growth prospects, amid an environment of improved conditions for financing and favourable institutional reforms.

Global pharma sector is growing briskly and is becoming more and more complex

Global revenues of pharmaceutical companies posted an average annual growth of 6% during the past 20 years, reaching c. $1.4 tr. in 2021 (vs $0.4 tr. in 2000), while it is projected that they could almost double by 2030 (to c. $3 tr.)[2]. About ½ of global pharmaceutical sales are manufactured in the US while Europe covers about ¼ of the market. It should be noted that during the past decade there was a gradual migration of production and research activities from Europe to emerging economies (such as China, India and Brazil) aiming to lower production costs. Indicatively, pharmaceutical R&D in the EU posted an average growth of about 3% during 2016-2020 (down from 5% during 2006-2010). On the contrary, the US accelerated its R&D activities, with average annual growth in the range of 6% to 8% during the same period. As a result, the US

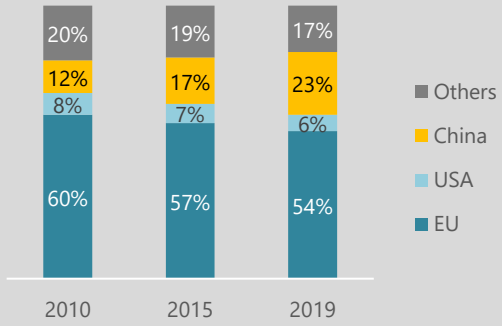
[1] McKinsey, "The era of exponential improvement in healthcare?", March 2019
[2] Statista Health Market Outlook

Share of new chemicals and biological entities



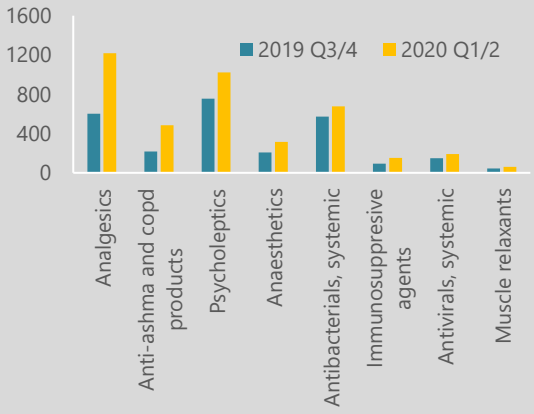
Sources: EFPIA, NBG estimates

EU imports of Active Pharmaceutical Ingredients:
(% of EU import volume)



Sources: ECIPE, NBG estimates

EU Shortages by product categories
(number of products most commonly used in COVID-19 treatment)



Sources: Technopolis Group, European Commission, NBG estimates

maintained its share of about ½ in terms of the number of new chemicals and biological entities, while the EU lost 10 percentage points of its share (from 32% to 22% respectively), going to emerging markets (from 7% to 17% respectively).

Against this background, pharma supply chains have become increasingly complex, with inter-regional trade covering 60% of total trade flows, up from 50% ten years ago (compared with a relatively stable share of 50%[3] on average for other industries). In particular, India and China cover[4]:

- 80% of global API production[5] (active pharmaceutical ingredients - i.e. pharma raw materials)
- 40% of finished pharmaceutical products sold in Europe

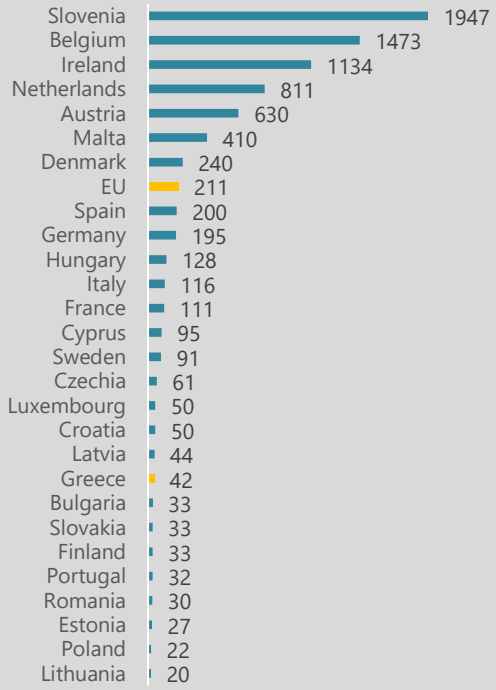
Due to this dependency on specific production countries, the outbreak of the covid pandemic created problems in global supply chains, driven by a disruptive mix of i) demand surge for certain types of drugs (either for immediate use or for stockpiling by hospitals, citizens or governments), ii) production limitations following the shutdown of factories due to quarantines and iii) logistical issues caused by border closures and export bans[6].

Following this covid-induced «code red» regarding import dependencies, EU has introduced a new Common Pharmaceutical Strategy

EU pharma industry was significantly affected by the covid supply shock, as its import dependency concerning APIs (Active Pharmaceutical Ingredients) has increased during the past decade, with extra-EU imports covering 56% in 2019, up from 40% in 2010, mainly due to higher imports from China (23% in 2019, up from 12% in 2010). During the first two quarters of 2020 ('first wave of covid'),

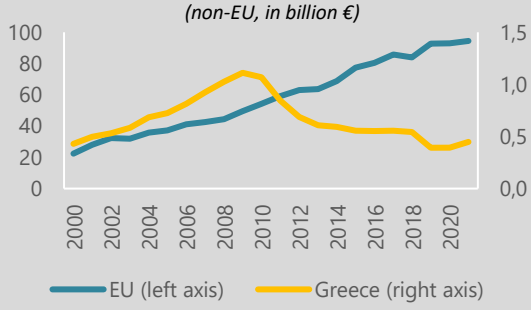
[3] McKinsey, "Four ways pharma companies can make their supply chains more resilient", September 2021
[4] Demo, "The pandemic and drug production courses", July 2021
[5] e.g. 90% of penicillin, 60% of paracetamol and 50% of ibuprofen
[6] Indicative examples of such issues during COVID were: i) the export curb on 26 APIs and formulations in India to avoid domestic shortages, ii) suspended operation of API and generics manufacturers in China due to quarantine (a survey by the Institute for Supply Management conducted between February and March 2020 found that 50% of suppliers (across industries) were operating at only 50% capacity).

Non-EU Pharmaceutical imports
(€ per capita)



Sources: Eurostat, NBG estimates

Pharmaceutical imports
(non-EU, in billion €)



Sources: Eurostat, NBG estimates

strong increases were posted in the number of shortage[7] notifications concerning the most commonly used covid treatments (about 56% higher shortages vs pre-covid levels, reaching up to double shortages for some medicines).

Amid those disruptions, the EU recognized the need for a common European Pharmaceuticals strategy[8] focusing on a patient-centered strategy aiming to ensure the quality and availability of medicines, while boosting the sector's global competitiveness. To be more specific, the strategy's main targets are:

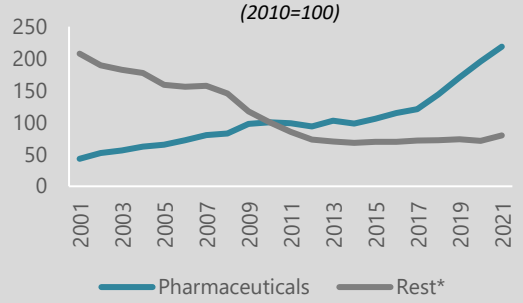
- Promoting R&D investments towards both pharmaceutical innovation as well as generics drugs, thus ensuring accessibility and affordability of medicines
- Creating a stable but flexible regulatory environment, offering legal certainty for investments while accommodating technological developments (as new players seek to enter the market - including technology companies)
- Promoting diversified supply chains[9], the importance of which became more evident through the covid pandemic and the recent geopolitical crisis in Europe (creating uncertainty about global trade flows).

Greek pharma is experiencing vigorous growth momentum

Considering both the challenges of the global environment as well as the opportunities of the European Pharmaceutical Strategy, Greece has the potential to stand out as a key agent of the EU pharmaceutical industry. The sector's willingness and readiness to step up is evident by its exceptional performance over the past 5 years - outshining both other Greek sectors as well as EU pharma manufacturers.

[7] European Commission, "Future-proofing pharmaceutical legislation — study on medicine shortages", November 2021
[8] European Commission, "Pharmaceutical Strategy for Europe", November 2020
[9] Special focus is directed towards issues of pharmaceutical shortages (which pre-dated the covid pandemic), mainly through better information and data sharing between parties as well as mitigation strategies.

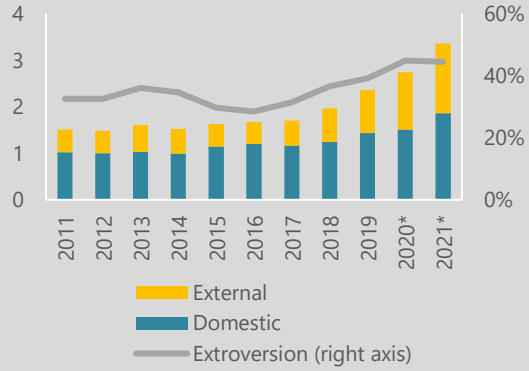
Industrial Production Index
(2010=100)



**excluding oil*

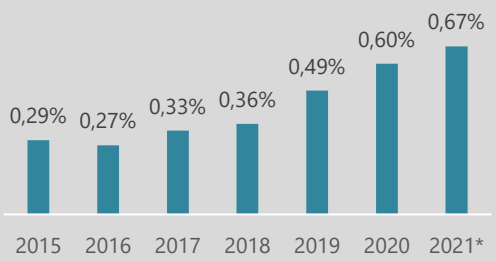
Sources: Eurostat, NBG estimates

Sales of Greek pharmaceuticals
(billion €)



**NBG estimate*
Sources: Eurostat, ELSTAT, NBG estimates

Greek pharma export value share in the EU
(estimate for EU countries)



**estimate*
Sources: Eurostat, NBG estimates

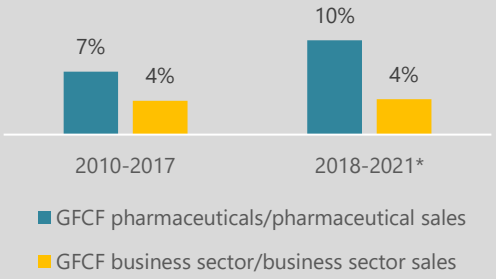
Greek pharmaceutical sales grew by about 80% during the past 5 years (to c. €3 bn in 2021, from €1.7 bn in 2017), mainly led by exports (+180% vs +35% for domestic sales). As a result, the sector's extroversion has increased to 45% in 2021 (from 30% of sales in 2017), while Greece's share in EU exports increased to 0.7% from 0.3% during the same period. The growth momentum has also been evident in terms of production volume, as the industrial production index grew by 81% during 2017-2021 (vs 43% in the EU and 7% for other Greek manufacturing). It should be noted that the recent production boom was accompanied by higher investments, with annual gross fixed capital formation in the range of €220 bn during 2018-2019 (vs €110 bn on average during 2011-2017). The increase in investment intensity (from 7% to 10% of pharmaceutical sales) widened the positive gap with the rest of the Greek business sector (with annual investments relatively stable at 4% of sales during the same period), however remaining lower than the EU average (about 14% of sales).

Never let a good crisis go to waste

Looking ahead, Greece is in an advantageous position to benefit from the newly introduced European Pharmaceutical Strategy, supported by both its recent dynamic performance as well as an improving institutional and funding environment. Specifically:

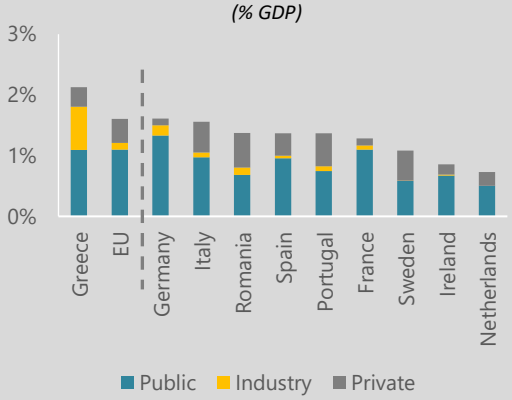
- **The Greek pharma sector appears fit to exploit export opportunities**: Pharma manufacturing is an important part of the Greek business sector, covering 7% of non-oil exports and 7.5% of manufacturing value added (vs 5% on average in the EU). The long-standing presence of pharma manufacturers (partly triggered by the fact that pre-crisis Greece has been a high health-expenditure market) ensures both an expertise in production methods and protocols as well as an effective participation in global networks. More importantly, a significant pool of specialized employees is available, who also offer a substantial cost competitive advantage. Pharma,

Gross fixed capital formation
(% sales)



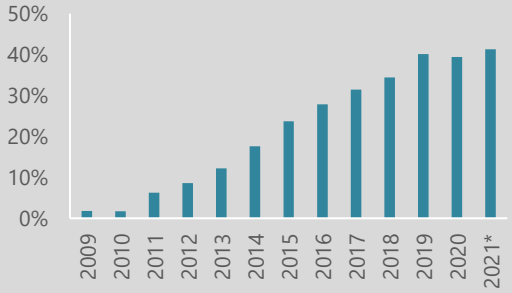
**estimate*
Sources: Eurostat, NBG estimates

Outpatient pharma expenditure
(% GDP)



Sources: IOBE, NBG estimates

Clawback & Rebate expenditure
(% of public outpatient expenditure including clawback & rebate)



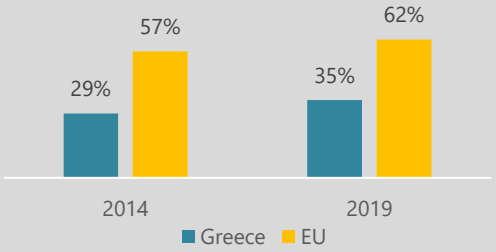
**estimate*
Sources: IOBE, NBG estimates

being a labor-intensive industry (with labor cost covering 22% of total cost, vs 16% for the EU manufacturing on average), benefits significantly from low unit labor costs. Since Greece's manufacturing enjoys relatively low unit labor costs (c. 20% lower than the EU average), the country is an attractive location for producing pharma ensuring easy access to the EU markets (by-passing cumbersome and time-consuming testing and regulatory procedures applied to imports from non-EU countries). Additionally, in terms of self-sufficiency, Greece appears to have less severe dependency issues compared to other EU countries, with extra-EU imports per capita of c. €40 (vs c. €210 on average in the EU). Furthermore, pharmaceutical imports in Greece from non-EU countries have decreased during the past decade by about 60% (vs an increase of about 70% in the EU).

- **Domestic growth potential through institutional reforms**: Greek pharmaceutical expenditure is relatively high (reaching about 2.4% of GDP in 2020 vs 1.5% on average in the EU), reflecting high public expenditure (as private sector's expenditure is close to the EU average). This is mainly a result of a low Greek GDP per capita (about ½ of the EU average), while pharmaceutical expenditure per capita is actually relatively low (but still one of the highest among OECD countries in PPP terms). As a temporary means to constrain public pharma expenditure, there is a provision for pharma industry's contribution to the budget in the form of clawback and rebate charges[10] (40% of total pharmaceutical expenditure in 2019-2021), ranking Greece as the country with the highest clawback-rebate charges in the EU (c.10% on average). Against this background, a viable solution could be the promotion of high-quality domestically produced generic drugs. Note that there is significant room for higher generics penetration as they cover just 35% of pharmaceutical sales

[10] The rebate applies in the form of a discount by pharmaceutical companies on the turnover that social security funds record, while clawback concerns the amount of money that pharmaceutical companies have to return to the State if there has been an overrun in the state budget for pharmaceutical expenditure.

Generics' penetration
(volumes share)



Sources: IOBE, NBG estimates

Investment plans
(ml €)

	2022	2023	2024	Total
Greek firms (Production)	85	80	75	240
Greek firms (R&D)	70	70	70	210
Multinational firms	150	150	150	450
Total	305	300	295	900

Sources: Data from PEF members, NBG estimates

volume in 2019 (vs 62% in the EU[11]). Partly, Greek generics have not reached their potential due to a relatively low price gap vs branded pharmaceuticals (about 35% lower vs 65% in the EU) based on current legislation[12]. While this measure aims to support Greek manufacturers of generics (who bear the high clawback burden), it actually creates a vicious cycle of low generics and high clawback (as higher-priced medicines lead to high pharma expenditure). A way to break this cycle is provided by the institutional reform (included in the RRF[13]) aiming to lower public expenditure while mobilizing investments and R&D through a partial offset of the relevant expenditures from clawback. Greek pharma manufacturers could utilize this reform as an opportunity to increase their productivity, thus a lower generics price (i.e. a higher gap vs branded medicines) would become viable. Under this scenario, the «branded-conscious» Greek consumers/patients would gradually shift from branded imported medicines to branded Greek generics (as a generalized shift to unbranded imported generics is considered almost unattainable for the Greek society). This would create second-round effects towards reducing pharmaceutical expenditure (as low-priced medicines increase their share in the mix), therefore leading to a virtuous cycle of increasing generics' share and lowering the clawback.

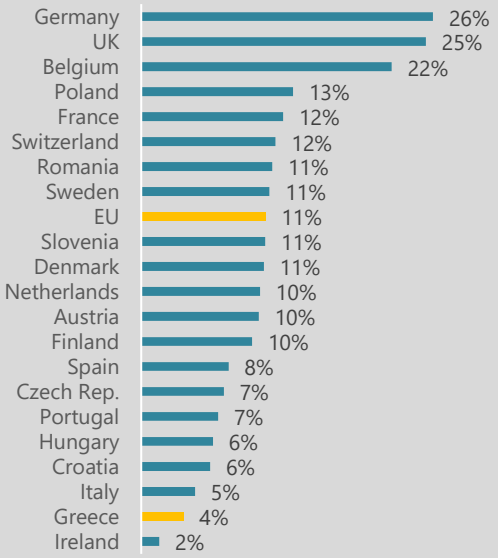
- **Financing opportunities and incentives** that could facilitate plans for capital investment and R&D are available in programs such as the Greek Investment Law and the Recovery and Resilience Facility (RRF), amounting to €30.5 billion up to 2026 (€17.8 billion in grants and €12.7 billion in loans). These

[11] Note that generics penetration increased during 2014-2021 from 29% to 33%, in line with the EU trend (keeping a gap of about 28 percentage points), in part boosted by a regulation change concerning the mandatory prescription based on the active ingredient (as opposed to specific – mainly imported – brands).

[12] Institutional developments have a significant impact on the sector, which is highly regulated due to its specific nature, as i) it affects human health while ii) supply-demand relations are highly complex, with an interrelated net of consumers (patients), choice-makers (doctors), funders (States) and producers (pharma companies).

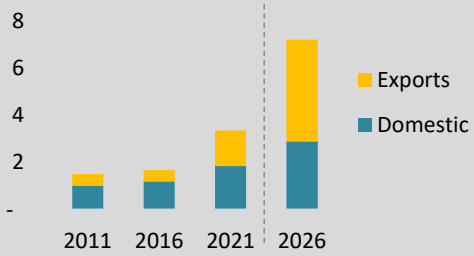
[13] The reform aims to a double effect until 2025: i) gradually decrease the relevant annual expenditure by about €0.4 bn (vs 2020 levels) by 2025 and ii) gradually increase the annual amount of the offset from investments (up to €0.1 bn by 2024). Note that the planned digitalization of the wider health system (RRF reform), with the use of big data could also improve the efficiency of policymaking and budgeting, while facilitating the containment of pharmaceutical expenditure.

R&D industry expenditure
(% of production)



Sources: EFPIA, NBG estimates

Potential Sales of Greek pharmaceuticals
(billion €)



Sources: Eurostat, ELSTAT, NBG estimates

amounts are expected to mobilize about €30 billion of private investments providing incentives for exports, size increase and R&D (including cooperation with academic institutions and research centers).

- **Investment appetite already evident:** To that end, there is an apparently growing momentum in terms of investments, based on already announced investment plans of c. €1 bn by large pharmaceutical companies for the next 3 years (i.e. more than double the average investment of the past 3 years). These plans concern both R&D (17 new research departments up to 2024 - almost doubling the current level), as well as production capacity additions (12 new factories, 29 new production units and 52 new production lines) focusing on raw material production, targeting higher self-sufficiency.

Despite the generally favorable environment, a word of caution is appropriate concerning the effects of the continuing energy crisis. Specifically, as the pharma sector is highly regulated in terms of prices, partly passing-through the recent spike in energy prices and transport costs to pharma prices is difficult. This could exert pressure on the competitiveness of Greek pharma manufacturers (especially for lower-priced medication).

The ultimate goal for Greece

Based on our estimates, the sales of the sector could almost double in the next 5 years (to €7.2 bn in 2026 from €3.4 bn in 2021), as the medium-term trend of Greek pharma sales[14] (c. 9.5% annually over past decade) will be boosted by an RRF multiplier (+20% over our baseline scenario for non-oil manufacturing).[15] Structurally speaking, this estimate could be achieved through the gradual convergence of Greece to the EU average in terms of i) extroversion (with exports from 45% of pharma sales to 60%) as well as ii) generics penetration (from 34% of pharma sales to 62%). Note that based on the current

[14] Adjusted for the expected increase in future inflation (see appendix)
[15] See appendix for the NBG Research Department's sales estimates for the Greek business sector up to 2026.

asset productivity of the sector, the abovementioned sales boost of €3.8 bn would require new investments of c. €2 bn (with about ½ covered by already announced investment plans).

All the above point to a unique opportunity for Greece to stand out as a key pharma producer in the coming years. Moreover, by leveraging on its comparative advantage in terms of human capital, evident in

- the availability of chemicals, biologists and pharmacists (about 0.3% of the population, vs 0.1% on average in the EU), and
- the strong academic environment (with Greek universities ranking among the top 500 globally in the fields of chemistry and biological sciences)

In order for this potential to be realized, pharma R&D should increase significantly to converge to EU levels (i.e. to 11% of production value from 4% currently). This would in turn require stronger cooperation between enterprises and academia - an area that Greece currently ranks very low. Under this scenario, Greece's human capital advantage could make a real difference and the country could develop into a comprehensive hub for the pharma industry across the board, from research to production.

APPENDIX: ESTIMATING SALES POTENTIAL FOR THE GREEK BUSINESS SECTOR

Methodology

Aiming to estimate sales potential for the Greek business sector, the NBG Research Department has examined sectoral data for 65 sectors[16] (using NACE codes). Specifically, for each sector we examine annual sales data (from ELSTAT) for the past 20 years (2001-2021), combined with data for the structure of the Greek business sector (sources: Eurostat, ELSTAT) and we estimate their trend over the next 5 years (2022-2026). Our approach is based on two main scenarios:

i) Baseline scenario: All sectors firstly recover from the pandemic sales drop (at latest until 2023 - with varying recovery speeds based on their performance so far) and then follow their historic trend until 2026 (adjusted for expected differences in future vs past inflation rates). Note that in sectors posting downward long-term sales trend in the past, we estimate future growth equal to expected inflation.

ii) Recovery and Resilience Facility (RRF) scenario: Considering the opportunities presented in the RRF actions, we expect an additional sales boost for each sector, benefitting from RRF to converge (or achieve) their long-term potential. The size of that boost in each sector is calculated considering:

   a. The size of their hidden dynamic (gap of current to potential sales), which in turn is defined by factors such as: export competitiveness, potential for high value-added products (e.g. less bulk food product sales), institutional improvements (e.g. land use planning - cadastre), country characteristics (e.g. geographic position advantages) as well as indirect effects from cluster development in other sectors (e.g. tourism benefits in food manufacturing)

   b. The degree in which they achieve that dynamic, which is defined by factors such as historic sales trend and policy directions (e.g. RRF incentives for digital and green investments).

Sales estimates

Based on our estimates, the Greek business sector could post a sales growth of about 50% during 2021-2026 (i.e. €150 bn increase), with about 1/3 of the increase resulting from RRF opportunities (boosting the baseline scenario by 2.3 percentage points, from 6% to 8% average annual sales increase). On a sectoral level, this transition is expected to bring the structure of the Greek business sector closer to the EU Med average. Specifically, the most notable changes are:

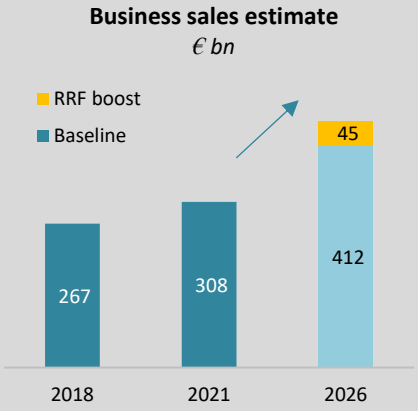
i. higher share of non-oil manufacturing from 17% in 2021 to 19% in 2026

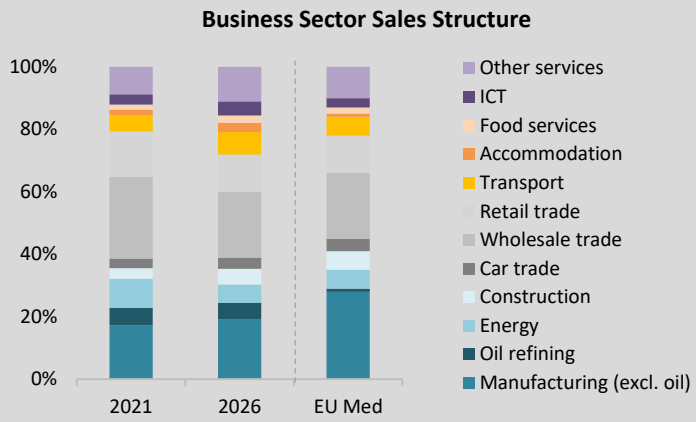
ii. higher share of accommodation, food and transport services (cumulative share from 9% to 13%) – driven by tourism growth

[16] Sectors with special characteristics have been excluded from the analysis, e.g. primary production (agriculture, aquaculture, mining), water supply, financials, public administration, health and education (sectors with strong public sector presence).

iii. higher share of construction (+2 percentage points) and ICT (+1 percentage point) – significantly boosted by RRF incentives

iv. with most growth potential concerning the productive parts of the economy, trade sectors are expected to decrease their contribution approaching the EU Med levels (cumulative share from 44% in 2021 to 37% in 2026).





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