HELLENIC BIO-PHARMACEUTICALS AND HEALTHCARE SECTOR

PROPOSAL

for a national R&D strategy for the period 2014 – 2020

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HBio
Hellenic BioCluster

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EXECUTIVE SUMMARY

In view of the Greek government's preparation of the Greek R&D program for the period 2014-2020, HBio has put together a Plan that it believes lays the foundations for a sustainable model of growth for the life sciences and bio-pharmaceutical sectors of Greece.

The Plan recognizes the present challenges that Greece faces and aims to propose a transition path from the current situation to the desired state of global and sustainable competitiveness of the target sectors and, as a consequence, of the country as a whole.

In summary:

- While Greece must cover a significant distance in order to catch up with its European and global counterparts, it has sufficient strengths that allow it to target some of the available global opportunities with a good probability of success. Program priorities should therefore aim to support these opportunities.

- Challenges such as limited size and industry fragmentation dictate a strategy of niche positioning in areas of clear and present unmet need, where the global community itself is in need of innovation.

- While we propose that the focus should be on the needs of the export-oriented segment of the industry, the important role of academia cannot be ignored. There must be measures that ensure that where appropriate:
    - The needs of industry are served on a priority basis by academic applied research.
    - The capacity of academia to come up with breakthrough solutions continues to be supported but should be directed to challenges that are more relevant to industry in the shorter term. While we support the notion of "science for science's sake" the question we presently need to address is: *how much can Greek society, at the present point in time, afford "science for science's sake"?*
    - The transition towards a state of closer and truer industry-academia collaboration is as smooth as feasible.

- The strength of the Greek IT industry and the expected benefits of potential synergies of the life-sciences/bio-pharmaceutical sector with the IT industry and other *related* areas of Greek strength cannot be overstated. This position is reflected in the plan.

- The plan proposes a set of accompanying measures that will address in parallel with the main initiatives, some of the identified weaknesses, both specific to the bio-pharma and healthcare sectors and to the country as a whole. For the proposed initiatives to be effective, there should be tight integration between these initiatives and the set of accompanying measures.

- In terms of financing, priority should be given, in order of decreasing amount, to (a) industry-lead research, (b) academic translational research and (c) collaborations with multinationals *that are tied to reciprocal benefits*. It is also proposed to support fewer but excellent projects so as to ensure that they are adequately financed.

- There should be an effort to define selection criteria that are specific to each support-action and metrics that reflect realistic success criteria.

- There should be a significant effort at the country level to build the Greek brand in general as well as the "science made in Greece" brand. This will take time and has to be "across the board", aiming to leverage where appropriate the country's reputation from areas of strength to those were, at present, there is no or negative brand value.

1. INTRODUCTION

Background

Greece is in the process of developing its strategic R&D plan for the period 2014 - 2020 that will identify the priority R&D areas, appropriate policy instruments, monitoring and control mechanisms that will bolster sustainable innovation, entrepreneurship and competitiveness at a world class level.

The Hellenic Biocluster (HBio) is the cluster of Greek bio-pharma and life sciences companies with a strong scientific, innovation and export orientation. HBio promotes the collaboration and exchange of information between its members, represents its members at international fora, liaises with other European and international bio-clusters and prepares position papers and recommendations on a variety of matters of relevance to its areas of interest.

This document presents HBio's proposal to the Hellenic government for a strategic plan (the "Plan") for supporting and guiding research, innovation and the international competitiveness of the Greek biopharma and life sciences sectors for the period 2014 - 2020.

Target Audience and Goal of the Proposal

The proposed Plan is aimed at government officials and organization decision-makers who are involved with the planning and implementation of Greece's R&D program for the period 2014-2020 and in particular the part of the program that relates to the bio-pharma, life sciences and healthcare sectors.

The goal is to present R&D priorities that our members feel are desirable and realistic and will contribute to the sustainable, international competitiveness of these sectors within the set timeframe. In addition to the priorities, the proposal discusses how, in HBio's opinion, financial, educational and program management choices can best serve the goals of the Plan.

Ultimately, this document serves as a communication tool between all relevant stakeholders who are interested in a life sciences and bio-pharma sector that best serves Greek society and promotes the competitiveness of Greek companies and organizations in the global ecosystem.

Structure of the document

This proposal is structured as follows:

Section 2 presents a list of top-level, principles, axioms and assumptions we have adopted that we feel do not require detailed justification and that provide background guidance for the proposals me make.

Section 3 is our SWOT analysis of the Greek bio-pharma and healthcare sectors. By choice we have focused on those items that have a material influence on our proposals. We have not included items that concern the Greek business environment in its totality, are common to all sectors and are or have been the remit of numerous other analyses.

Section 4 presents our main proposals for the Plan. The proposals naturally reflect our SWOT analysis and are further analyzed in section 4.1 according to their "smart specialization" compatibility. In other words we assess whether and in what way, the proposals are "smartly specialized" to the present Greek circumstances.

Section 5 discusses criteria and metrics to be used for implementing the Plan proposals. Section 5.1 presents prioritization criteria that should be applied in order to assess the size of the financial support to be received and the best timing for launching each initiative within the programmatic period covered. Section 5.2 then discusses selection criteria to be applied when evaluating proposals. Finally section 5.3 discusses success criteria and metrics to be applied at the final program assessment stage.

Section 6 focuses on accompanying measures including competitions and specific educational initiatives we feel are essential for addressing some of the weaknesses that affect the bio-pharma and healthcare sectors, in particular in relation to their innovation and global competitiveness potential.

Section 7 presents our broad-stroke proposal for the allocation of the available funds according to criteria such as the priority areas proposed, the nature of the grantees etc.

Section 8 discusses proposals for the role of academic research in the new framework.

Finally, section 9 presents basic concepts and example proposals for creating a Greek bio-pharma and healthcare sector brand, that are realistic, convincing and will help accelerate the international awareness of this sector.

2. BASIC PRINCIPLES, AXIOMS AND ASSUMPTIONS

In preparing the proposed strategic Plan we identify a set of basic principles and assumptions that have guided our work. They are as follows:

1. Greece (like many other developed countries) can only hope to prosper by focusing on products and services that are either "knowledge-intensive" or have a significant differentiating quality, since it has neither the market size, nor the low cost to compete on any other basis.

2. Having at the present time, small and fragmented industries, Greece must focus on niche offerings that exploit unique properties of our products and environment and do not depend on volume or low cost. Over time Greece must seek to build a reputation for quality and seek to be an active participant in emerging value chains.

3. Within the global economic web we must start by becoming an "active contributor" aiming to grow over time into an "important" node, where capable.

4. We recognize the importance of synergies to sustained and systematic innovation, within existing and especially in new value chains that are being created, and our choices and actions will be aligned with this.

5. Where lacking the necessary resources, we must strongly consider partnering with global players, aligning, where feasible, our output with their requirements and helping them compete in the global arena (on a kind of OEM/ODM basis). We should work to become and be perceived as a component of their success aiming to grow this role over time. Where strong and innovative, we should not shy away from leading by example.

6. The goal of the Plan is to make the Sectors competitive at the EU/global level, and not simply increase the present competitiveness level or make Greece competitive only at the regional level.

7. The Plan adopts a "forge ahead" stance. This means that it concentrates on identifying and focusing on the global opportunities and challenges of the industry and only to a much lesser degree on the weaknesses (e.g. unfavorable/unstable taxation etc.) of the current Greek environment, which it is assumed will be the remit of other government initiatives.

8. We recognize that in the final count, certain choices must be made at the political level. Akin to the "entrepreneurial attitude" and the "gut feeling" basis of many successful decision-makers, some of the recommendations are made on the basis of their potential downstream benefit, rather than the basis of shorter-term metrics.

9. While we recognize the important role of academia, at this point in time the Plan must have a significant industry-led character with academia contributing to market oriented initiatives.

10. It is paramount to support actions that promote *synergies* between companies and organizations so as to increase the critical mass of the available Greek companies in specific sectors and address the fragmentation of the industry. These synergies may be either within or across sectors as for example in the case of mobile health applications.

11. The Plan will aim to establish the Greek biopharma and life sciences companies and institutions as *global* niche players by the year 2020.

12. We believe that in the present time of industry reorganization, Greek companies and institutions, far from being at a disadvantage, are presented with significant opportunities since in an emerging environment and during the creation of new value chains where the new "rules of the game" are in flux and there are no clear market leaders, the relative disadvantage of the Greek companies is diminished. This belief should be reflected in the Plan.

13. The Plan must ensure that the Sectors do not end up in a "caught in the middle" position, where they do not offer a niche, differentiated or highest quality product/service nor do the enjoy the benefits of lowest cost supplier.

14. The Plan must strike a balance in its actions targeting existing Greek companies with strong export performance or potential, start-ups and multinationals that are based in Greece and are prepared to partner with Greek industry stakeholders.

15. Greece needs a number of "quick wins" that will serve as examples of good practice and contribute to the change towards a more "healthy entrepreneurship" mindset, both within the industrial/academic community and the society at large. This "healthy entrepreneurship" mindset should ideally convince academia that is skeptical of translating research into commercial products. This can best be achieved by a number of "*showcase projects*" with high-impact, high-visibility potential that will be well funded.

16. There needs to be a rationalization of eligible costs towards activities that *directly* contribute to value addition and away from purchases of fixed assets which means support of foreign imports. Knowledge intensive activities require primarily the support of personnel costs.

17. In allocating the funds, there should be a move away from the "social support" practices of the past, towards a policy of supporting fewer proposals with a better chance of success. Given the critical nature of these, selection and monitoring of such projects should be of the highest quality standards.

18. We recognize the need to increase exports and international commercial collaborations to be of paramount importance. We believe that the optimum approach to achieve results sooner rather than later and with greater chances of success should focus on the needs and priorities of companies/academic groups with the following characteristics in order of decreasing priority:
    a. Having strong export orientation and performance to date (exports 40% or greater of total revenue)
    b. Having strong, internationally competitive science and are close to exporting or increasing the ratio of their exports
    c. Seeking or having collaborations with multinational companies in Greece
    d. Start-ups with excellent science/products/services in the making

19. This plan focuses on actions that target commercial excellence. For completeness, we briefly consider societal, educational and employment implications and provide relevant suggestions.

20. The activities of the Plan that are adopted by the government must be *tightly integrated into a coherent whole* so as to maximize their expected impact. This means that the top level goals selected, the projects, the success criteria, the accompanying measures and the management structures put in place, must all be well aligned to each other. For example, educational initiatives that aim to teach generic "business plan writing for novices" should at best be very conservatively funded.

21. While we recognize the utility of understanding industry value chains, the need to identify “novel value chains” that result from historically non-traditional partnerships and promise a sustainable competitive advantage has led our analysis to be based primarily on identified global opportunities and trends. Existing value chain links are processed, where relevant, primarily as a “reality check” for the feasibility of our proposals.

3. SWOT ANALYSIS

Any SWOT analysis at a national sector level as broad and important as health care is at risk of itself being too broad and hence less useful as a policy development tool. In the following SWOT analysis, we apply our "forge ahead" stance to identify those positive elements (strengths and opportunities) that relate to goals that are realistically achievable and to those negative elements (weaknesses and threats) that are actionable and relate specifically to the industry itself. Systemic weaknesses of the Greek business environment as a whole (e.g. changing legal and financial frameworks, excessive bureaucracy etc.) are not discussed here since they are covered in detail in numerous other strategic analyses and proposals to the Greek government.

Strengths

S1: Greece has a small but sufficient number of very good generics companies with strong export orientation and international competitiveness. The export-oriented companies all have a strong network of international clients and collaborators that could be selectively leveraged to achieve desired outcomes. With the right incentives these companies could exert a "pull" effect on other (smaller/niche) companies further acting as a potential bridge between these Greek sub-contractors and their international clients/collaborators.

S2: Greece has a small number of highly export oriented companies that are competitive (and in some cases market leaders) in niche segments that could – with the right incentives - coalesce into *viable consortia*. These niches include: pre-clinical testing, clinical trials, diagnostics and companion diagnostics, drug repositioning, indication expansion, super-generics and drug delivery.

S3: There is a satisfactory drug manufacturing capacity with GMP certification and related expertise that could be made available to the international community.

S4: Greece has a high number of highly qualified personnel in a variety of *synergistically related* areas (academics, medical doctors, bio-scientists, IT professionals, clinical trials investigators etc.). The pockets of academic excellence could be leveraged in certain areas including the discovery and limited development of New Chemical Entities (NCEs).

S5: Greece has a very strong IT sector and some brilliant engineers that can be usefully leveraged in a number of emerging Sector challenges and opportunities, including Big Data analytics, mobile health (m-Health), tele-medicine, patient empowerment, patient compliance, support for the elderly, healthcare insurance and sales support. The country's participation in the "Open Government Partnership" makes available as a resource a host of public data sets that could fuel innovation in these fields.

S6: Greece has one of the richest flora in the world and enjoys an excellent reputation for its Greek-Mediterranean cuisine. Combined, these assets can be leveraged in the emerging markets of nutraceuticals, Cosmeceuticals, herbal medicinal products, food supplements and functional foods. Greece's good reputation offers a convenient springboard for branding efforts in these emerging markets. There is also tremendous opportunity for synergies between the red- and green-bio fields, the latter of which should, and is, a priority of the Greek government.

S7: Greece enjoys an excellent reputation as a tourist destination with favorable climatic conditions, amenities and services of relevance to medical, healthcare and wellness tourism. While not directly related to the core of the biopharma industry, initiatives in this space could act in a "demand pull" capacity for a host of related services provided by the combined red- and green bio sectors of Greece. Done right, such synergies could help put the smaller suppliers in front of international clients and support their own independent exports, leveraging in a multiplicative capacity any investments in this area.

S8: Following the recent deployment of its e-prescription system by the ministry of health, Greece is a European leader in the field, creating many opportunities for value adding services.

Weaknesses

W1: The Greek bio-pharma and healthcare industry is fragmented and of small size.

W2: The large Greek companies have failed to date to assume the role of "innovation attractors" for the available SMEs and the academic groups. Additionally there is a lack of a collaboration attitude amongst Greek entrepreneurs and large company owners.

W3: Available funding for industry focused, translational R&D has, and will continue to be very limited compared to international standards. To date there has not been a real demand for internationally competitive industrial R&D, the VC culture and market are only just emerging and private investors have kept a distance from high-tech, high-risk propositions. Finally, standard investment exit models (e.g. IPO) are not available in the Greek sector for technology companies, frequently forcing innovators to export their technology abroad.

W4: Supporting expertise in the regulatory, quality management, IP, financial and related domains has been lacking, increasing the relevant costs and acting as an additional hurdle for Greek companies. In the healthcare industry, thorough knowledge of the regulatory requirements and expertise in the implementation of relevant quality management systems are prerequisites for a successful commercialization process. In some product categories, such as telemedicine and health apps, there is a lack of awareness of these requirements, while in other product categories the relevant expertise is limited.

W5: With some notable exceptions, the Greek bio-pharma and healthcare sector suffers from a lack of branding in the domain.

W6: Industry-academia collaborations have been highly opportunistic and not subject to strict commercial-value-generation criteria. As a consequence, the potential benefits of these collaborations have not been reaped and effort will have to be expended to bridge this gap.

W7: There is a dearth of C-level executives with experience in international business development, high-tech financing, company valuations and other disciplines of immediate importance for the creation and sustenance of a competitive industry.

W8: Greece's capacity to supply patients in some therapeutic areas is already stretched due to number of trials initiated from overseas multinational companies' headquarters. Particularly in therapeutic areas with increased interest in biomarkers and companion diagnostics such as oncology, haematology and cardiology

Opportunities

O1: We consider the present state of flux and reorganization that the international bio-pharma and healthcare sectors are presently experiencing as the biggest opportunity for the Greek Sectors. Increased competition and cost pressures are powerful drivers that are opening up larger and established players to smaller/newer ones offering unique products and services.

O2: There is increased pressure for clearer product differentiation and cost reduction. Cost Effectiveness Analysis (CEA) and Budget Impact Analysis (BIA) address the two important questions of "how better is one therapy/drug over another?" and "can we afford it – even if it is better?" These challenges are of great importance to generics companies that are seeking to increase value addition and gain competitive advantages via better formulations, drug delivery, drug repositioning, drug-device and combination-drug opportunities. Greece has some very strong representatives in all these areas.

O3: The global challenge captured by concepts such as "total health cost" and "integrated therapies" creates opportunities for synergies between various stakeholders.

O4: The emerging nutraceuticals, cosmeceuticals, herbal medicinal products, food supplements and functional food markets offer a significant opportunity for value-adding synergies between the Greek food and bio-healthcare sectors.

O5: The prohibitive cost of clinical trials (CTs) is creating opportunities for technologies that increase their predictability, reduce the risks to CT participants and reduce their overall cost. Furthermore, the difficulties in recruiting CT subjects for multi-centric CTs in combination with the "tightening" of the regulation in overseas markets creates a strong demand for CT centers.

O6: There is a very significant amount of public, freely accessible big data repositories that provide exciting opportunities to groups that can think out of the box and are IT-savvy. Exploiting these assets is low cost and is driving the creation of new value chains in healthcare, bio-pharma and other areas.

O7: Changing demographics and the drive for personalized medicine in the western world are creating opportunities for new niche products and services, the discovery and development of which often depends on the ability to exploit relevant big data sources and clever IT applications.

O8: The livestock industry is itself facing a number of challenges regarding livestock health and potentially toxic effects to humans from increased use of antibiotics. This creates a need for solutions, including those that could be transferred (repositioned) from the related domain of human health where a significant body of knowledge is available for exploitation.

Threats

T1: The increasing cost pressures on the healthcare system is commoditizing the industry with all the implications of such a state.

T2: Competitors that are equally good and cheaper (both out with *and* within the EU)

T3: International pharmaceutical companies are entering rather dynamically in the generics (including the value added generics) space, thus increasing competition.

T4: Payers and healthcare providers (hospitals and doctors in private practices alike) are increasingly exercising their prescription selection rights. As a consequence, not well-differentiated products or products whose price is not well justified in the eyes of these decision makers, will fail.

T5: Large IT multinationals (IBM, Oracle, SAS, Google etc) are entering the healthcare sector presenting formidable competition to the smaller, less innovative companies whose product/service is “IT intensive”.

T6: The continuous re-organizations, restructurings and buy-outs can threaten the cash flow of smaller companies.

T7: The emergence of non-chemistry-, non-surgery-based treatments may threaten in the long term those players that are potentially affected and do not follow developments in these fields.

T8: A possible threat for Greece (where there is a lack of critical mass of companies) is that its excellent companies are bought out by multinationals *before* any significant benefits they bring are shared within the Greek industrial ecosystem.

4. STRATEGY PROPOSALS

Overview

HBio proposes a strategy for the support and development of the Greek bio-pharma and healthcare sectors that focuses on five priority goals for the period 2014-2020:

- Goal 1: Establish Greece as a globally competitive, *niche* player in three broad areas:
  - Development of value added pharmaceutical products (including generics) and treatments
  - Innovative and high IT-content products and services for the healthcare sector
  - High synergy innovative applications and services
- Goal 2: Support a small number of high profile, high impact "showcase projects".
- Goal 3: Strengthen industry-led, industry-academia collaborations
- Goal 4: Support a set of accompanying measures to address current weaknesses
- Goal 5: Encourage collaboration with multinationals in Greece

Proposals for R&D Priority Areas

Goal 1: Establish Greece as a globally competitive, niche player in three broad areas

Based on our SWOT analysis, we propose the support of the following three priority areas:

Area 1. Development of value added pharmaceutical products and treatments
This area targets the Greek pharmaceutical industry and aims to support the development of well-differentiated products and low cost treatments in therapeutic areas of unmet need. The following more specific R&D activities are proposed:

- Improved formulations /super generics/ value added pharmaceutical products
- New drug Delivery options
- Drug repositioning / Indication Expansion
- Drug combinations
- Drug-device combination treatments
- Biomarkers, diagnostics, companion diagnostics and clinical trials (including commercialization planning for promising candidates and design and implementation of proof of concept studies)

Area 2. High-IT content products and services for the healthcare sector
This area aims to promote and support the potential of products and services that exploit the strong synergies between healthcare sector and specifically the IT sector where Greece is strong. The following more specific R&D activities are proposed:

- mobile-health and biosensors
- Big Data Analytics
- Care for disadvantaged groups (elderly etc.)
- Tele-medicine services
- Drug development products and services

Area 3. High synergy applications
This area aims to promote and support the potential of products and services that exploit the strong synergies between the healthcare sector and other related sectors. The following more specific R&D activities are proposed:

- Nutra/Cosmeceuticals/food supplements
- Herbal medicinal produts
- Livestock health
- Medical tourism
- Functional foods
- Manufacturing processes for the pharma industry

Goal 2: Support a small number of high profile, high impact "showcase projects"

Showcase Projects should have high clarity goals addressing a true and preset need of the international community, have strict proposal selection criteria, promise significant export potential and be well funded.

HBio proposes the following Showcase Projects (SPs):

Within Area 1

- SP1: Greek pharmaceutical product to Phase II: will aim to develop a value adding pharmaceutical product entirely within Greece and successfully complete a Phase II study

- SP2: Repositioned compound to Phase II: will aim to develop a repositioned pharmaceutical product (or other compound) entirely within Greece and successfully complete a Phase II study with a view to out-license it to a multinational or raise funds for its further development by the Greek sponsor(s).

- SP3: Drug Device Combination Treatment: will aim to develop a drug device combination treatment (including for example companion diagnostics platforms) entirely within Greece and successfully complete a Phase II study

Within Area 2

- SP4: IT in the service of Healthcare: will aim to develop a high-profile, high impact in terms of exports potential or job-creation potential application that is data/knowledge/IT-intensive

Within Area 3

- SP5: Livestock health: will aim to develop a better preventative treatment (less toxic for human consumers) for a selected disease that affects livestock
- SP6: Discovery services (within areas 1, 2 and 3) combining strengths in Big Data Analytics with Big Data Acquisition platforms (with facilities currently available both in academia and industry) aiming to offer state-of-the-art services to multinational companies

Goal 3: Strengthen industry-led, industry-academia collaborations

While industry-academia collaborations could be strengthened via the participation of academic groups in consortia receiving grants from the other proposed goals, this goal is specifically targeting collaborations the outcomes of which create innovation at the level of internal company capabilities (such as manufacturing, new product development, testing etc.).
An example instrument for supporting this goal is the status of "affiliated entity" for companies wishing to collaborate with University groups. Such a status allows companies to participate in university postgraduate and PhD programs, hosting students at their premises to solve a specific R&D challenge they are facing.

Goal 4: Support a set of accompanying measures to address current weaknesses

HBio proposes a set of accompanying measures that target identified weaknesses of the Greek business environment should also be supported within the Plan. Examples of such measures include:

- Educational programs in selected areas as detailed in Section 6 of this proposal.
- *Innovation competitions* (see also Section 6) with a bias (but not exclusively for) towards young entrepreneurs and emerging applications in the health sector. These should be high profile events organized on a yearly basis, preferably funded to the level of a Showcase Project, with the contribution of sponsors. The aim should be to contribute to the speedier building of the Greek brand and to change attitudes and the acceptance of innovation and entrepreneurship within the business and academic communities as well as the Greek society at large.
- Initiatives that promote the Greek brand in the healthcare and bio-pharma space.
- A project that will assess the success of the Plan. This must include an assessment of the *change* in the status of the "Greek brand".

Goal 5: Encourage collaboration with multinationals in Greece

HBio proposes that a certain small proportion of the available funds should be directed to activities that promote the collaboration of Greek companies with the local subsidiaries of pharmaceutical multinationals, the goal being to expose Greek beneficiaries to world class players and encourage them to develop world class solutions.

Smart Specialization

For the purpose of assessing the proposed Plan for the Greek bio-pharma and life sciences sectors, we apply the concept of "smart specialization" first presented in the policy documents of the EU for the HORIZON-2020 program.

Smart Specialization is understood to mean a set of Plan priorities that promise to render the Greek bio-pharma and health sectors *globally and sustainably competitive,* taking into account Greek strengths and weaknesses *as compared to other regions, EU and global,* and not simply within Greece. Smart specialization is therefore seen as a 'filter' applied to the plurality of options suggested by the SWOT analysis presented above. It is an 'eligibility criterion' that the proposed Plan actions must meet before they can be considered for funding by the Hellenic government.

A specific action item in our proposed Plan, is "smart specialization compatible" if the following conditions apply:

- It builds on a Strength or targets a global Opportunity in the life-sciences and bio-pharma sectors identified in our SWOT analysis
- Identified Weaknesses have a minor impact on the item, or we have a 'contingency plan' for them, or finally they act as a 'conditionality' for the implementation of the proposed item
- Identified Threats have a minor effect, are common to all stakeholders internationally, can be avoided or they act as a 'conditionality' for its implementation

Table 4.1 overleaf presents our smart specialization compatibility analysis.

- Column 1 "Proposed Item" lists the specific proposals of the Plan.
- Column 2 "Drivers" lists a combination of one or more Strengths and/or Opportunities identified in our SWOT analysis that create a *positive context* for the proposed item.
- Column 3 "Pitfalls" lists, where relevant, any developments that could negate or jeopardize the effort if they materialize or are not managed properly.
- Column 4 "Challenges" lists a combination of one or more Weaknesses and/or Threats identified in our SWOT analysis that create a *negative context* for the proposed item.
- Column 5 "Checkpoints" lists a set of foreseen contingency actions or other observations that illustrate why and how the challenges are manageable in the present context.

Note: In columns 2 and 4, relevant SWOT items are presented in the format "Letter-number" referring to a corresponding item in the SWOT analysis. For example S2 is Strength item 2 and T3 is Threat item 3.

1	2	3	4	5
Proposed Item	Drivers	Pitfalls	Challenges	Checkpoints
Improved pharmaceuticals formulations	S1, S2, S3, S4, O1, O2,	CEA and BIA should probably be taken into account, involving payer organizations and (academic?) experts in health economics	W1, W3, W4, W5, W6, W7, T2, T3, T8	While these challenges are true, there are a small number of companies that have a track record in the space. Government support *given with appropriate criteria* can help increase these examples. Threats T2 ad T3 should be reflected and accounted for in the project proposals that are funded.
New drug delivery options	S1, S2, S3, S4, O1, O2	As above	W1, W3, W4, W5, W6, W7, T2, T3, T8	As above.
Drug repositioning Indication Expansion	S1, S2, S3, S4, S5, O1, O2, O6, O7	As above	W1, W4, W5, W7, T3, T6, T8	As above.
Drug combinations	S1, S2, S3, S4, S5, O1, O2, 06	As above	W1, W3, W4, W5, W6, W7, T2, T3, T8	As above.
Drug-device treatments	S1, S2, S3, S4, S5, O1, O2, 03	Must ensure relevant regulatory know-how is available	W1, W3, W4, W7, T6, T8	As above.
Biomarkers, diagnostics, companion diagnostics and clinical trials	S1, S2, S4, S5, O2, O3, O5, O7	Close synergy with one of the above initiatives is highly desirable	W1, W3, W5, W7, T2	To ensure synergies and address W1, funded actions should be in areas of existing expertise
mobile-health	S4, S5, O3, O6, O7	High impact applications should be selected with a view to global showcase potential	W1, W3, W5, W7, T2, T5, T8	Because of the comparatively low investment needed and the trans-border nature of IT, these weaknesses are less critical here. T5 suggests the need for a focus on speed, quick distribution capability, and a highly focused and innovative nature for the project proposals that are funded.

Table 4.1: Smart specialization compatibility analysis

1	2	3	4	5
Proposed Item	Drivers	Pitfalls	Challenges	Checkpoints
Big Data Analytics	S4, S5, O3, O6, O7	Assess where in the "hype cycle" this is and plan according to degree of risk-taking that is acceptable.	W7, T2, T5, T8	This is an emerging field and the weaknesses and threats are not seen as "Show stoppers". Some care should be exercised in relation to prioritization (see Hype Cycles comments in section "Prioritization Criteria"
Care for disadvantaged groups	S4, S5, O6, O7	Focus on rare and orphan diseases may be desirable	W1, W3, W4, W5, W7, T3, T5, T8	As for mobile-health and Big Data analytics. Cleverly positioned projects could mitigate these weaknesses and threats but this must be reflected in the selection criteria of the relevant program call(s) for proposals.
Tele-medicine services	S4, S5, O3, O6, O7	Effort should build explicitly on past efforts and demonstrate how lessons learned are accounted for. Sound business models and commercialization plans must accompany R&D proposals. Medical devices and personal data protection regulations must be accounted for.	W7, T2, T5, T8	This is an emerging field and the weaknesses and threats are not seen as "Show stoppers". Some care should be exercised in relation to prioritization (see Hype Cycles comments in section "Prioritization Criteria"
Drug development services	S1, S2, S4, S5, S6, O2, O3, O5, O6	Services should contribute directly to value creation and where relevant care should be taken to ensure that appropriate certifications are available.	W1, W2, W3, W4, W6	Some of the "Big item" proposals (e.g. the development of value-added generics) are expected to create sufficient initial demand that will support the further development of this sector. The exploitation of all appropriate synergies should be a selection criterion for funding projects.

Table 4.1 (cont'd): Smart specialization compatibility analysis

1	2	3	4	5
Proposed Item	Drivers	Pitfalls	Challenges	Checkpoints
Nutraceuticals Cosmeceuticals	S1, S4, S6, S7, O3, O4, O7	We propose a balance between market leaders and start-ups. Explore complementarities with initiatives for other sectors (e.g. ag-bio)	W1, W2, W5, T2	With the participation of strong Greek companies – some of which have recognizable brands – from these target industries these weaknesses are mitigated.
Medical tourism	S4, S6, S7, O3, O4, O7	Should go beyond simply "bringing patients to nice Greek destinations"	W7, T2	Main challenge is probably an organizational and how to target the higher end of the market
Functional foods	S2, S4, S6, S7, O3, O4, O7	Incentivize Greek food companies, preferably ones with international brand	W1, W2, W5, T2	As for nutraceuticals and cosmeceuticals
Manufacturing processes for the pharma industry	S3, S4, S5,		W2, W6, T2	Highly targeted and carefully selected projects are mandatory
SP1: Greek Generic drug to Phase II	S1, S2, S3, S4, S5, O1, O2, O6	Clear demonstration of unmet need IP and ownership of asset should be clearly allocated (contractually) and in place as funding pre-requisite	W3, W4, W7, T2, T4, T8	Government funding could help overcome some of W3. W4 and W7 could and should be addressed by the accompanying measures proposed. T2 and T4 call for innovation at multiple levels that are addressed by other elements of this Plan.
SP2: Repositioned compound to Phase II	S1, S2, S3, S4, S5, O1, O2, O6, O7	As above	W3, W4, W7, T2, T4, T8	As above.
SP3: Drug Device Combination Treatment	S1, S2, S3, S4, S5, O1, O2, 03	As above	W3, W4, W7, T2, T4, T8	As above.
SP4: IT in the service of Healthcare	S4, S5, S6, S7, O1, O2, 03, 05, O6, O7	Efforts should be end-user driven, not IT-driven.	W2, W3, W4, W6, T3, T5	Will need t ensure the participation of credible end-users (e.g. hospitals, payers, government organizations, patient groups etc.)

Table 4.1 (cont'd): Smart specialization compatibility analysis

1	2	3	4	5
Proposed Item	Drivers	Pitfalls	Challenges	Checkpoints
SP5: Livestock health	S1, S2, S3, S4, S5, S6, O8	Collaboration with international element strongly desirable	W1, W3, W5, W6	Apply strict selection criteria Consortia behind proposals must be right
SP6: Discovery services	S1, S2, S3, S4, S5, S7, O1, O2, O3, O6, O7	Collaboration with international element (existing or potential) strongly desirable	W1, W2, W3, W4, W6	As above.
Goal 3: Strengthen industry-led, industry-academia collaborations	S1, S2, S3, S4, O6	See section "The role of academia"	W6	See dedicated section "Bridging the Industry-Academia Gap"
Goal 4: Support a set of accompanying measures to address current weaknesses	S1, S2	These should probably be "front loaded" in the Plan.	W2, W3, W4, W5	Actions need to be highly focused on specific issues of immediate need and interest to the industry.
Goal 5: Encourage collaboration with multinationals in Greece	S2, S3, S4, O1, O2, O5, O6, O7	Ensure that funded actions have a clear benefit for Greek stakeholders as well.	W1, W4, W6, T2	W4 is considered an impediment to date and is being addressed by the proposed accompanying measures. Specific incentives could also be adopted by the government, in order to promote these collaborations.

Table 4.1: Smart specialization compatibility analysis

5. CRITERIA AND METRICS

We discuss here criteria and metrics to be used for implementing the Plan proposals. These are organized in three basic categories: prioritization criteria, selection criteria and success criteria.

Prioritization Criteria

We have identified a set of criteria that we have applied in order to help prioritize the recommendations made. We organize these criteria in the 3 main categories:

Industry importance and expected impact

These criteria reflect our assessment of the importance of a proposed focus area and the impact we expect the Greek industry to have on these. They are as follows:

- International contracts/collaborations are signed sooner rather than later.

Impact to Greek bio-pharma and life sciences sectors

- Support of Greek pharmaceutical products exports
- Support of Greek services exports

Timing

These criteria attempt to answer the question:

> At what time and in what order should the government launch each of the proposed Plan initiatives?

We propose the following criteria in order of decreasing importance:

- Initiatives promise greater return for less government financing to start with
- Degree of synergism and cross-disciplinarity
- Proposal contains a “platform” technology/solution
- Position of technology in the “hype cycle”

Selection Criteria

Selection criteria for the proposed initiatives and project to be funded should, where possible, be specific and not "general purpose". We propose the following indicative list of criteria:

- Existing exports and/or clients and/or collaborations (the later preferably not EU Project collaborations)
- A convincing SWOT analysis for the proposal with smart specialization compatibility checks
- Time to market criteria
- Degree of synergy criteria

Future versions of this document will analyze these criteria in more detail.

Success Criteria

HBio believes that the Plan must adopt sets of success criteria that are specific to the initiatives and actions to be supported; in other words not a "one size fits all" approach but one that measures the attainment of true value creation, innovation, social and other objectives. We propose 4 groups of success criteria as follows:

1. Financial Criteria
    i. Exports
    ii. Turnover
    iii. Valuation
2. Social Criteria
    i. Number of new jobs created
3. Innovation Criteria
    i. Number of patents filed/granted
4. Competitiveness Criteria
    i. Market Share
    ii. Brand/product visibility
    iii. Number of international markets

Future versions of this document will analyze these criteria in more detail.

6. ACOMPANYING MEASURES

HBio recognizes the need for a set of accompanying measures that will further support the main R&D activities proposed. We focus here on educational activities and competitions.

Educational Activities

HBio recognizes the important role of continuing education and its potential contribution to the sustainable competitiveness of the industry as a whole. Presently, there exists a broad range of needs, targeting many different stakeholders and at a variety of levels of seniority. Nevertheless, HBIO believes that there are certain priorities that must be respected in order to create an alignment between clear and present needs of the industry and the knowhow that must be developed in order to address these needs successfully.

With the above in mind, HBIO proposes the following priorities for educational programs of immediate relevance and expected contribution to the bio-pharmaceuticals and life sciences sectors:

Biopharma Company Valuation: Presently, major financial institutions in Greece that could spearhead the local VC market lack the specialist knowledge required to assess opportunities related to high tech and life-sciences related ventures and their potential value. As a consequence, they are incapable – even if willing – to invest in what they consider "high or unquantifiable risk" proposals. Given that such a capacity is a precondition for the development of a VC market that in the long term will be in a position to support innovative companies, HBIO considers this to be one of the first priorities of a targeted continuing education initiative.

Drug approval paths for regulators: To date, the Greek National Organization for Medicines (ΕΟΦ) has focused primarily on the approval of generics and novel drugs that have been approved either in the EU or the USA. There is a lack of experience in other approval paths, for example the 505b(2) path of the FDA for repositioned drugs or other approval path options that are relevant to differentiated generics, drug-device combinations and similar applications. In line with making the above activities R&D priorities of the Greek industry, local regulators must be able to supply the relevant expertise.

Intellectual Property Law: "New Chemical Entity", "Method of Use" and other types of patents of relevance to the emerging health sector are highly specialized fields of expertise that are an essential ingredient of an industry that aims to be competitive at the global level. Presently there is a dearth of qualified IP attorneys and Patent Office examiners in Greece, a reality that acts as a very real impediment to local innovation and its translation into marketable value.

Bio-Ethics: A corollary of the proposal to establish Greece as a regional center for clinical trials is that all personnel involved with CTs, from doctors to care-givers to CT CROs must be fully aware and compliant with international bio-ethics and patient rights guidelines and law. This is a relatively young field but one where Greece must be fully up-to-date and also abe to contribute to the global debate.

Pharmacoeconomics: As the pressure to reduce the total cost of healthcare increases, so the need for executives who have a deep understanding of pharmacoeconomics increases. Such executives are needed by all companies but also by healthcare providers and payers alike.

Regulatory and quality management: Medical devices and pharmaceutical industries are heavily regulated. Furthermore, the regulatory framework is undergoing constant evolution as it follows industry developments. A successful product commercialization strategy requires expertise in the implementation of relevant quality management systems (e.g. ISO13485) and deep knowledge of the regulatory requirements. The Greek industry has to develop and maintain current its competences in the regulatory and quality domains and local government bodies should be able to provide the relevant expertise.

Certifications: there is a need to ensure that all active players in the bio-pharma and healthcare sectors are aware of and possess all the necessary internationally recognized certifications (GMPs, GLPs, bio-ethics etc.) that are required for their operation.

Proposed Instruments

HBio proposes that the government adopts a flexible set of instruments for implementing its industry-oriented educational program.

1. **Expert Personnel**: support for hiring or sub-contracting expert personnel in the above educational priority areas.

2. **Courses with certifications**: support for continuing education courses in the above educational priority areas.

3. **Events**: support for organizing international events in the above priority areas.

4. **Internships**: National and international internships (for students and company executives) to acquire specialized expertise.

Competitions

HBio proposes a set of innovation competitions with a bias (but not exclusively for) towards young entrepreneurs and “emerging” applications in the health sector. These competitions should not be similar to the many "innovation competitions" organized by a host of Greek organizations as of lately. We propose *thematic* competitions focused on *big item challenges of international interest*, with a high degree of synergism, open to all (companies, academic groups, individuals, from Greece and abroad) that will serve the following goals:

- promote the *Science in Greece* brand
- promote the collaboration between companies and universities
- offer a high profile opportunity for start-ups or individuals to try out new ideas
- advance the state of the art in challenging areas or showcase potential novel value chains and/or business models
- act as an example of synergies between the high-tech and industrial/academic sectors of Greece and its tourism sector. We see such initiatives as serving very well the aim of the tourist industry for thematic tourism, in this case education/science/business tourism.

Examples of competitions include:

- Mobile applications for health
- Gamification of discovery in bio-pharma
- Gamification for enhanced patient compliance
- Drug-device combination therapies

7. FINANCING

While HBio does not intend to propose a detailed plan for allocating the funds available for the bio-pharma and healthcare sectors, we present here some basic principles that we believe will contribute to a well balanced Plan.

- Funds should be allocated between existing Greek organizations, startups and foreign multinationals as follows:
  - Existing organizations (companies and universities): 60%
  - Foreign Multinationals: 20%
  - Start-ups: 20%

- The showcase projects should be funded to the tune of 2-4M€ each. Projects SP1, SP2 and SP3 in particular should be close to the 4M€ mark.

- Eligible costs should include:
  - Personnel
  - IP protection
  - Business development
  - Subcontracting (qualified)
  - Durable equipment (to a very limited extent)

- Within the proposed priority areas funds should be allocated as follows:

Goal 1: Establish Greece as a globally competitive, *niche* player in three broad areas:	**60**
Development of value added generics and treatments	30
Innovative and high IT-content products and services for the healthcare sector	15
High synergy innovative applications and services	15
Goal 2: Support a small number of high profile, high impact "showcase projects".	**10**
Goal 3: Strengthen industry-led, industry-academia collaborations	**15**
Goal 4: Support a set of accompanying measures to address current weaknesses	**5**
Goal 5: Encourage collaboration with multinationals in Greece	**10**
Total	**100**

8. THE ROLE OF ACADEMIA

To date, the relationship between industry and academia in Greece has been at best "patchy" and is summarily described as in Figure 8.1.

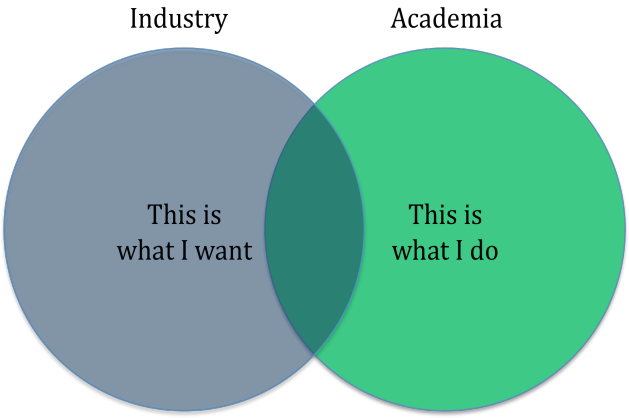

Figure 8.1: Industry and Academia collaboration in Greece is limited

There has been limited overlap, usually within the context of EU or national R&D projects, with very few examples of subcontracting, licensing or other traditional forms of true commercial collaboration. There have been many reasons for this situation, but one that may be directly relevant to the goals of the proposed Plan is the limited ability of the industry to "absorb" academic research output and the lack of an appropriate framework within academia that makes such collaborations commercially viable.

While we believe that in the present circumstances, the needs of industry should assume center stage, we recognize that the present and potential contribution of the academic establishment of Greece, if aligned with these needs, could prove to be a major competitive advantage for the country.

The challenge we face is that we must devise a plan that allows Greece to transition from the current state into the desired one. This plan should:

- Ensure the immediate support of industry with academic groups working on present challenges related to industry
- Ensure the long-term independence of academic research and the ability to come up in a 'bottom up' fashion with breakthrough concepts that could benefit all in the longer term.
- Ensure that the transition is smooth without risking to disrupt the main effort and goal.

For this we propose that the following principles are applied to the funding and prioritization of academic R&D:

- While we support the notion of "science for science's sake" the question we need to address is " how much can Greek society, at the present point in time, afford science for science's sake?" For this reason, we propose to give first priority to academic research that has strong sponsorship approval by one or more industrial partners. The goal here is to encourage academic institutions to work in challenging problems the solution of which will offer tangible benefits to their industrial collaborator within a short timeframe. These projects should be led by the industrial partner.
- Support academic led proposals of high synergistic content, that address some globally interesting challenge.
- Support academic research into basic science providing projects have a multinational bio-pharma company as a sponsor.

Last and certainly not least HBio strongly encourages the government and the academic community to create a clear and workable framework that actually allows (if not encourages) the collaboration of industry with academia in the basis of some sound and clear principles. IP ownership, licensing agreements, legal framework must all be crystal clear if academia is to ever begin considering such collaborations on a commercial - and not EU project – driven basis. Failing this, the desire of all for bridging this gap, will remain just that, a desire.

9. MARKETING OF THE GREEK LIFE-SCIENCES BRAND

HBio believes that it is essential to support, in parallel with the R&D activities, initiatives that help create and market the Greek life-sciences and bio-pharma brand. HBio further believes this should be part of a broader plan to promote the Greek brand for multiple target audiences.

While true value creation, differentiation and quality are the ultimate prerequisites of sustainable competitiveness, we believe that branding activities must be planned and executed almost from day one of the program, in order to help accelerate the international awareness and acceptance of products and services of Greek origin.

Marketing plan characteristics

HBio proposes a marketing action plan with the following characteristics and goals:

- The plan will take time (needs 4-10 years of consistently positive messages) and will be backed by all governments, present and future in a consistent way.

- The plan will build on positive concepts that are related with Greece, associating in clever and creative ways new goals (e.g. Greece as an emerging technological player) with globally accepted positive connotations (e.g. Greece and nutrition, Greek flora, tourism, the sea).

- The plan will create *marketing messages* and *labels* that are sector specific, felt at the subconscious level as *credible coming from Greece*, unique, novel and *of present global relevance*. Messages should aim to capture present global sentiments in each sector and where 'unmet needs' are being addressed, should not shy away from leading the way by proposing a 'new way' at the global level and creating appropriate *labels* of global appeal.

- To enhance emotional attachment, messages must be tailored to local markets and aim to link the Greek item being promoted with local issues/capabilities/goals/aspirations (a piggy-back approach).

- There will be messages strongly promoting the benefit and opportunities arising from *synergies* – both within and across sectors.

- The plan will have a national component (targeted at Greeks and aiming to provide examples of good practices and change "attitudes") and an international component (targeted at the international markets)

Proposed Examples of Marketing messages

Proposed Message 1
Goal: to accompany general purpose advertisements showcasing Greek healthcare

Greek Pharmaceuticals – value for money

Rationale of terms in message

- **Greek Pharmaceuticlas**: creates/raises awareness of a product with low-to-mid international recognition
- **Value for money**: there is a big international debate presently on this issue. Just like with Japanese cars in the '90s and Korean later, this claim can help build a name for Greek pharmaceuticals associating with them an attribute (low cost) that is a requirement in many markets

Proposed Message 2
Goal: to accompany general purpose advertisements showcasing Greek healthcare

Greek biopharma – contributing to future healthcare

Rationale of terms in message

- **Greek Biopharma**: creates/raises awareness of a product with low-to-mid international recognition
- "**contributing**": is compatible with the 'size' of the Greek biopharma industry and "humble claims"
- "**future healthcare**": talks to the many issues currently faced by the industry and is a term recognized internationally at the present time

Proposed Message 3
Goal: to accompany general purpose advertisements showcasing Greek healthcare

Great Nature – Good Health – Greece

Rationale of terms in message

- Plays on the 3 "G"s, reinforcing the association of "great" and "good" with "Greece"
- Exploits positively perceived association between beautiful Greek nature, cuisine and good life expectancy statistics and Greece
- Offers integration/synergistic opportunities between sectors such as: agriculture, nutritional/beauty products, healthcare, tourism, high tech

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