EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

EUCOPE

Pricing & Reimbursement / Market Access Working Group Meeting

Brussels, 21 November 2019

Competition Law Compliance Policy

EUCOPE brings together representatives innovative companies to discuss common issues, challenges and trends affecting the pharmaceutical industry. This activity can be perfectly legitimate. However, certain competition law risks may arise in relation to EUCOPE's activities.

EUCOPE's European Union ("EU") compliance policy ("Policy") explains these competition law risks and aims to ensure compliance by all members and EUCOPE staff with the rules applicable in the EU. EUCOPE itself and its members are subject to these rules when engaging in any EUCOPE related activities. Any anticompetitive behavior adopted by a member can result in serious financial, criminal and/or disciplinary penalties, as well as other harm (e.g., reputational harm) for EUCOPE, represented companies and for meeting participants personally.

Competition Law Compliance Policy

There are certain matters which **should not** be discussed with competitors before, during or after any such meetings. These include:

- Territorial restrictions, allocation of customers, restrictions on types of services, or any other kind of market division;
- Prices, price changes, conditions of sale (including payment terms and guarantees), price differentials, discounts;
- Current market conditions and issues, including industry pricing policies or patterns, price levels; capacity (including planned or anticipated changes regarding those matters), except where limited to the discussion of historical or public information;

[cont'd]

Competition Law Compliance Policy

- Individual costs, cost accounting formulas, methods of calculating costs;
- Individual company figures on market shares, sources of supply, capacity;
- Information as to future plans of individual companies concerning technology, capacity, marketing or sales; and
- Matters relating to individual suppliers or customers.

Attention: these rules equally apply to informal discussions before, after, or during each meeting. If any sensitive information is discussed or disseminated, insist that the discussion be terminated immediately and make sure that your objection is recorded in the minutes. If necessary, leave the meeting and immediately inform EUCOPE's General Counsel.

I.
Welcome / Next Events / Meeting agenda and objectives

Chairs

Agenda (1/3)

I. Welcome / Next Events / Meeting agenda and objectives

Chairs

II. The EURIPID 2nd Dialogue Stakeholder Meeting

- Summary and conclusions
- Next steps

Rajesh Chauhan, BioMarin

III. Seven secret ingredients for successfully launching and commercialising a company's first drug in Europe

- Understanding what drives a product's value and how to fully extract it

Christian Schuler, Simon-Kucher & Partners

Agenda (2/3)

IV. EU-Proposal on Joint HTA

- Comparison of the EUnetHTA methodology v. HTA processes in France and the UK

  Stephen Norton, MAP BioPharma

V. New Italian Decree on P&R Procedures: upcoming changes

Claudia Garimberti, Regulatory Pharma Net

VI. France: The PLFSS 2020 – implications for the pharmaceutical sector

Alexandre Regniault, FranceBiotech

Agenda (3/3)

VII. Further Country Updates

- UPDATE : main principles governing transparency and anti-kickback in France

  Sébastien Pradeau, Fieldfisher

VIII. AOB / End of Meeting

Chairs

Upcoming Events

- 25 November 2019: EUCOPE OMP Workshop, Brussels [developers only]
- 11 December 2019: EUCOPE policy lunch "Rare diseases and the EU OMP Regulation: addressing gaps in the economic data", Brussels
- 20 February 2020: OMP Working Group Meeting, Brussels
- 26 February 2020: Members Meeting, Brussels

II.

The EURIPID 2nd Dialogue Stakeholder Meeting

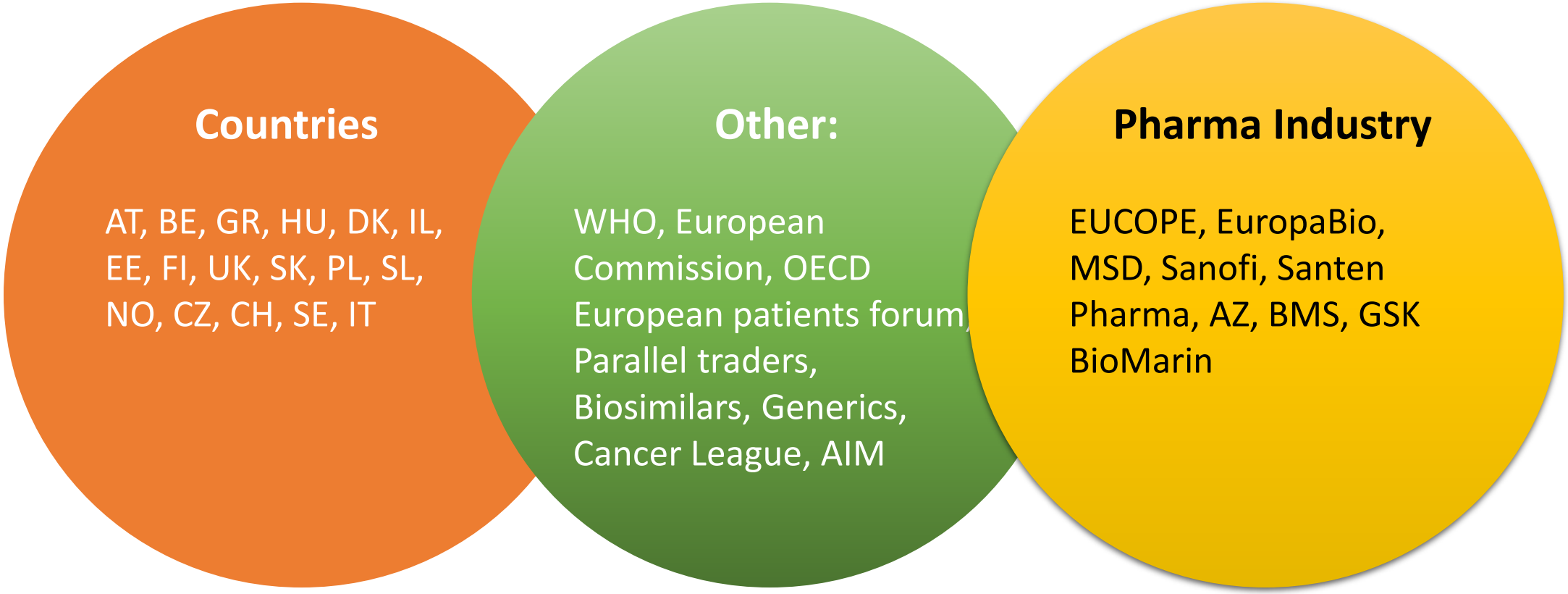
Rajesh Chauhan, BioMarin

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Feedback from the 2nd EURIPID stakeholder meeting

23 Sept 2019, hosted by NEAK, Hungary

There was broad representation from a range of stakeholders..



EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

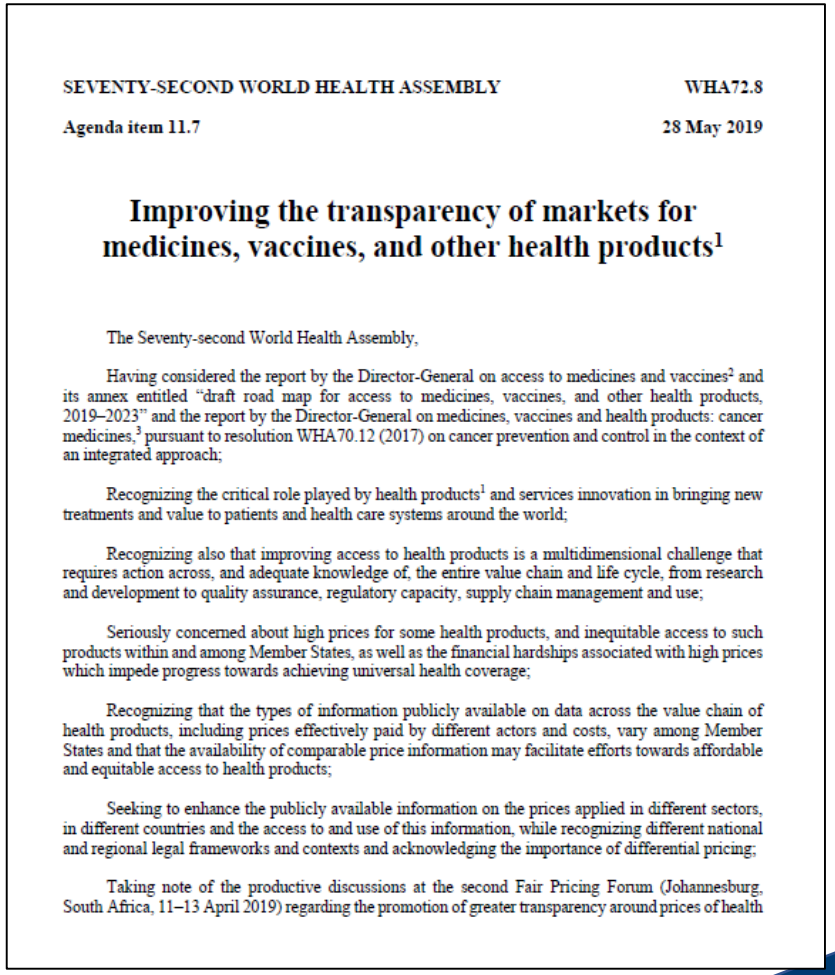
The WHO report on Pricing of cancer medicines formed the foundation for the price transparency resolution

- Strengthening pricing policies
- Improving efficiency
- Improving transparency
- Promoting cross-sector & cross-border collaboration
- Managing demand-side factors
- Realigning incentives for R&D

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

The WHO presented on price transparency…

- Seriously concerned about high prices for some health products ..
- Seeking to improve the transparency of funding [public and private sector funding for R&D] across the value chain
- URGES Member States to share information on net prices
- Improve the reporting, such as on sales revenues, prices, units sold…
- Monitor the impact of price transparency on affordability..
- Biennially convene the Fair Pricing Forum.. to discuss the affordability and transparency of prices and costs
- WHO does not have means to enforce the implementation of the Transparency Resolution but the Director-General is requested to submit a report on progress at the next WHA



SEVENTY-SECOND WORLD HEALTH ASSEMBLY WHA72.8

Agenda item 11.7 28 May 2019

Improving the transparency of markets for medicines, vaccines, and other health products[1]

The Seventy-second World Health Assembly,

Having considered the report by the Director-General on access to medicines and vaccines[2] and its annex entitled "draft road map for access to medicines, vaccines, and other health products, 2019–2023" and the report by the Director-General on medicines, vaccines and health products: cancer medicines,[3] pursuant to resolution WHA70.12 (2017) on cancer prevention and control in the context of an integrated approach;

Recognizing the critical role played by health products[1] and services innovation in bringing new treatments and value to patients and health care systems around the world;

Recognizing also that improving access to health products is a multidimensional challenge that requires action across, and adequate knowledge of, the entire value chain and life cycle, from research and development to quality assurance, regulatory capacity, supply chain management and use;

Seriously concerned about high prices for some health products, and inequitable access to such products within and among Member States, as well as the financial hardships associated with high prices which impede progress towards achieving universal health coverage;

Recognizing that the types of information publicly available on data across the value chain of health products, including prices effectively paid by different actors and costs, vary among Member States and that the availability of comparable price information may facilitate efforts towards affordable and equitable access to health products;

Seeking to enhance the publicly available information on the prices applied in different sectors, in different countries and the access to and use of this information, while recognizing different national and regional legal frameworks and contexts and acknowledging the importance of differential pricing;

Taking note of the productive discussions at the second Fair Pricing Forum (Johannesburg, South Africa, 11–13 April 2019) regarding the promotion of greater transparency around prices of health

The EURIPID collaboration responded to the EU Parliament call for price transparency..

The EU Parliament asked EURIPID to respond to their question regarding a call for greater transparency

EURIPID responded to this call but this response was not shared with industry and still has not been shared despite numerous requests.

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

The afternoon focused on 3 working groups..

1

Transparency Working Group:
Increasing transparency of pricing (access to EURIPID, questions of real prices)

2

EPR Monitoring Working Group
Monitoring the uptake of the recommendations of the EURIPID guidance document on external reference pricing

3

Patients' Access Working Group:
Measuring patients' access to medicines with the help of EURIPID (methodology and integration of volume information).

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Industry should have access to the database

- Industry does not currently have access to the EURIPID database
- Industry cannot be held accountable for the content unless appropriate governance measures are in place
- The database cannot offer variable access to company only content.
- A process is necessary for making amendments, an appeals process is necessary e.g. if data is found to be inaccurate.
- Currently data is added but the veracity of the data is not assessed

EURIPID suggested demonstrating the site ‘live’ at the next meeting to allay industry fears on content

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Researchers can gain access to the database

- EURIPID state they do not have the bandwidth to undertake research on the database
- They are open to researchers willing to analyse the data
- Rules around access for researchers remains unclear - activist groups could obtain data for anti-industry perspectives
- A strong rules based governance framework needs to be established
- The national authorities met the following day to discuss researcher access (industry were not invited)

Most groups are keen for greater price transparency (industry stands alone here..)

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

- The primary objective of the EURIPID database is to improve access – link between price and access was clearly stated
- Industry highlighted the risk of reduced access (an unintended consequence of greater transparency) however there was a lack of consensus with this perspective
- Industry disagreed on the sharing of confidential arrangements but strong support from other parties.
- Some countries are inserting volume data into the database
- Industry highlighted the legal barriers to sharing of confidential information e.g. competition law which prohibits sharing of confidential price arrangements (some EURIPID members felt this was not an issue)
- EURIPID and the majority of the audience were of the view that a step by step approach should be taken toward price transparency (how and what is still to be determined).

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Suggested areas for EUCOPE to intervene..

- EURIPID response to EU Parliament call for price transparency
- Industry access to the database + governance framework
- Researcher access
- Unintended consequences
- Step by step approach to greater transparency to be clarified

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Any Questions..?

Reminder of EURIPID..

- **EURIPID Collaboration** is a voluntary and strictly non-profit cooperation between mostly European countries on building up and maintaining a database with information on national prices and pricing regulations of medicinal products in a standardized format.

III.

Seven secret ingredients for successfully launching and commercialising a company's first drug in Europe

Christian Schuler, Simon-Kucher & Partners

Seven Secret Ingredients for Successfully Launching and Commercializing a Company's First Drug in Europe

Understanding What Drives a Product's Value and How to Fully Extract It

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

November 21, 2019

Christian Schuler, Senior Partner
Joerg Tritschler, Director

Munich Office
Luise-Ullrich-Str. 14
80636 Munich, Germany
Tel. +49 89 544793 647

Zurich Office
Loewenstr. 1
80636 Zurich, Switzerland
+41 44 226 50 40

Medical . Health Care

Simon-Kucher team introduction

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Christian Schuler
Senior Partner

Munich office
Luise-Ullrich-Str. 14
80636 Munich
Germany

Tel: +49 89 544793 647
christian.schuler@simon-kucher.com
www.simon-kucher.com

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Joerg Tritschler
Senior Director

Zurich office
Loewenstrasse 1
8001 Zurich,
Switzerland

Tel: +41 44 22650 67
joerg.tritschler@simon-kucher.com
www.simon-kucher.com

Source: Simon-Kucher & Partners.

Simon-Kucher & Partners at a glance

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Best consultancy in marketing, pricing and sales

Financial Times

Marketing, brand, pricing

1 **Simon-Kucher & Partners**
on par with
McKinsey & Company
⋮
Boston Consulting Group

Source: *Financial Times*, list of the UK's Leading Management Consultants, January 2018

brand eins/Statista

Marketing, sales, pricing

1 **Simon-Kucher & Partners**
⋮
Boston Consulting Group
McKinsey & Company

Source: *brand eins Thema* special edition: Consulting – industry report from *brand eins Wissen* and *Statista*, online survey, 2014 - 2019

Capital

Marketing, sales, pricing

1 **Simon-Kucher & Partners**
on par with
Boston Consulting Group
McKinsey & Company

Source: *Capital*, survey of the best consultancies in France, 2016, 2018 (conducted every two years)

Forbes

Marketing, brand, pricing, sales

Simon-Kucher & Partners
★★★

Source: *Forbes*, survey of the best management consulting firms in the US, October 2016, 2018 (conducted every two years)

MT Magazine/Erasmus University

Strategy consulting

1 **Simon-Kucher & Partners**
⋮
Boston Consulting Group
McKinsey & Company

Source: *MT Magazine*/Erasmus University: *MT1000 2018*, survey of the best strategy consultancies in the Netherlands, Dec. 2018

Bilanz Magazine/WGMB

Marketing and sales

1 **Simon-Kucher & Partners**
⋮
Boston Consulting Group
McKinsey & Company

Source: *Bilanz Magazine*/WGMB: survey of the best management consultancies in Switzerland, January 2019

World leader in pricing

World leader in giving advice to companies on how to price their products
BusinessWeek

The world's leading pricing consultancy
The Economist

Pricing strategy specialists
The Wall Street Journal

In pricing, you offer something nobody else does
Professor Peter Drucker

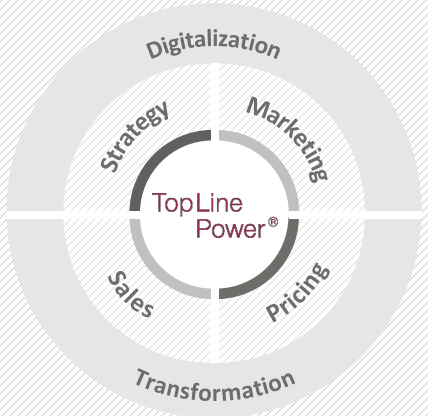
Global presence

38 offices worldwide, >1,300 employees, $360m revenue in 2018

Amsterdam
Atlanta
Barcelona
Beijing
Bonn
Boston
Brussels
Cairo
Chicago
Cologne
Copenhagen
Dubai
Frankfurt
Geneva
Hamburg
Hong Kong
Istanbul
London
Luxembourg
Madrid
Mexico City
Milan
Mountain View Munich
New York
Paris
San Francisco Santiago de Chile
São Paulo
Shanghai
Singapore
Stockholm
Sydney
Tokyo
Toronto
Vienna
Warsaw
Zurich

Source: Simon-Kucher & Partners.

>3,500 projects in the last three years



- Growth and competitive strategies
- Product portfolio (re-)design
- Pricing excellence
- Sales strategies and sales channel optimization
- Customer-centric digital approaches
- End-to-end transformation toward commercial excellence
- …

We are the trusted advisor of big pharma, but also understand the needs of emerging biopharma companies

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Projects by company type

Pharmaceuticals ('Big pharma')

- Pricing and market access strategies for **8 of the 10 best-selling pharmaceuticals** in the world
- Trusted pricing advisor for **24 of the 25 largest pharmaceutical** companies

Medical devices / diagnostics

- Worked for **8 of the 10 leading medical device and diagnostic** companies
- Addressed difficult commercial challenges for **paradigm-shifting technologies**

Biotech

- Advised **7 of the 10 largest** as well as > 75 small to midsized biotechnology companies
- Assisted in commercializing **complex scientific and medical innovations**

We recognize that emerging companies need a partner that:

- ✓ Has a deep history of experience working with small biotech companies in a variety of business situations
- ✓ Understands the importance of each of your assets
- ✓ Recognizes the urgency of implementing the right strategy / getting the right answers for your team
- ✓ Brings a mix of both scientific and business expertise to each and every engagement
- ✓ Drives alignment across all levels of the organization, including C-level / senior leadership
- ✓ Integrates the perspective of potential partners / larger companies into strategic decision-making
- ✓ Commits to your team's success in the long-term, not just through a single short-term engagement
- ✓ Remains flexible throughout the process, recognizing that your needs may change in the short-term and long-term

Source: Simon-Kucher & Partners internal data, collected 2018.

Simon-Kucher & Partners has vast experience with gene and cell therapies

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

No one has completed more projects in this space

We have unparalleled experience with gene & cell therapies …

- **20+ gene & cell therapy products** supported in various projects
- **Various project types carried out**, addressing different strategic questions *(list not exhaustive)*
  - Pricing and market access strategy
  - Contracting and payment models
  - Market landscape assessment
  - Phase III payer-rationalized clinical trial design
  - Negotiation excellence support and mock negotiation
  - AMNOG negotiation support
  - P&MA roadmap development
  - Commercial forecasting

… in numerous markets

- **Broad country scope in all projects**, addressing various country-specific challenges and questions *(list of countries not exhaustive)*

North America	
Europe	
Asia	
LATAM	
Australia	

Source: Simon-Kucher & Partners.

Additionally, we have unparalleled, cross-industry experience in helping emerging, high-potential companies succeed

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Simon-Kucher is THE Unicorn adviser: We have worked with >30 unicorns.

23andMe | Airbnb | Dropbox | Etsy | Eventbrite | Evernote | LegalZoom LifeLock | New Relic Nutanix | PagerDuty | Roblox | Rubrik | Stripe | Twilio | Uber | Workday | Zendesk | Zillow / Trulia

Types of projects

- Monetizing Innovation
- TopLine Power Assessment
- Loyalty program design
- Growth hacking
- Business and revenue model design
- Two-sided market monetization
- Actionable customer segmentation
- Packaging and pricing
- Migration strategy, cross-sell & up-sell
- Mobile monetization strategy
- …

Testimonials

"Simon-Kucher was a great partner during our research phase. We appreciated their support, expertise and partnership throughout the process of developing Uber Rewards."
Barney Harford, COO, Uber

"The pricing & packaging work Simon-Kucher did for us was game changing, up there with the most successful projects we've ever done."
Nels Gilbreth, Head of Commercial Strategy, Eventbrite

Source: Simon-Kucher & Partners.

Executive summary: Identifying and extracting value

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

More and more biopharma companies are emerging world-wide

While the clear majority commercializes their lead product on their own in the US, only a fraction pursue independent commercialization in Europe

What drives going it alone and how to excel doing so

Focus of today

Value generation	Extraction of value
Willingness-to-pay + volume assessment	7 secret ingredients for success

Source: Simon-Kucher & Partners; Pictures: colourbox.com.

Disclaimer: Every situation is different, but key patterns and critical success factors can be isolated

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

iStock/phototechno

Focus of this research:

- Retrospective assessment of common value drivers for successful commercialization in Europe
- Recognition of key success factors derived from year-long project experience and interviews with 18 senior commercial executives
- Reflection of secondary research and analysis of 20 products and companies: Detailed analysis of resulting +4,500 data points
- Illustrative thought-provoking hypothesis to tackle critical challenges when launching your first drug in Europe
  - Applicable to US and European-based companies considering their first launch in Europe

Limitations of this research:

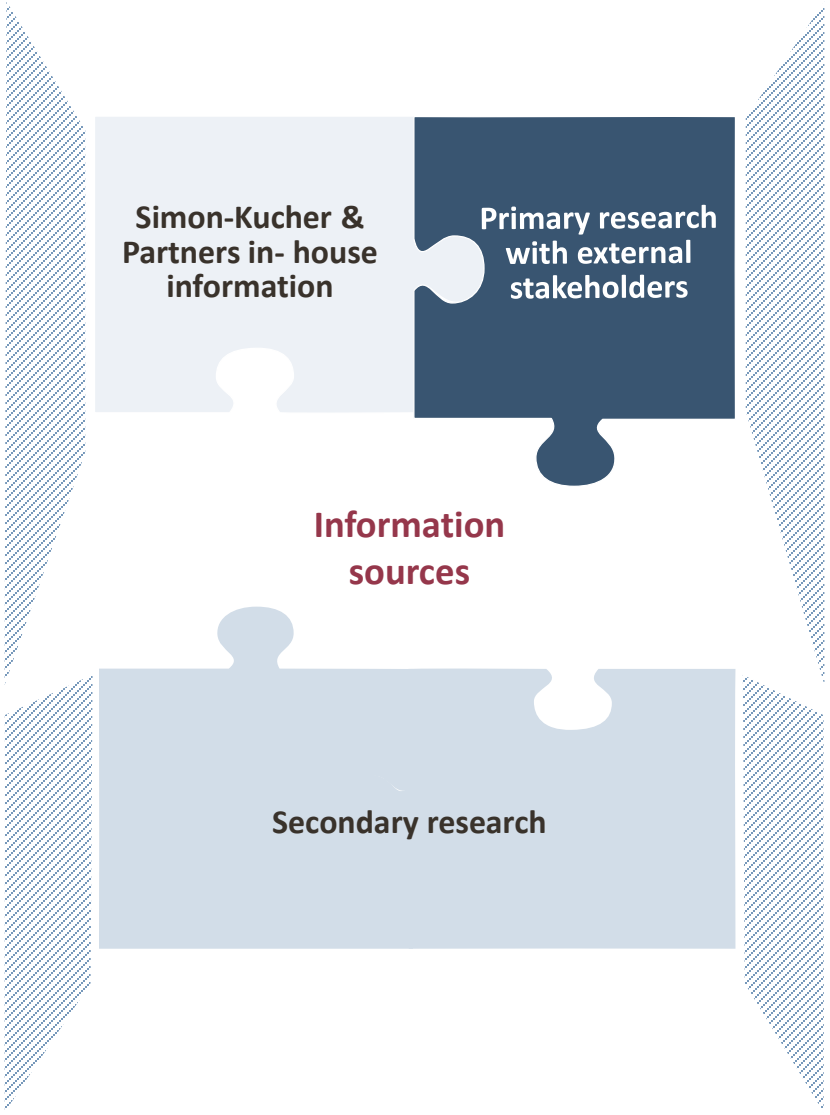
- Addressing all challenges and capabilities: Every case / launch has unique challenges
- Detailed forecast and blueprints
  - Every disease area and drug is different
  - Different pricing potentials and revenue upsides (and road blocks)
  - Different investment requirements to extract a drug's full commercial value potential

Source: Simon-Kucher & Partners.

This research is based on in-depth research from a variety of sources

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

- **Extensive experience in industry P&MA**
- **"Finger on the pulse":** Regular work in P&MA assignments
- **Understanding of product and organizational challenges and opportunities** from previous projects, especially in indications with high unmet medical needs and need to shape the market
- Sophisticated **skills** in identifying **market opportunities, forecasting**, and eventually **realizing** those **opportunities**



- In-depth **qualitative discussions** in a **one-on-one setting with pharma executives** (early stage to emerging biopharma)
  - **Internal functions**: Commercial, P&MA, Medical, Marketing
  - **Total interviews:** 18
- **Discuss:**
  - Current thoughts on **critical commercial activities, duration, responsibilities and rationale**
  - Specific **launch challenges** for orphan drugs (product and disease area-specific)
  - **Lessons learned from other products / companies** (What was / is done? What worked? What did not work?)

Topic research:

- Front running: Little academical research available
- Specialized websites, commercial intelligence platforms
  - Global Pharma
  - Evaluate Pharma
  - Etc.

Product / company research:

- Available **public information / industry reports** on disease area, unmet needs, disease prevalence, competitors, price level, etc.
  - **Drug information:** EMA, Global Pharma, country-specific authorities such as G-BA (GER)
  - **Price information:**: IHS Markit and / or local price databases such as Lauer-Taxe (GER)

Source: P&MA = Pricing and market access; G-BA = Gemeinsamer Bundesausschuss.

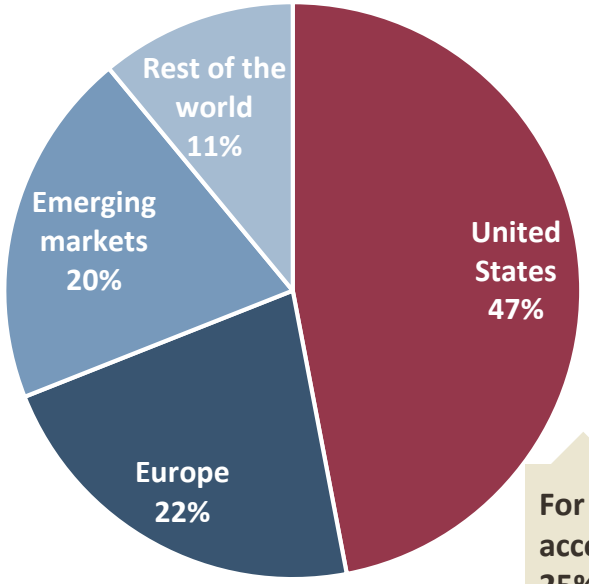
Europe (EU-5) is the second biggest market for pharmaceuticals, however, only a fraction of emerging biopharma companies tackle it on their own

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

From 2005 to 2019 only 3% of EMA approvals were driven by emerging US-based biopharma companies.

Europe accounts for ~22% of pharma sales…

Global pharmaceutical sales by region (2018)

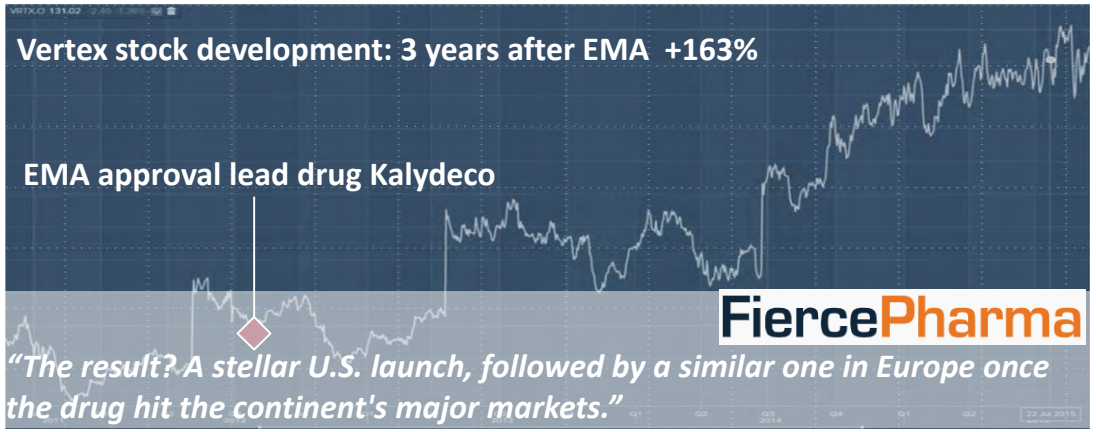


For highly innovative drugs, US can account for 60-70% and Europe for 20-25% of global sales

EU-5 accounting for nearly 18% of world-wide sales:

… hence, expansion to Europe has significant upsides but bears also large entrepreneurial risks

UPSIDES:



DOWNSIDES:

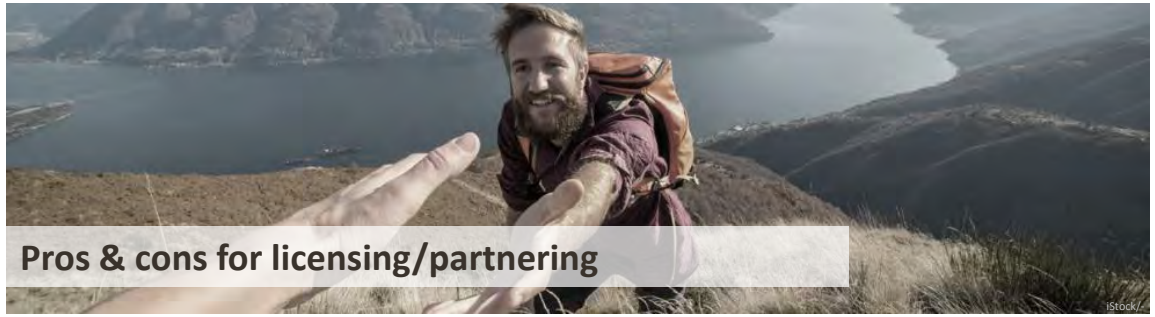
Source: Simon-Kucher & Partners, Efpia: The Pharmaceutical Industry in Figures 2019; Eikon; Statista; IMS. Iqvia.com.

Going to Europe on your own has significant commercial upsides and allows to keep control of your lead asset(s), but bears also significant risks

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Pros & cons for making the leapt to Europe on your own

- ⊕ Highest **financial rewards**
- ⊕ Retain **ownership**
  - Asset positioning
  - Strategy execution
- ⊕ Leverage potential for **future pipeline**
  - Fully integrated international operations
  - Knowledge generation
- ⊖ High **risk**, no safety net
- ⊖ Resource **intensive**
  - High (upfront) capital requirements
  - Timeframe for realizing revenue
- ⊖ Moving outside **core competency**



Pros & cons for licensing/partnering

- ⊕ Less **risky**
- ⊕ **Faster monetization** of asset
- ⊕ **Synergies** and upside with potential partners
  - Potentially pooling of resources
- ⊖ **Contract terms** and revenue split depend on negotiation skills
  - Product undervaluation
  - Opportunistic re-negotiation
- ? Limiting **company valuation**
- ? Increased **organizational complexity** ⊖
- ⊖

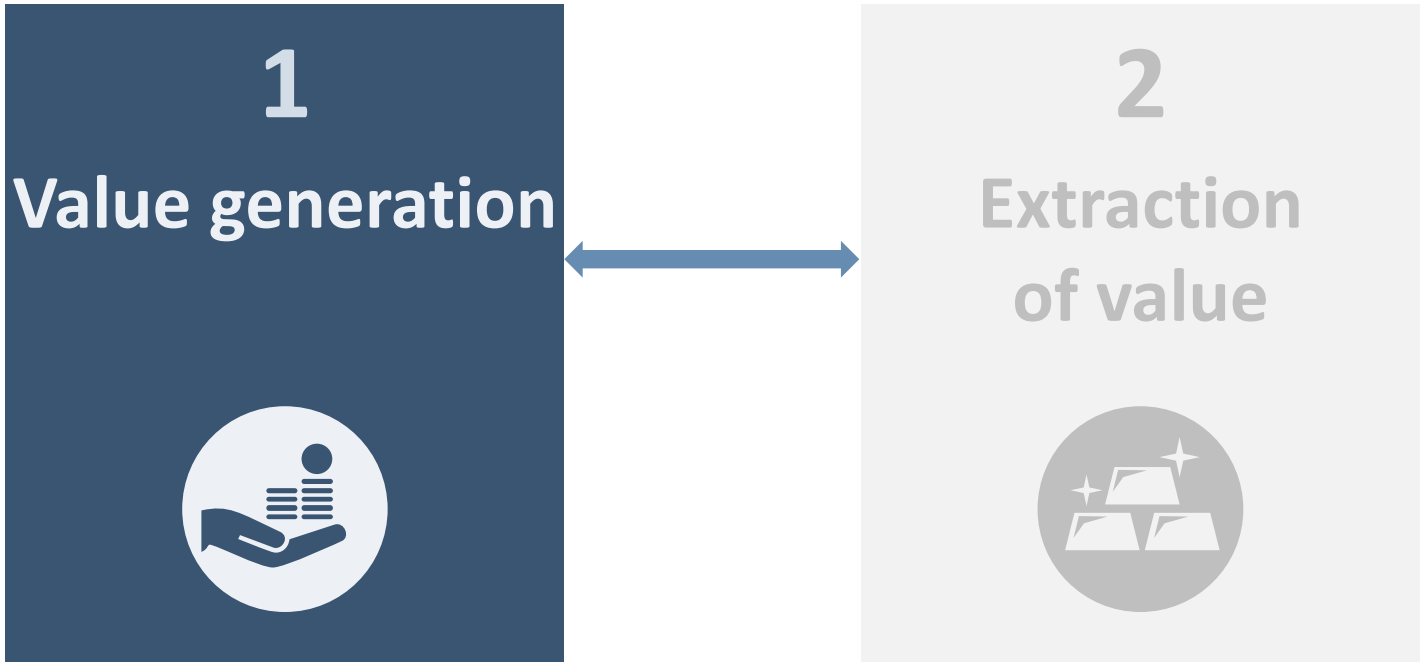
Central business question(s)

- Is independent commercialization the most favorable go-to-market strategy?
- What is required to make your first drug launch a success?
  - What drives and limits value extraction of such companies?
  - How can the go-to-market strategy be optimally executed?

Source: Simon-Kucher & Partners, Efpia: The Pharmaceutical Industry in Figures 2019; Eikon; Statista; IMS. Iqvia.com.

Let's first focus on the value drivers that determine the therapeutic value of a drug in Europe

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants



Willingness-to-pay + volume assessment

7 secret ingredients for success

Source: Simon-Kucher & Partners.

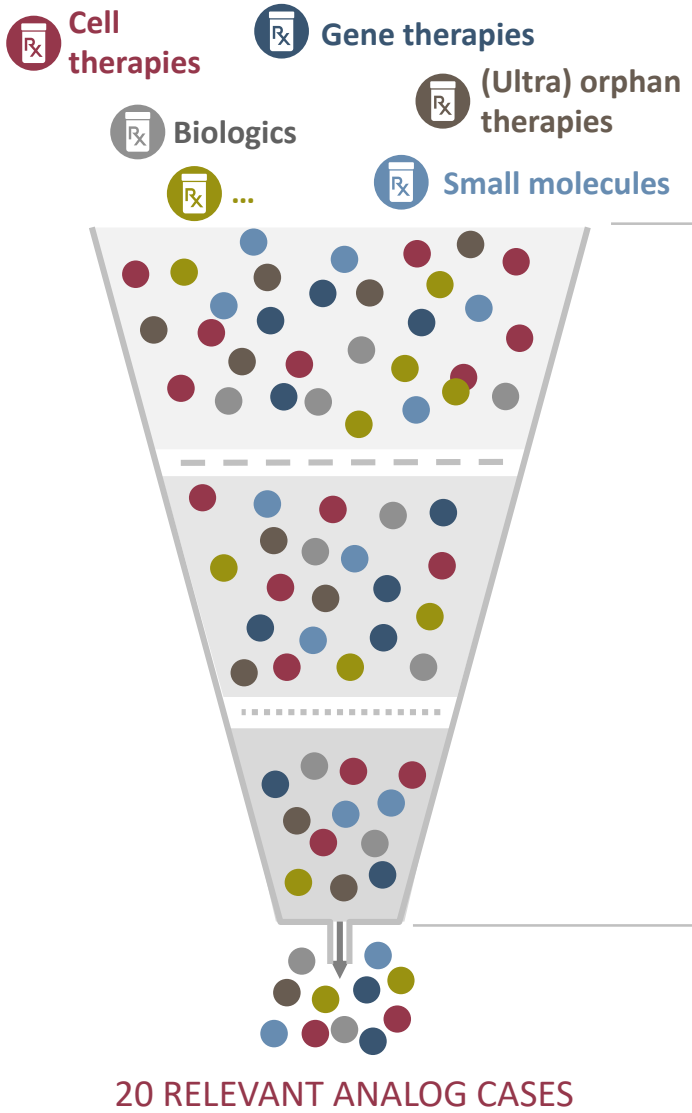
There are many potential price and access drivers for going it alone… but which ones are the most important?

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Source: Simon-Kucher & Partners.

Benchmark selection:
Focus on US-based biopharma companies from 2005 to June 2019

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants



We scanned all first marketing authorizations from 2005 to June 2019

Conceptual

In total: 653 observations were made

Recommended criteria for selection of analogs:

- **Time of launch:**
  - Between January 2005 and June 2019
- **Drug status:**
  - Innovative: No generics, no biosimilars, no hybrid applications
- **Commercialized**
  - EU (and) US
- **Company characteristics:**
  - US-based*
  - Focus on lead product for Europe: No previous major licensing deals or EU commercial experience

Transferrable findings: Despite US-based sample, we and our expert believe today's findings are applicable for US- and European-based companies launching their first drug in Europe

Source: Simon-Kucher & Partners; *One Australia-based company included.

Overview of the selected analog products and respective emerging biopharma companies

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Backup

Drug	Inn	Company	Indication	Year of EMA approval	Orphan designation	Comment
Mepsevii	vestronidase alfa	Ultagenyx	Mucopolysaccharidosis VII	2018	✓	At time of publication: Only launched in GER w/o no negotiated price
Onpattro	patisiran	Alnylam	hATTR, Stage 1 or 2	2018	✓	
Rubraca	rucaparib	Clovis Oncology	Ovarian cancer 3L+ (BRCA / platinum sensitive)	2018	✗	Had their EMA approval in 2018 but only launched in March 2019 with two indications (3L and maintenance)
Tegsedi	inotersen	Akcea	hATTR, Stage 1 or 2	2018	✓	
Zejula	niraparib	Tesaro (during late-stage of launch GSK)	Maintenance ovarian cancer platinum-sensitive	2017	✓	Included because advance stage of commercialization at M&A with GSK in contrast to other companies (e.g., Onyx)
Galafold	migalastat	Amicus	Fabry disease with an amenable mutation	2016	✓	
Ocaliva	obeticholic acid	Intercept Pharma	Biliary cholangitis	2016	✓	
Hetlioz	tasimelteon	Vanda Pharmaceuticals	Non-24-Hour sleep-wake disorder	2015	✓	
Translarna	ataluren	PTC Therapeutics International	Duchenne muscular dystrophy	2014	✓	
Iclusig	ponatinib	Ariad Pharmaceuticals	CML or Ph+ ALL	2013	✓	
Provenge	sipuleucel-T	Dendreon	Asymptomatic or minimally symptomatic metastatic (non-visceral) castrate-resistant prostate cancer	2013	✗	
Kalydeco	ivacaftor	Vertex Pharmaceuticals	Cystic fibrosis (one copy of the G551D mutation	2012	✓	
Revestive	teduglutide	NPS Pharmaceuticals	Short bowel syndrome	2012	✓	
Cinryze	C1 inhibitor	Viropharma	Angioedema attacks	2011	✗	
Esbriet	pirfenidone	Intermune	Mild-to-moderate idiopathic pulmonary fibrosis	2011	✓	
Abraxane	nab-paclitaxel	Abraxis Bioscience	Metastatic carcinoma of the breast	2008	✗	
Revlimid	lenalidomid	Celgene	2L+ multiple myeloma (+ dexamethasone)	2007	✓	
Soliris	eculizumab	Alexion	Paroxysmal nocturnal haemoglobinuria (PNH)	2007	✓	Indication expansion to children happened later
Naglazyme	galsulfase	Biomarin	Mucopolysaccharidosis VI	2006	✓	
Scenesse	afamelanotide	Clinuvel UK	Erythropoietic protoporphyria (EPP)	2014	✓	Australia-based company. Included due to similar context: Ex-European, English-speaking

Source: Simon-Kucher & Partners.

✓ yes ✗ No

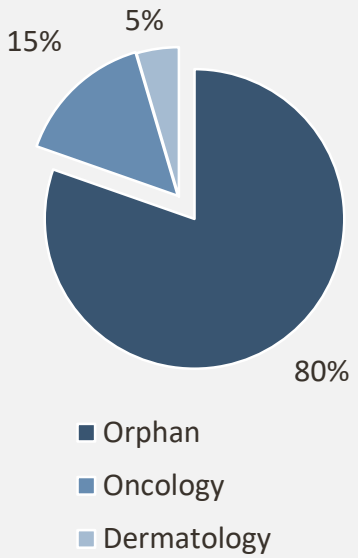
Analog cases aim at fulfilling targeted needs: Targeting a small patient population with high unmet needs

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

All four characteristics are considered key value driver for a successful commercialization.

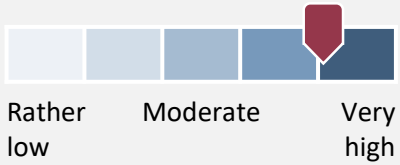
Market entrant characteristics: Targeted needs

DISEASE AREA



Dominated by orphan drugs

UNMET MEDICAL NEED



High unmet medical need / severity

PREVALENCE

ø **2.6** patients
in **10k** people

Small but targeted patient population

Realized high price potentials

Average EU-5 yearly treatment cost

Economic upside for value creation beyond patients' needs

Source: Simon-Kucher & Partners; analog research (n = 20); * Excluding one drug having only launched in Germany with no negotiated price available; inclusion of this drug would lead to average treatment cost of around 180,000 euros.

Orphan drug: Countries / regions can vary in how they treat rare diseases from a regulatory and public policy standpoint

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Orphan drug / rare disease regulation & policy instruments

	Europe - EMA	US - FDA	Japan - PMDA
Prevalence justifying the orphan disease designation	5/10,000	7.5/10,000	4/10,000
Scientific and technical assistance	✅(free/reduced)	✅(paid service)	✅(free)
Accelerated procedure for market access	✅(not guaranteed but likely)	✅(not guaranteed but likely)	✅
Market exclusivity	10 years	7 years	10 years
Tax reductions	Fees reduction	Tax credit and fees reduced	Tax reductions for R&D expenses

Specific regulations / advantages encouraging the development of orphan drugs exist in almost all countries / regions

Source: Simon-Kucher & Partners; EMA, FDA, PMDA.

Orphan drug: In some European countries, the P&MA processes can also differ for orphan drugs

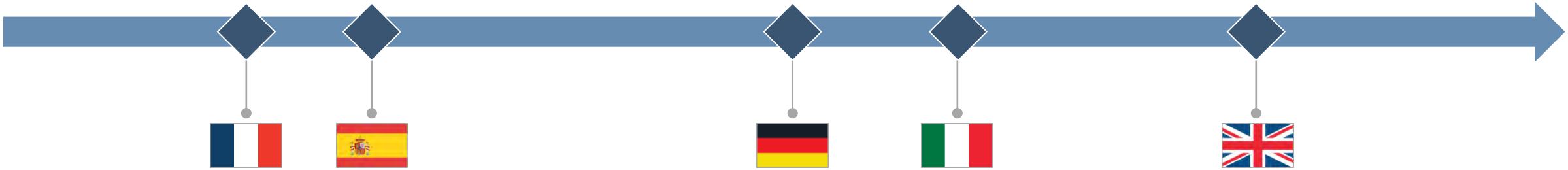
SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Orphan drug-specific processes and impact on P&MA

Orphan drugs are handled just as non-orphan drugs

Increasing specificity for orphan drugs

Orphan drugs have distinct P&MA processes



- No difference in P&MA process and no impact on time to market
- ODD makes drug eligible for Article 14, benefiting from orphan clause enabling a price >€50k/patient/year in exchange for a negotiated sales cap (a pay-for-performance scheme can be negotiated on top or as an alternative to the sales cap)

- No impact on overall P&R process
- Lower mandatory discount for orphan drugs: 4% instead of 7.5%

- Special process used in AMNOG benefit evaluation; orphan drugs are automatically assumed to provide a benefit, at the very least "not-quantifiable" in the AMNOG evaluation[1]
- Not required to demonstrate patient relevant benefit vs. defined appropriate comparator

- National Healthcare Plan for Orphan Diseases
- National orphan drug center, registry and network
- May accelerate and ease P&MA negotiations: can be expedited for orphan drugs with the "100 days procedure" and for rare disease drugs are granted innovation status (rarely realized)

- NHS England Specialised Services
- If NICE decides not to review a rare disease drug, it may be assessed directly via NHS
- HST process for ultra-orphan drugs gives consideration to nature of condition and impact on patients
- No impact on time to market, but may increase willingness to pay

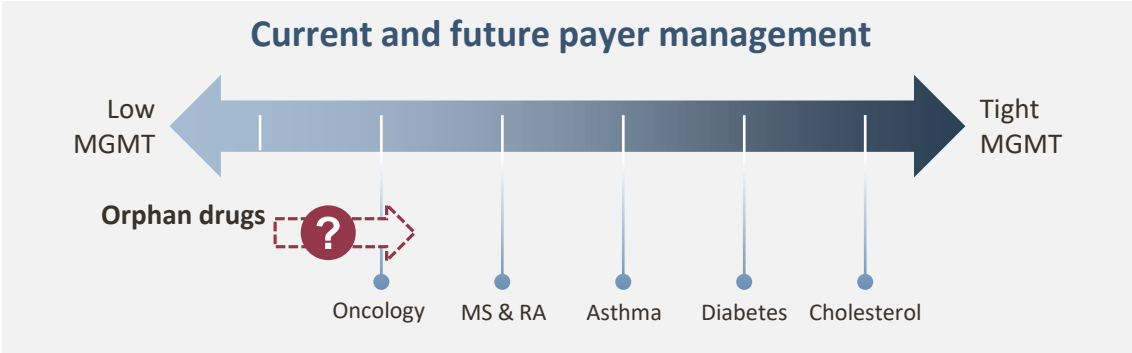
Source: Simon-Kucher & Partners. AMNOG: Act for restructuring the pharmaceutical market in statutory health insurance; EMA: European Medecines Agency; HST: Highly specialised technology; ICER: Institute for Clinical and Economic Review; NHS: National Healthcare System; NICE: National Institute for Health and Care Excellence; ODD: Orphan Drug Designation; P&MA: Price and Market Access; P&R: Price and Reimbursement. (1) Applies for orphan drugs ≥€1m and not exceeding €50m sales per year, if sales are >€50m per year, standard AMNOG review holds.

Orphan drug: However, orphan drugs are increasingly becoming a target of significant payer pushback, thus no guaranteed stand-alone success factor

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

With increasing number of orphan drug designations and sales, orphan drugs are not rare anymore…

… and payers have and will start to imply policies trending towards handling orphan drugs in the same manner as non-orphan



Recent example: Germany

The law for more safety in the provision of medicinal products (GSAV) has been passed in July 2019

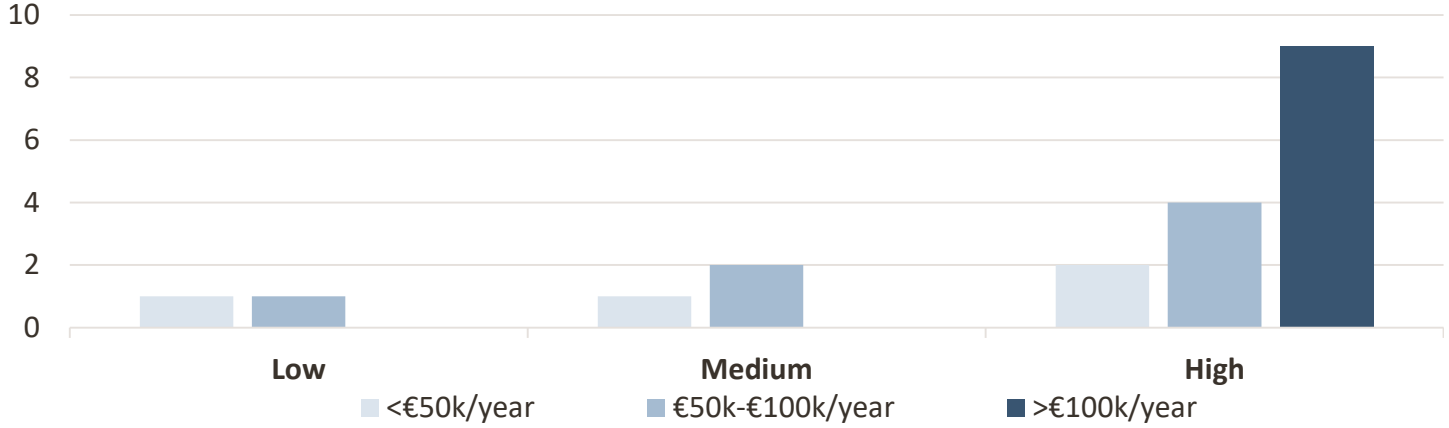
- Redefinition €50 million threshold: Outpatient, private, and inpatient sales considered (instead of out-patient only)
- G-BA entitled to demand creation of RWE (registry) data
- G-BA may perform regular benefit re-assessment with registry data
  - If data not available or does not allow for quantification of benefit, price cuts are most likely inevitable

Source: Simon-Kucher & Partners; IMS Health – When small becomes big: The new challenges or Orphan drug in Europe.

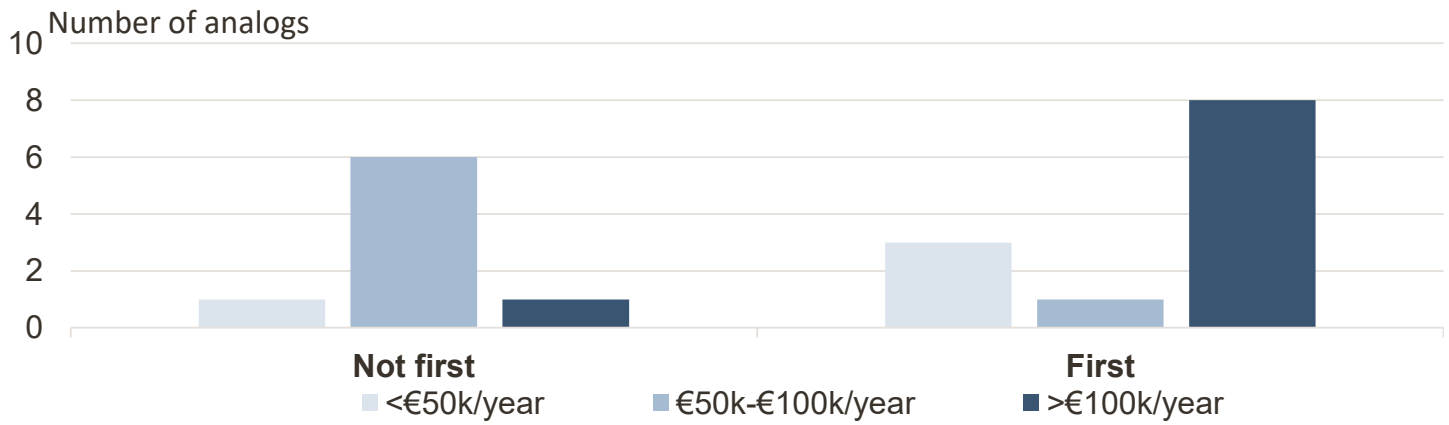
Unmet medical need: Drugs for a disease with a high unmet medical need or that are first-to-treat a disease tend to achieve higher prices

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Relationship between price and unmet need of the disease



Relationship between price and first-to-treat the disease



Key insights

Directional only

- Analog research indicates that products for diseases with high unmet medical need tend to achieve higher prices
- Analogs show a trend towards higher achievable prices for drugs that target diseases for which no other treatment option exist at the time of launch
- … but drugs which target a high unmet need area and for which no direct competitors exist market shaping and education is of upmost importance
- However, those factors are not exclusive drivers
  - For example, a higher price benchmark in a disease area with lower unmet need (assuming increased need for meaningful differentiation potential)

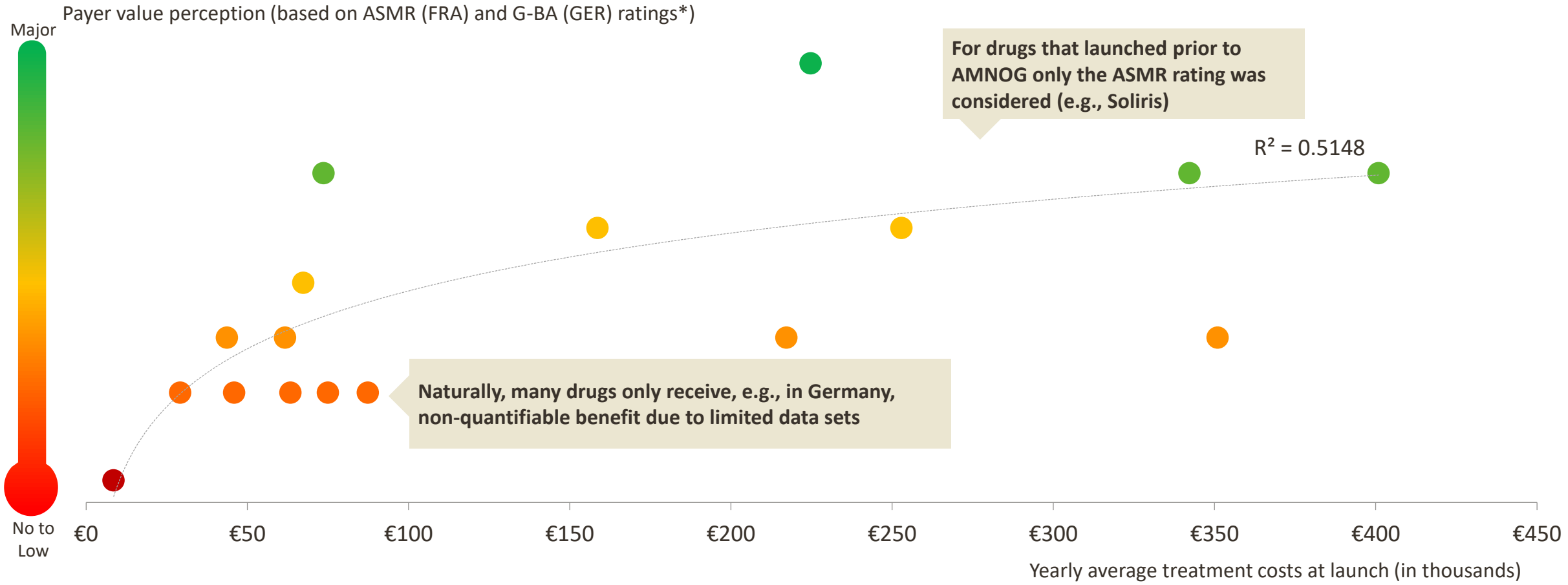
Source: Simon-Kucher & Partners; Historical exchange rates at launch; Germany net ex-manu prices shown included mandatory discount, 7%/16% or negotiated whichever is applicable; Spain net ex-manu prices for drugs launched after 2010 include 4% mandatory discount for drugs with EU orphan drug designation and 7.5% for non-orphan drugs and no discount otherwise; Italy net ex-manu prices include 5%+5% discounts; Assumed average patient weight: 76kg; otherwise trial population considered; No wastage assumed.

Therapeutic improvement: Drugs serving a high unmet benefit from a better payer value perception and are able to achieve very high prices often

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Perceived therapeutic improvement by payers vs. average annual treatment cost at launch

Directional



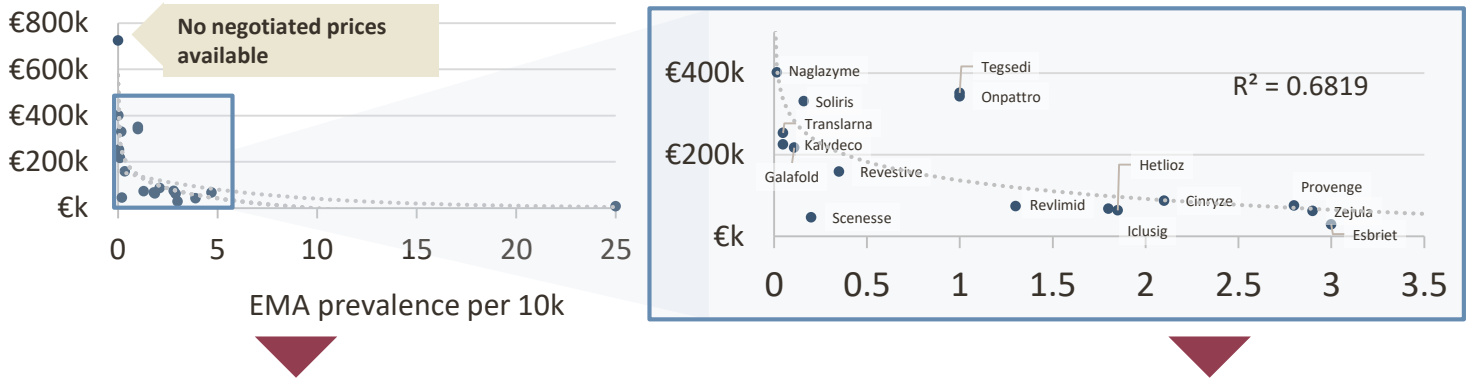
Source: Simon-Kucher & Partners. * Highest outlier excluded due to high price not having undergone any price negotiations yet. Average ASMR and G-BA benefit ratings were calculated on a 5 point scale with 4 =best possible rating and 0=worst possible rating. G-BA ratings for orphans from 1 to 4 (5 and 6 were excluded due to sample structure) were converted to a 5 point range to match the ASMR scale; Assumptions for price calculations: Historical exchange rates at launch; Germany net ex-manu prices shown included mandatory discount, 7%/16% or negotiated whichever is applicable; Spain net ex-manu prices for drugs launched after 2010 include 4% mandatory discount for drugs with EU orphan drug designation and 7.5% for non-orphan drugs and no discount otherwise; Italy net ex-manu prices include 5%+5% discounts; Assumed average patient weight: 76kg; otherwise trial population considered; Vial splitting/no wastage assumed.

Disease prevalence: There is a strong relationship between price and the size of the eligible patient population

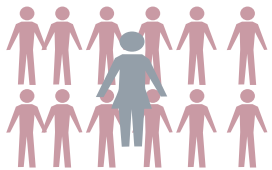
SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

A small patient population is a key driver for achieving high prices (important to control budget impact)

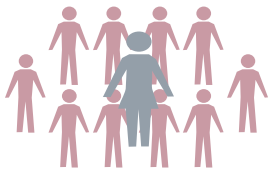
Average annual cost per patient in EU-5*



Smaller target populations require smaller commercial infrastructures ….



Primary care:
High sales rep to MSL ratio



Specialty care:
Medium sales rep to MSL ratio

Focus

Targeted needs:
Lower sales rep to MSL ratio

… at a high price tag for your product, the rewards can thus be substantial

Key insights

- The analogs show a strong relation between achievable price and disease prevalence
  - Very high prices are almost only exclusively possible for ultra-rare disease drugs as the budget impact would otherwise be too high
- Whilst low prices are not reserved for technologies with high prevalence, high prices are reserved for low prevalence treatments
- Further, the average number of patients targeted by analogs with a price tag <€50k is considerably larger than the average number of patients of the more expensive analogs

"For fewer stakeholders you need less infrastructure…but that also means there is no margin for mistakes."
- Chief Commercial Officer, US-Based biotech

Source: Simon-Kucher & Partners; Historical exchange rates at launch; Germany net ex-manu prices shown included mandatory discount, 7%/16% or negotiated whichever is applicable; Spain net ex-manu prices for drugs launched after 2010 include 4% mandatory discount for drugs with EU orphan drug designation and 7.5% for non-orphan drugs and no discount otherwise; Italy net ex-manu prices include 5%+5% discounts; Assumed average patient weight: 76kg; otherwise trial population considered; No wastage assumed.

Summary: Addressing the needs of a targeted (orphan) disease population may unlock substantial business opportunities

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Drug characteristics

Orphan drug

- High unmet medical need
- Small patient population (esp. pediatrics)
- First (effective) treatment
- High degree of therapeutic improvement

Marketing & pricing upside

Freedom to shape and educate the market

+

High price tag

(Business) Opportunity

Potential for independent, "do it yourself" commercialization

"Orphan is no guarantee for success. Yes, most likely most of upcoming launches led by emerging (bio-)pharma companies will have orphan status, but it is the underlying factors like unmet medical need, therapeutic improvement or targeted patient population that drive the value potential."

- Global Head of P&MA, US-Based Biotech

"Personally, I believe a high price tag is key to make economics work. Think about it, any patient contributing more than €100,000 per year can theoretically cover one FTE."

-SVP Commercial, US-Based Biotech

Source: Simon-Kucher & Partners; analog research (n = 20).; expert interviews (n=18).

Company characteristics: A solid cash position and a pipeline that can leverage the "to be built infrastructure" in Europe are considered as very important

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Key characteristics one year prior to EMA approval.

Number of FTEs (global)

473
(40 to 2,000)

The numbers of FTEs is largely driven by US-business. For Europe, you need to design your organizational structure based on your needs and ideas.
-Chief Commercial Officer, EU-based biotech

Cash position

€389m
(€41m to €1.5bn)

Under full scale, we estimate with approx. €100m per year for EU operations in total cost while revenues are only slowly starting to pick up.
- VP Commercial, US-based biotech

Free cash flow

-€107m
(-€431 to €79m)

Due to the investments in EU infrastructure and ongoing R&D activities, it takes time to reach a positive free cash flow unless you divest other non-strategic assets to generate additional revenue.
- Chief of Staff, US-based biotech

Pipeline strength

You need to launch a new drug or major indication expansion every 3-4 years to fully leverage your organizational structure.
- VP Commercial, US-based biotech

Most frequent EU HQ locations

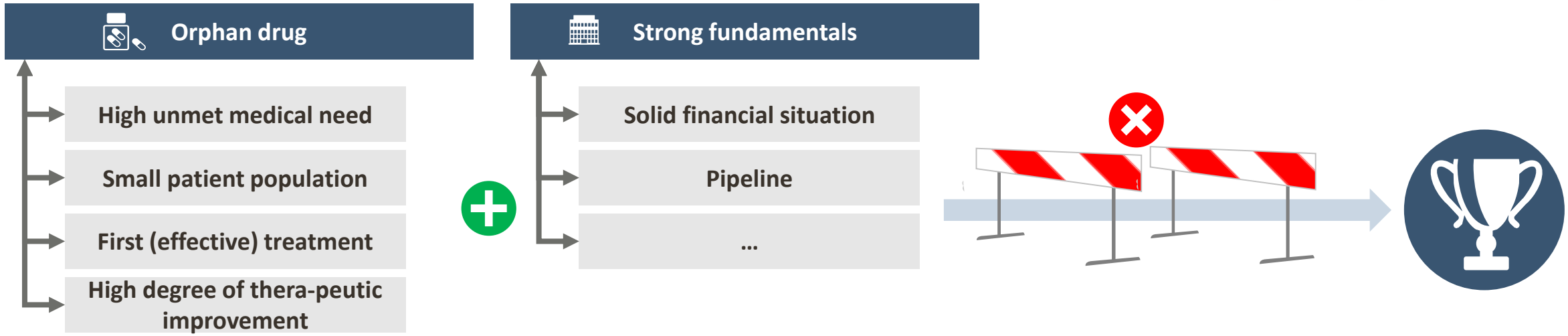
1. UK
2. Switzerland
3. Ireland
4. GER / NDL

Today, no one would open an HQ in UK. You want to look for good flight connections, tax benefits, cluster knowledge but also an attractive location to attract talents.
- SVP Commercial, US-based biotech

Source: Simon-Kucher & Partners, analog research (n = 20).

However, only a thorough assessment and strategic planning will allow to turn a promising (orphan) drug into a commercial success

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants



Orphan drug and other (company) characteristics are no guarantee for success as significant (access) hurdles are continuously increasing

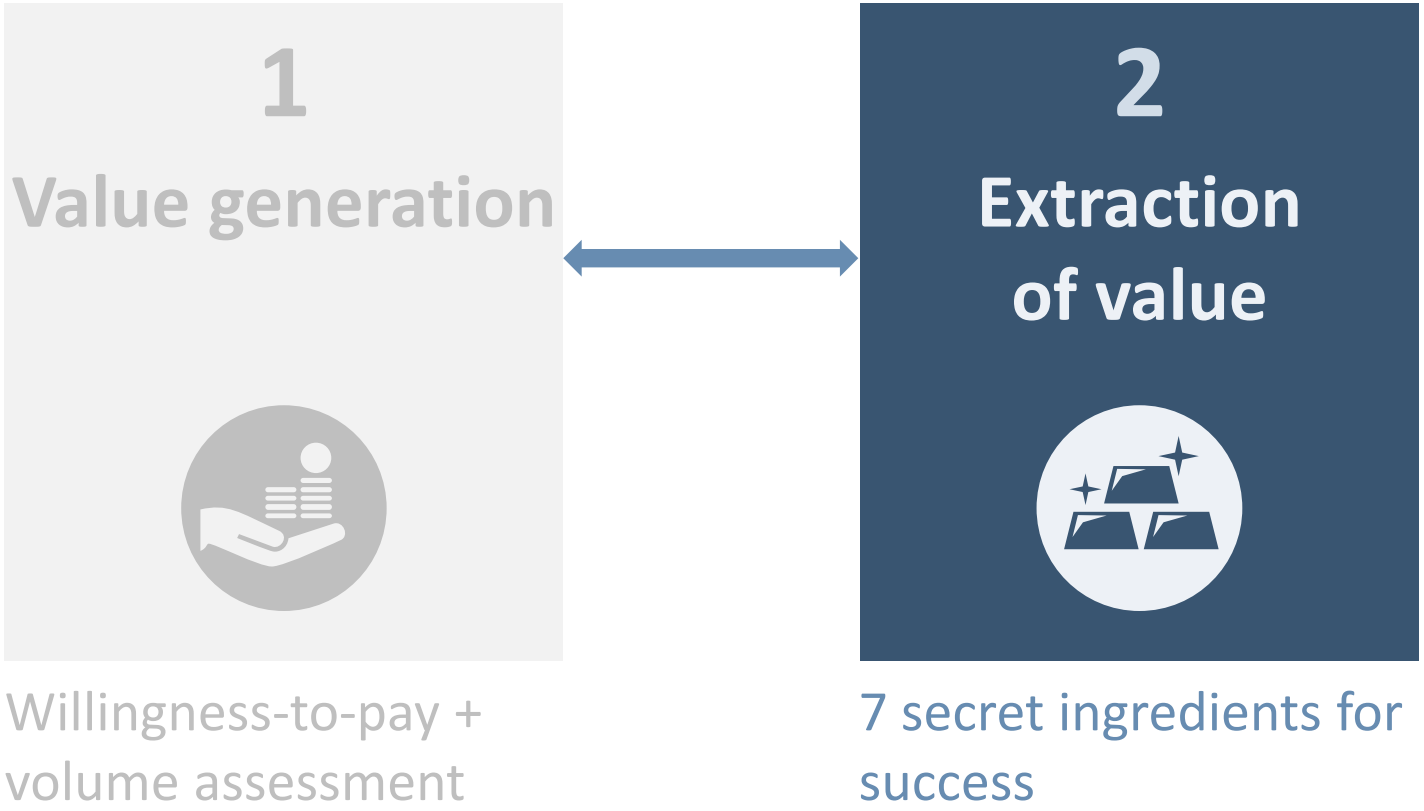
- **External hurdles**
  - Stricter national payer management: Increased data requirements, budget pressure, and use of innovative contracting schemes
  - More stringent international payer management: Increased use of external (i.e. international) price referencing to restrict prices
  - Shortening product life cycles and increased competitive pressure from all sides
- **Internal hurdles**
  - Lack of experience in establishing commercial operation and actually bringing a product to market in Europe

- **True product value must be critically assessed and continuously challenged**
- **True product value defines commercial potential and as such the go-to-market strategy**

Source: Simon-Kucher & Partners; analog research (n = 20).; expert interviews (n=18).

Now, let's consider on how to extract the value to make the launch in Europe a commercially viable strategic option

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants



Source: Simon-Kucher & Partners.

Starting point: Commercializing a drug independently requires an extension of core competencies, especially if commercialization is planned in several regions

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Skillset requirements for emerging biopharma

Current skill set | **Required skill set**

	R&D	Pre-clinical	Phase I	Phase II	Phase III	P&MA	Marketing & sales
Development process	Biopharma start-ups / biotech				“Big pharma competencies”		
Key competencies	▪ R&D ▪ Clinical development				▪ Finalization of clinical development ▪ Regulatory processes ▪ Unlocking P&MA ▪ Commercialization		
Comparative advantages	⊕ Agile & light structures ⊕ Close connection to academia (provision of basic research, funding & IP) ⊕ Rapid adoption of technological & digital advancements				**Operate and execute on global scale (US, EU, beyond)** ⊕ Financial means to fund capital-intense Phase III trials ⊕ Expertise with approval & regulatory processes and P&MA on global scale ⊕ Management of significantly growing payer requirements ? Plug & play structure for commercialization ⊕		

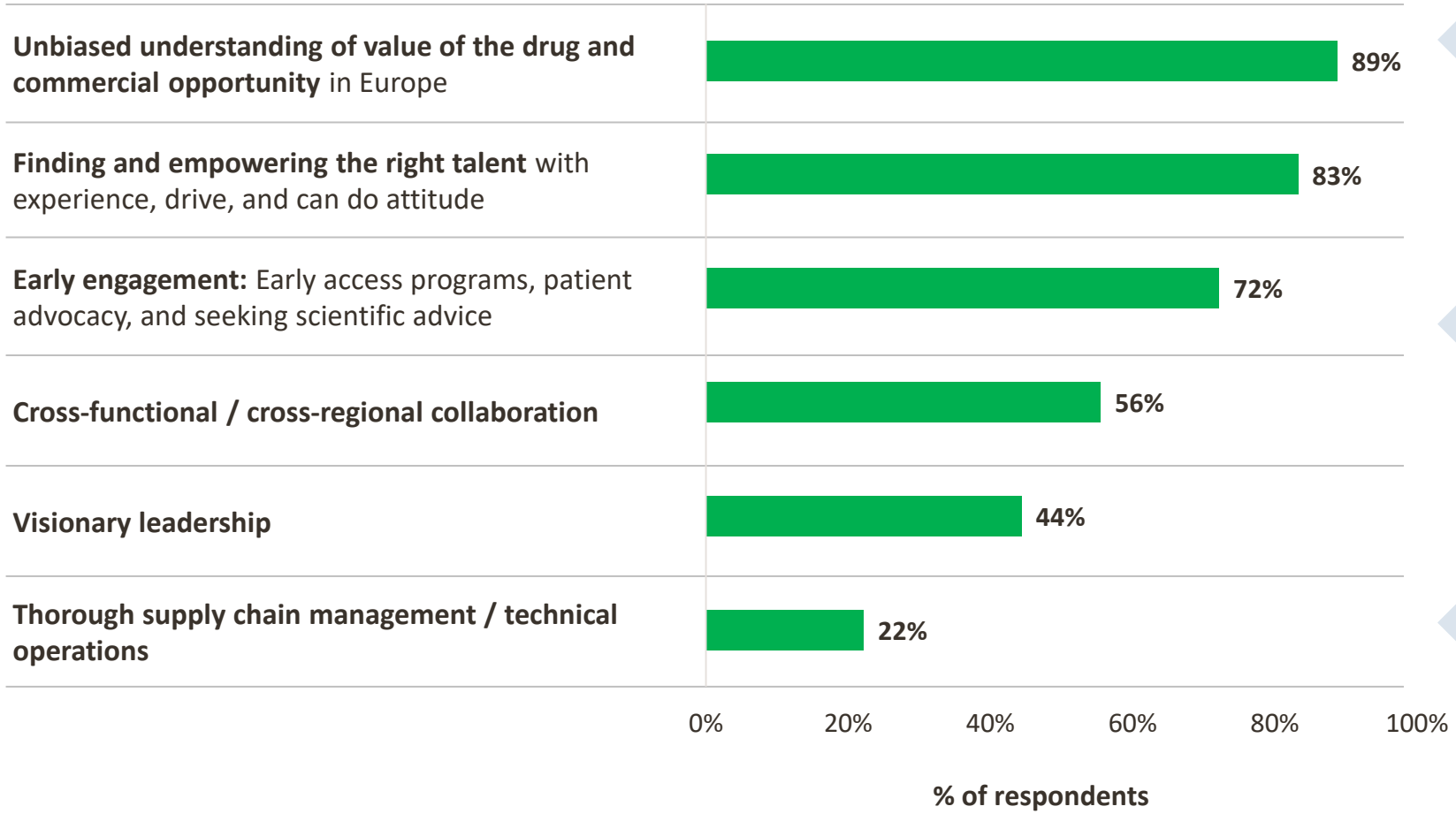
Source: Simon-Kucher & Partners.

The secret ingredients take into account most frequently mentioned best practices which are considered key to success…

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Overview of unprompted mentioned best practices.

Best practices



"Your drug potential is like your polestar. It will dictate your commercialization strategy, hence, you should not be misguided."
- CEO, US-based biotech

"We consider the early access program and early engagement in general as one of the key tools to create patient and commercial value as well as to learn as a company."
- CCO, US-based biotech

"Of course we have a launch timeline, but adhering to it is very hard, there is so much to take care of…also from an operational perspective."
- Chief of Staff, US-based biotech

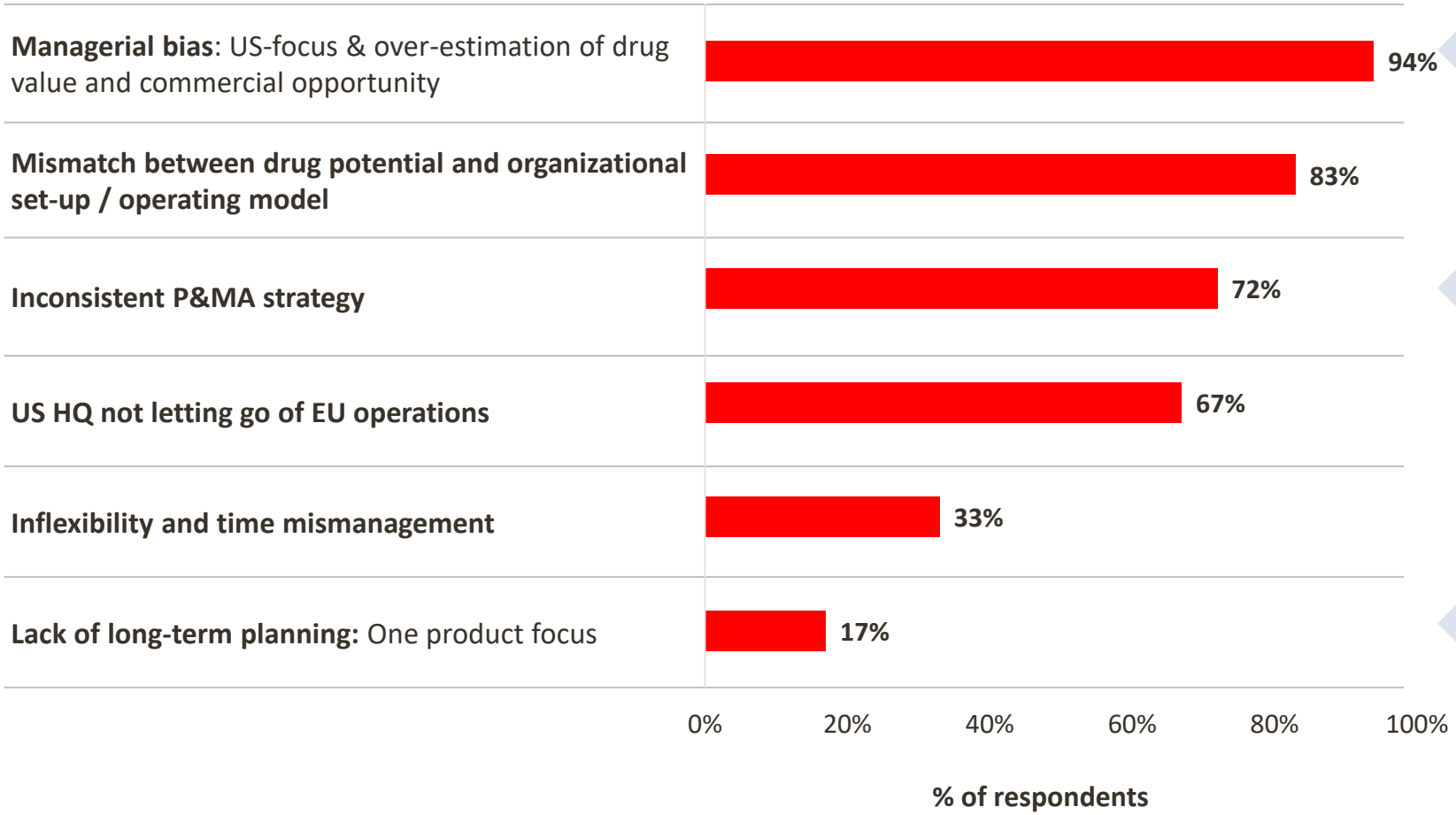
Source: Simon-Kucher & Partners; expert interviews (n=18); Note that %s will not add to 100% given that respondents were able to give multiple answers during the interviews.

Additionally, the secret ingredients mirror worst practices as well

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Overview of unprompted mentioned worst practices.

Worst practices



"Managers want to play on their home turf and tend to forget to consider better options."
- SVP Medical Affairs, US-Based biotech

"Your P&MA strategy defines how much value you can at max extract from your product, if you don't get this right, the best marketing in the world cannot help you."
- Regional GM, US-Based biotech

"The hiring requirements are immense. You need people that can educate the US to get the freedom needed but also excel in that given freedom."
- Regional GM, US-based biotech

Source: Simon-Kucher & Partners; expert interviews (n=18); Note that %s will not add to 100% given that respondents were able to give multiple answers during the interviews.

The seven secret ingredients for successfully launching and commercializing a company's first drug in Europe

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Source: Simon-Kucher & Partners.

The seven secret ingredients for successfully launching and commercializing a company's first drug in Europe

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Source: Simon-Kucher & Partners.

Emerging biopharma companies are often too focused on either research or the US market and may miss business opportunities

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

94% of commercial experts believe that in (early) stages executives of emerging biopharma company have a too limited strategic scope. Main pain points are a lack of business acumen and neglecting international opportunities

Research focus

- Focus on optimizing the "biologic" or scientific aspects of the drug
- No defined long-term commercial strategy, considering lead asset and future pipeline
- Neglecting:
  - Critical reflection of commercial potential and positioning of asset
  - Payer-rationalized clinical trial design
  - Visionary leadership to transition from R&D mode into a revenue-driven, commercial strategy
- …

"Payer and patient relevant data will always trump the biological aspects of a drug with regard to commercial aspects."
-Commercial Officer, US-based biotech

US-focus

- Focus on home turf and presumably biggest business opportunity
  - Additionally, US-focus driven by experience and origin of managers / founders
- Copy paste mind set: No individual approach for internationalization
- Neglecting time, investments, and product data package needed for international expansion
- No knowledge and capabilities to master complex market access environment of EU-28 markets (and beyond)

"Most companies that end up out-licensing or partnering have just not prepared early enough and were too focused on the US-business."
- Vice President Marketing, EU-based biotech

Source: Simon-Kucher & Partners; Expert interviews (n =18).

To pave the pathway to a successful commercialization beyond the US and purely regulatory requirements, a broadening of the mindset must occur early

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Exemplary overview of key topics to should have on your radar when moving through clinical development stages.

Price and market access potential (beyond US)

Country-specific P&MA requirements

Payer (data) requirements / payer rationalized clinical trial design

Regulatory requirements

Current P&MA trends

Patient reality: Patient journey, stakeholders, true pain points

Product value, drug usage and volume estimates

True patient and prescriber pain points

Drug positioning

Competitive landscape

Top-3/4 areas to enlarge managerial scope

Broaden your perspective and overcome limited perspectives in early stages (ideally in Phase I or II) by:

- Analog, secondary, and primary research with the right stakeholders
- Hiring commercial / P&MA experts who have business acumen and international commercial experience
- Collaborate with external vendors to overcome lack and barriers of knowledge

Source: Simon-Kucher & Partners; Expert interviews (n =18).

The seven secret ingredients for successfully launching and commercializing a company's first drug in Europe

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

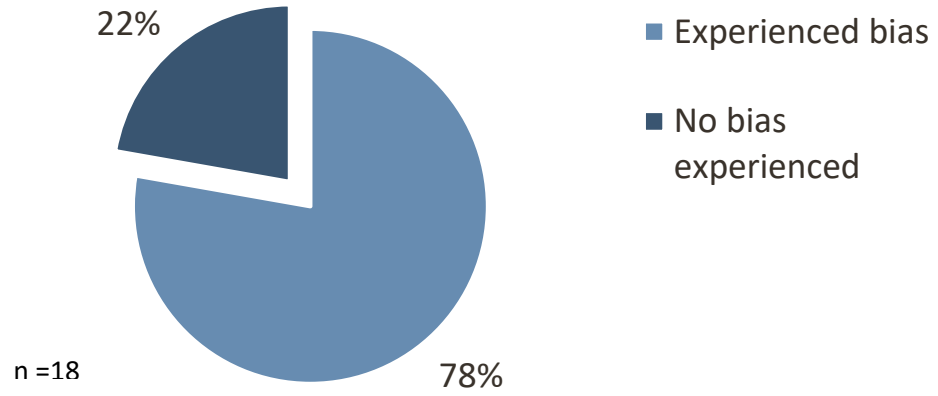
Source: Simon-Kucher & Partners.

Management biases are commonly observed in emerging biopharma companies

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

They are especially critical in early stages or when only a couple of senior executives decide on the future of a company.

Majority of respondents reported to have experienced managerial bias obstructing informed decision making



The smaller the company is or the more power its executives have, the greater the impact these errors in thinking can have in the long-term

Commonly reported biases:

Exemplary

- **Mustering courage:** Overestimating therapeutic improvement of "their" drug based on false assumptions
  - Failing to identify opportunities to differentiate
  - Misalignment of product value and commercialization strategy
- **Conservatism:** Reluctance to update their beliefs in the face of new evidence
  - No constant challenging of attractiveness and requirements to launch on their own
  - No assessment of payer requirements beyond the US

"At my former employer, one executive wanted not to launch in Italy due to his negative experience... How can you rule such opportunity out without even truly assessing it?!."

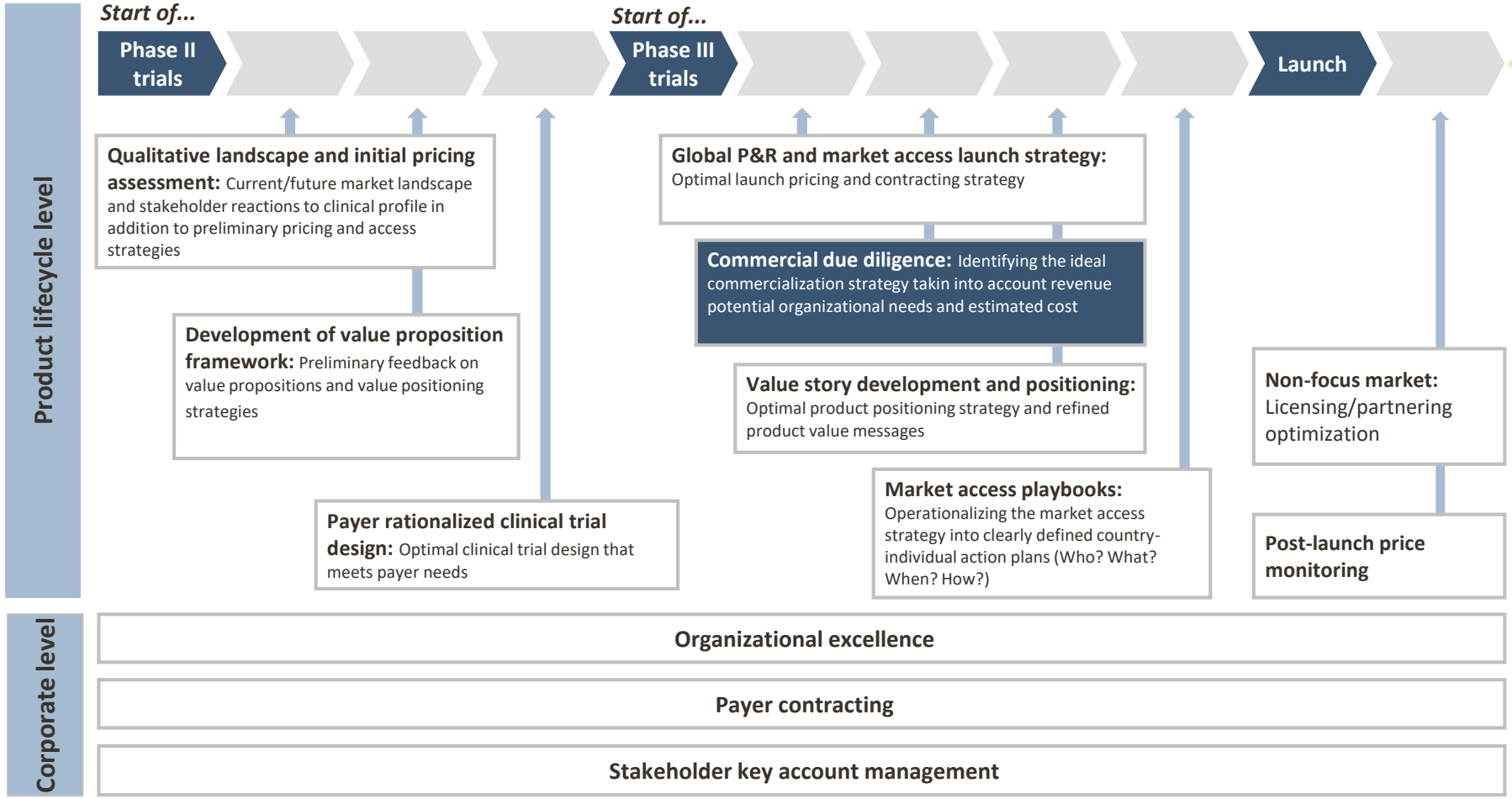
- Global Head P&MA, EU-based biotech

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Often, external perspectives are the most effective way to de-bias executives / whole companies

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

All of our participants, regardless of whether they had worked with Simon-Kucher in the past, acknowledged the importance of external consultancies in bringing in fresh perspectives or challenging existing mindsets.



Activities to understand the true value of your asset

- **Assess the business potential: Price x Volume** *(to be informed about partnering for trial development and commercialization)*
- **Optimally build the clinical development strategy** of a new compound and to decide:
  - Which indications to pursue / launch sequencing
  - Payer-rationalized trial design
- **Develop a targeted value proposition framework**
  - Addressing payers', physician's, and patients' needs
- **Understand existing the P&MA challenges & hurdles** and how to mitigate them

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Commercial Due Diligence will allow you to identify the ideal commercialization strategy

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

A risk-adjusted NPV (rNPV) will be calculated after considering the revenue potential and commercialization costs for different scenarios to identify the most likely and most favorable one.

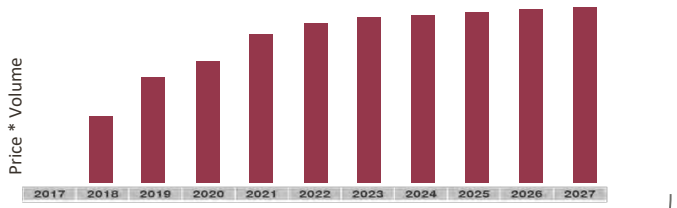
Conceptual

Estimated revenue potential for EU countries

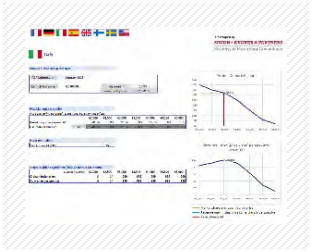
EU organizational needs and estimated cost of commercializing in the EU
(derived from P&MA and prescription volume assessment studies)

Annual profit/loss net present value (rNPV)
+
Decision on partnering, licensing, or going it on your own

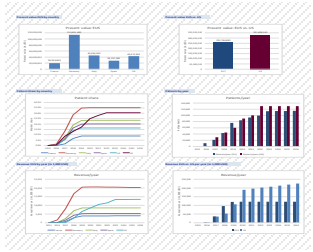
Revenues



Optimal price



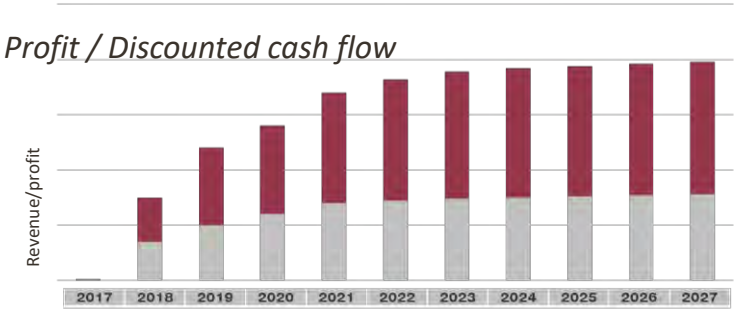
Sales forecast



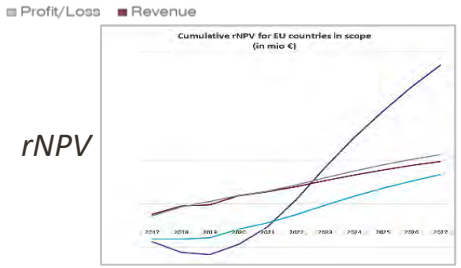
FTE requirements & salaries per country considering different organ set-up options

Additional expenditures

Profit / Discounted cash flow



rNPV



Source: Simon-Kucher & Partners.

The seven secret ingredients for successfully launching and commercializing a company's first drug in Europe

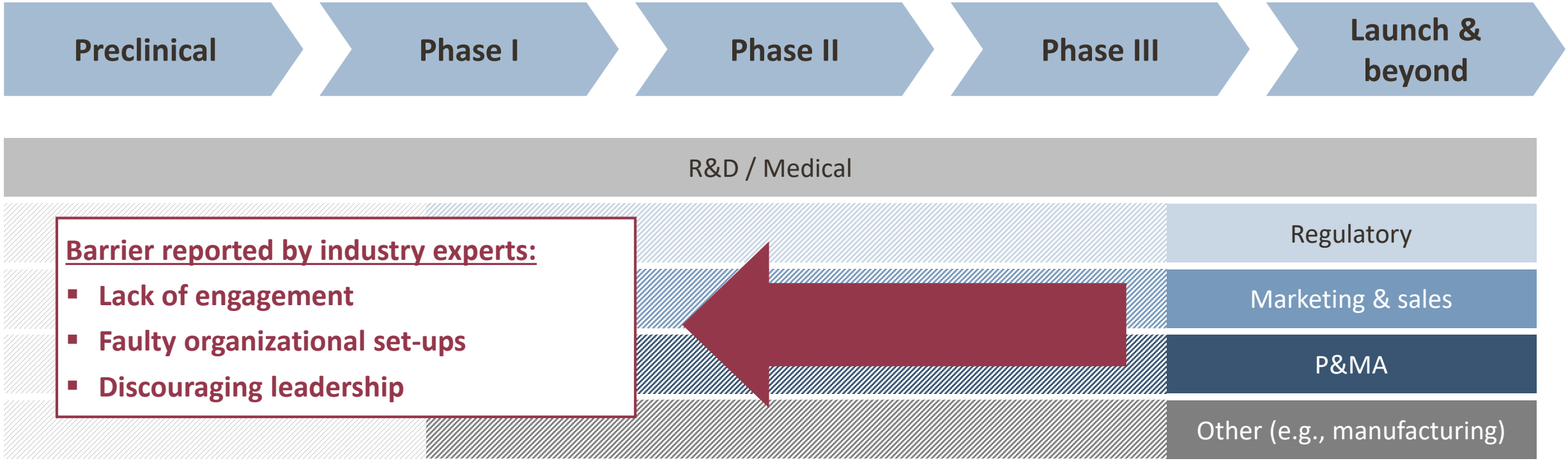
SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Source: Simon-Kucher & Partners.

Products cannot be developed and commercialized following a silo approach

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

From silo approach to functionally-integrated R&D



Expert insights:

- Shift of decision-making from physicians to payer-supported treatment guidelines/algorithms
- Early engagement with regulatory and HTA authorities required
  - Study design can have key influence on P&MA potential
- Close cooperation between R&D, P&MA, medical, marketing, and even non-primary functions required throughout different development stages

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Upside of breaking the silos: Companies integrating the P&MA function to help guide R&D show a higher profitability

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

From silo approach to functionally-integrated R&D

Simon-Kucher & Partners life sciences industry study

Involvement of P&MA team in early development
(Phase I / Phase II)

Take into account payers' needs and value drivers early
(Phase I / Phase II)

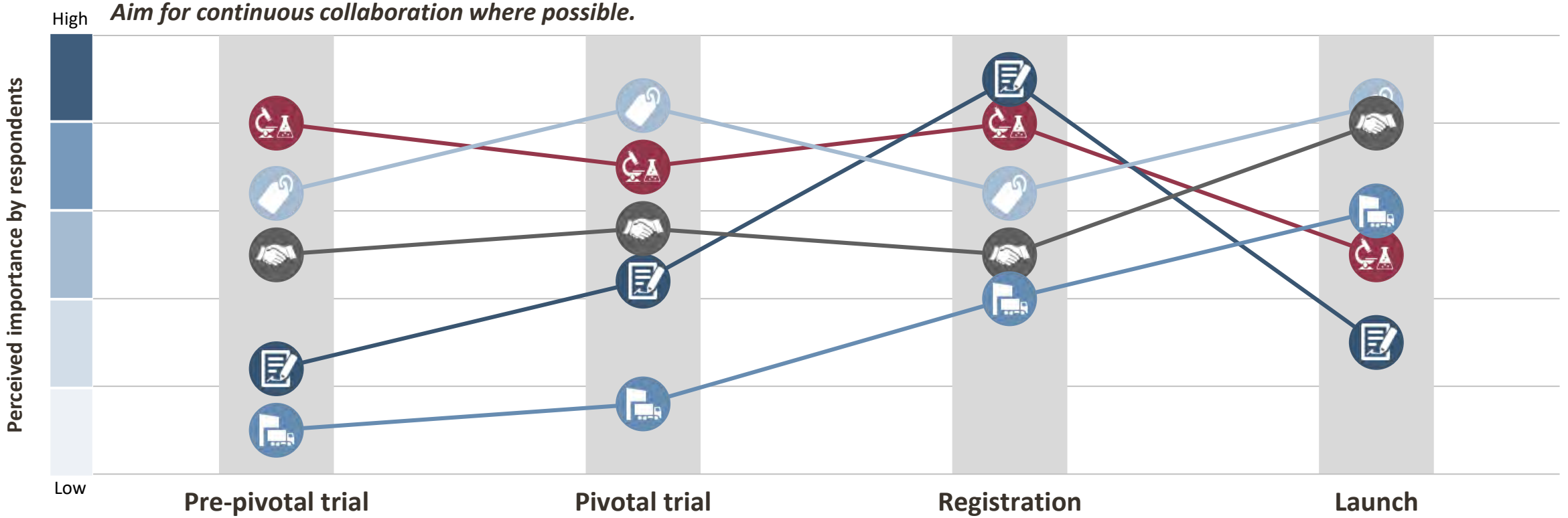
	Companies with >20% EBITDA margin		Companies with <20% EBITDA margin
Involvement of P&MA team in early development (Phase I / Phase II)	67%	VS.	55%
Take into account payers' needs and value drivers early (Phase I / Phase II)	80%	VS.	36%

Source: Simon-Kucher & Partners; Simon-Kucher Life Sciences Industry Study 2017.

Over time, different functions beyond primary functions such as regulatory come into focus

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Aim for continuous collaboration where possible.



Insights

Pre-pivotal trial
- R&D driving clinical development
- P&MA to support development of access-oriented trial program (payer-rationalized trial design)

Pivotal trial
- P&MA understanding the potential value of the lead asset
- R&D / medical finishing and managing trials
- Medical engaging with key (prescribing) stakeholders

Registration
- Regulatory driving the registration
- Medical engaging with KOLs and patient advocacy to create awareness / early access

Launch
- P&MA unlocking full potential
- Commercial extracting the potential
- Logistics enabling extraction

R&D / Medical | Regulatory | P&MA | Commercial | Technical operations

Source: Simon-Kucher & Partners; Expert interviews (n =18).

The seven secret ingredients for successfully launching and commercializing a company's first drug in Europe

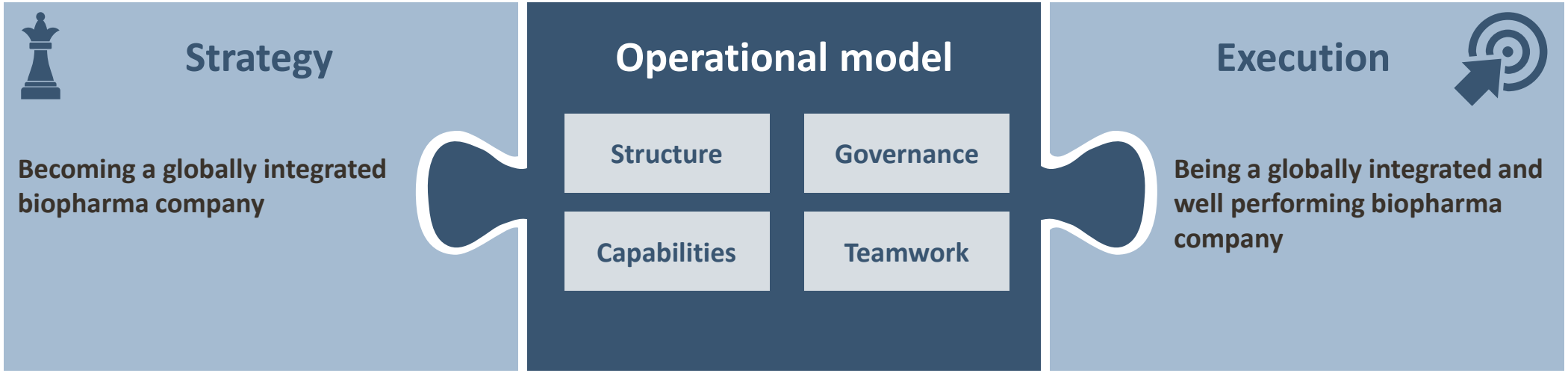
SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Source: Simon-Kucher & Partners.

A regional operating model allows to execute the strategy successfully

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

The operating model is the link between strategy and execution.



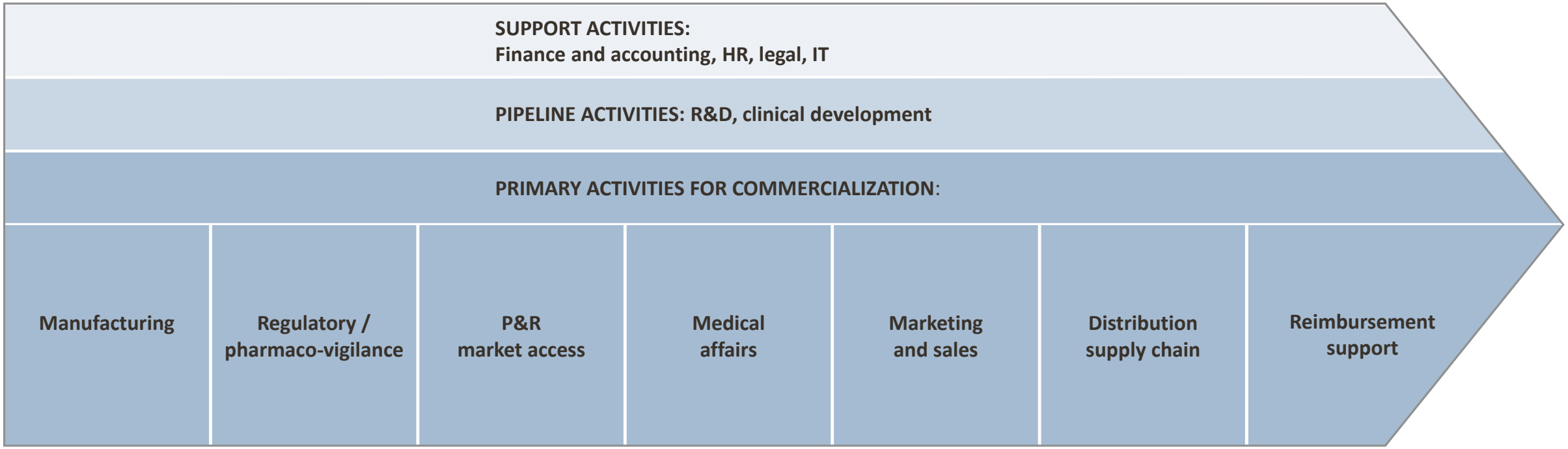
The operating model is considered a decisive success factor and its set-up requires a thorough understanding of your drug:

- 83% of our respondents believe having the wrong organizational set-up is a common trap impeding strategy execution
- Key concern is building/designing an operating model that is not tailored to the specific requirements of the 'to be' commercialized asset

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Organization: The value chain is the foundation to design an organizational set-up

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants



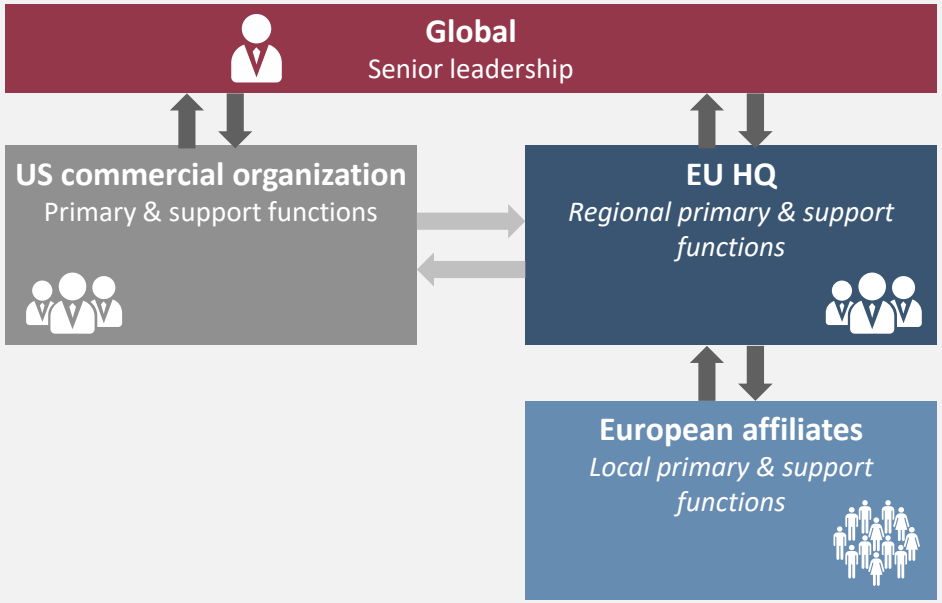
YOU MUST BALANCE 5 VARIABLES WHEN ASSESSING WHAT FUNCTIONS TO BUILD IN EUROPE AND WHETHER TO HIRE THESE INTERNALLY VS. EXTERNALLY (OUT-SOURCING)

1. Necessity of Europe-specific function vs. one global function in the US
2. Ability of your company to develop capabilities
3. Efficiency / capabilities of third-party vendor
4. Synergies with your company's future pipeline
5. Alignment of your company's and third-party vendors' goals

Source: Simon-Kucher & Partners.

Organization: Regardless of revenue potential or cash position, a lean and efficient organization in the EU commercialization should be targeted

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants



Experts point out commonly 3 considerations to design an efficient organizational structure

- **Lean structure**: Cost in line with revenue potential of drug
  - No unnecessary duplication of roles on all levels
- Stimulating **cross-functional / cross-country collaboration**
- **Empowering** the regional and local teams

General considerations:

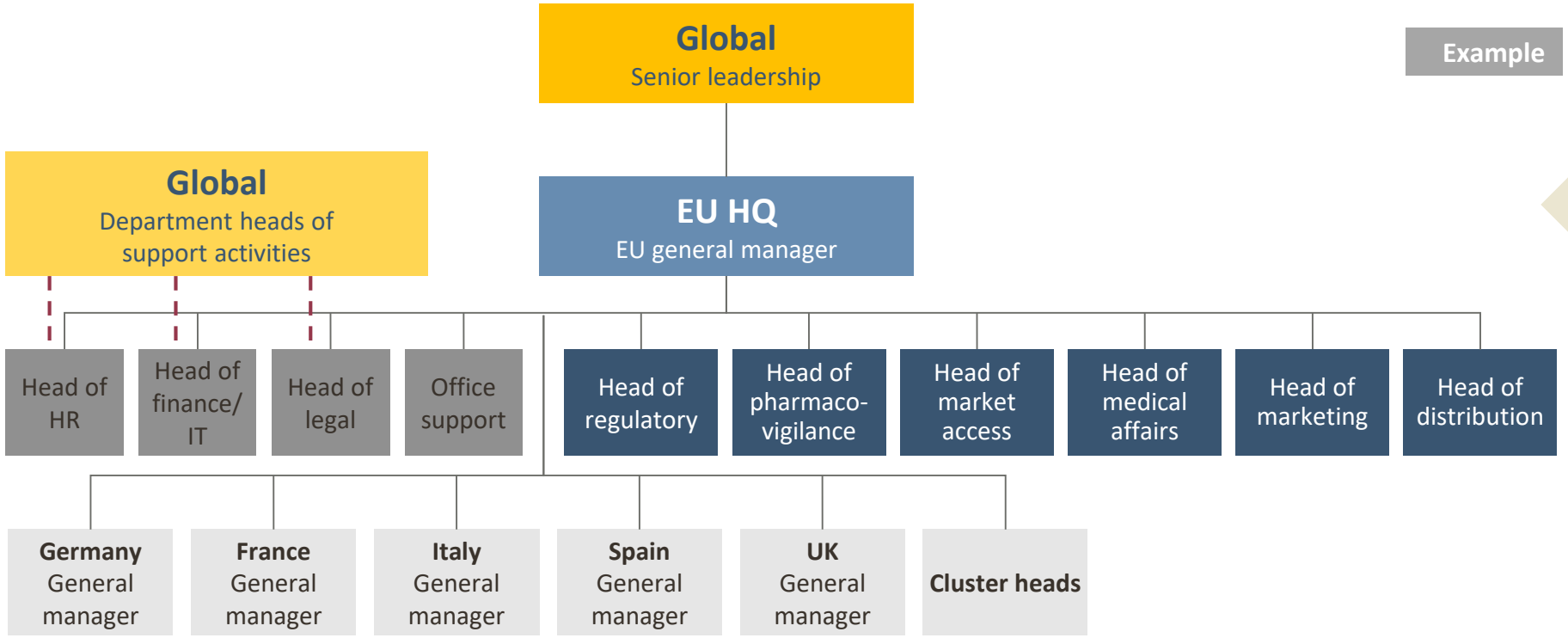
- A lean organization will grant agility to quickly **scale the organization** to the needs of the market once reimbursement is granted
- Resources should be used **efficiently** to **avoid redundancies** between the EU HQ and Affiliates
  - Aligned **market entry strategies designed** by Regional; tailored and executed in collaboration with affiliates
  - EU HQ marketing for collaborating closely with the EU affiliates to ensure a consistent and robust marketing approach, rather than duplicating efforts
  - The EU HQ supports P&MA processes in all countries
  - …

Opportunities to share resources with the US are limited

- Synergies are limited, and regional and local expertise is required
  - Opportunities for resource sharing
  - Regulatory if launches are not closely in sequence
  - Support functions
- In order to make resource sharing work, Global must free up those resources: Adding responsibilities on top won't work

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Organization: Department heads and affiliate general managers report to the EU general manager



Example

EU HQ primary activities

EU HQ support activities

EU affiliate functions

Reporting FTE to the EU general manager

Dotted line reporting to global department head

"You can always add dotted lines, but establishing cross-functional collaboration is key. This requires a certain amount of guidance from senior management."

– Chief Commercial Officer, US-based biotech

Outsourcing:

- Support functions can be outsourced (or supported from the US). Remember to consider:
  - Transaction costs
  - Degree of involvement of support functions (legal and HR) and overtime
- Non-strategic support tasks, such as payroll or dossier writing, can be outsourced to agencies
  - Depending on the number of external vendors, consider hiring a head of PMO to ensure effective management and alignment

Source: Simon-Kucher & Partners; expert interviews (n=18).

Organization: On affiliates level, most respondent believe a hybrid structure is the most efficient organizational set-up

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Different options to design the affiliate structure exist. From very lean to fully fledged organizations, everything is possible.

Lean structure

- No role duplication between EU HQ and affiliates
- *GM + MSLs + Reps*

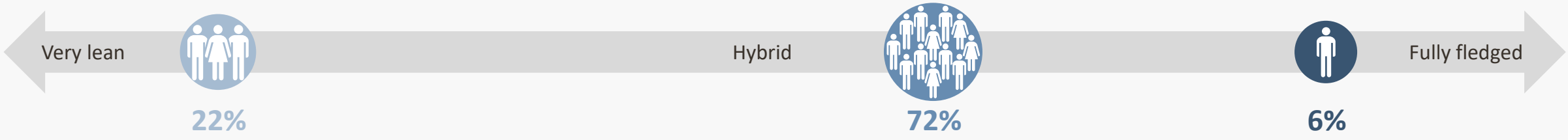
Hybrid structure

- Duplication of few key functions between EU HQ and affiliates
- *GM + P&MA + Medical affairs + MSLs + Reps*

Fully fledged structure

- High degree of role duplications
- *GM + P&MA + Commercial + Finance Medical affairs + MSLs + Reps + …*

PREFERENCE OF RESPONDENTS



22%

"For cluster markets like Nordics, a lean structure is efficient. Some companies just hire one FTE, i.e., the GM to manage one cluster on their own."
- Chief Operating Officer, EU-based biotech

72%

"This requires the affiliate team to be comfortable to operate in cross-functional roles. The GM may support P&MA negotiations and P&MA may need to support Medical Affairs."
- CEO, EU-based biotech

6%

"Despite all cost consciousness, I doubt it is possible to hire so many cross-functionally skilled people. Hence, I believe there will be role duplications."
- Regional GM, US-based biotech

However, every case requires individual assessment of drug, disease area, strategic objectives, and financial means of executing company

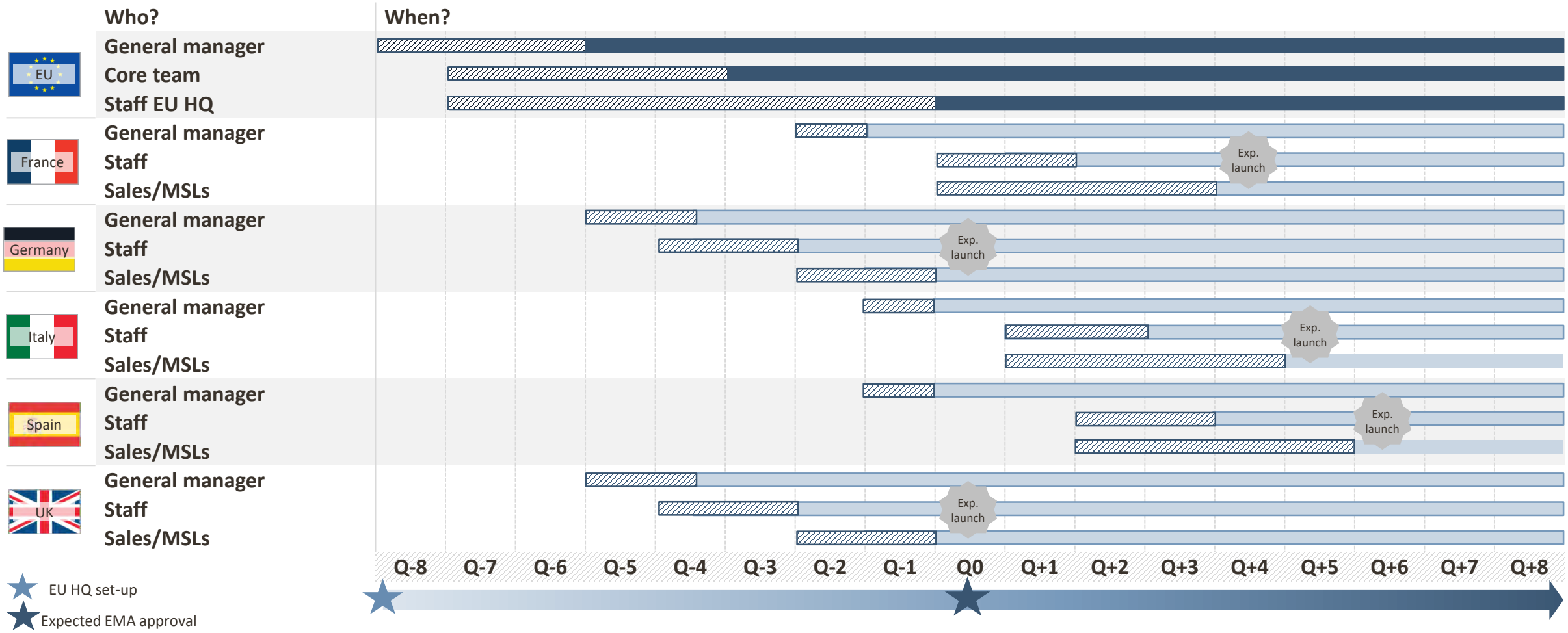
Source: Simon-Kucher & Partners; Expert interviews (n =18).

Project example: The set-up and hiring timeline should take into account different reimbursement timelines and potential up and down side scenarios

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Anonymized example

Affiliate teams should be built up following a sequential approach dependent on expected end of country-specific price negotiations / launch.



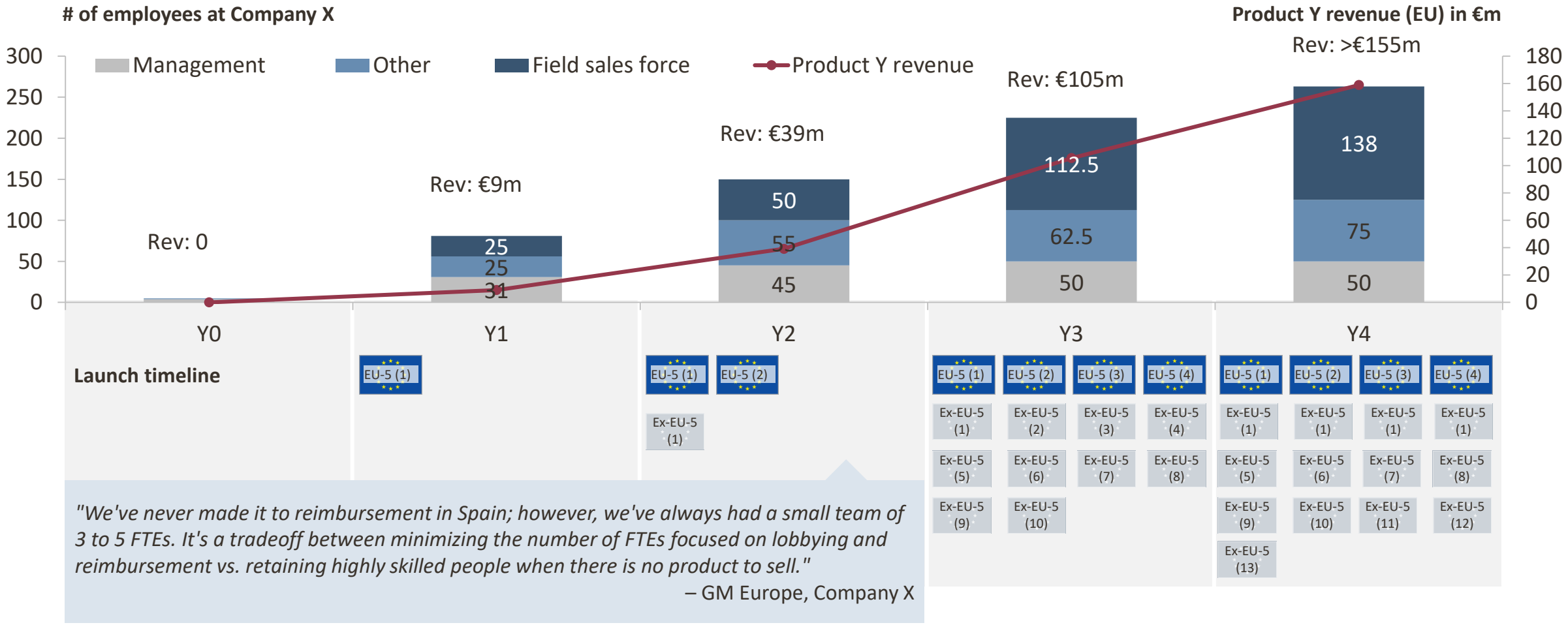
Source: Simon-Kucher & Partners; Project example.

Best practice: Company X prioritized smaller countries / shorter launch timelines and was only fully staffed upon reimbursement

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Hiring timeline and revenue development

Anonymized example



"We've never made it to reimbursement in Spain; however, we've always had a small team of 3 to 5 FTEs. It's a tradeoff between minimizing the number of FTEs focused on lobbying and reimbursement vs. retaining highly skilled people when there is no product to sell."

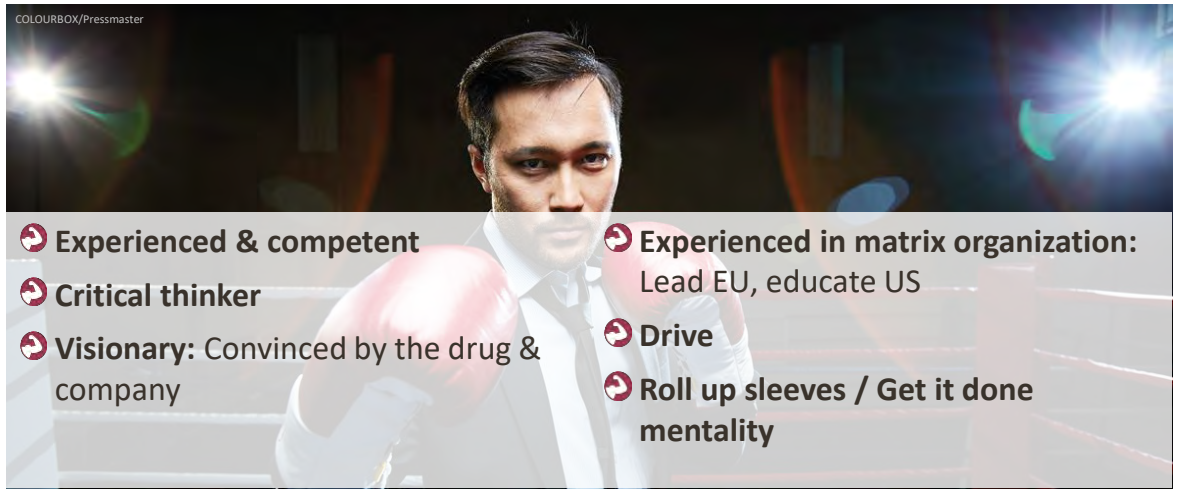
– GM Europe, Company X

Source: Author's own analyses based on external anonymized interviews (n=18); press releases of company X.

Capabilities, teamwork and governance:
Your performance is only as good as the weakest link in the chain

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

General hiring requirements: Qualities to look for



- Qualities apply more or less to any (key) personnel
- First hire: Country GM who hires regional lead functions (e.g., P&MA)
  - High time requirements: Regional GMs report of up to 50% of their time spent on recruiting
- Be willing to go beyond just offering exciting role descriptions and make your venture also financially attractive (e.g., stock-based compensation)

"I am often surprised by the lack of thoroughness in the initial hiring process of key personnel. You need experience, but also people who are willing to roll up their sleeves."

-- Chief Commercial Officer, US-based biotech

Tools and methodologies to enable collaborative ways of working (non-exhaustive)

- Hire staff and leaders with needed mind set
  - Executives and supportive staff alike must support this way of working
- Creation of cross-functional roles
  - Set shared objectives
- Promote cross-functional and international knowledge exchanges
  - Reserving considerable travel budget for face to face meetings / meeting technology
- Standardize procedures: Establish central KPI tracking platform, plug and play IT platforms
  - Measure performance from multiple angles

"Draw a clear line between giving input and making the ultimate decisions. I believe the ones being accountable should also make the last call."

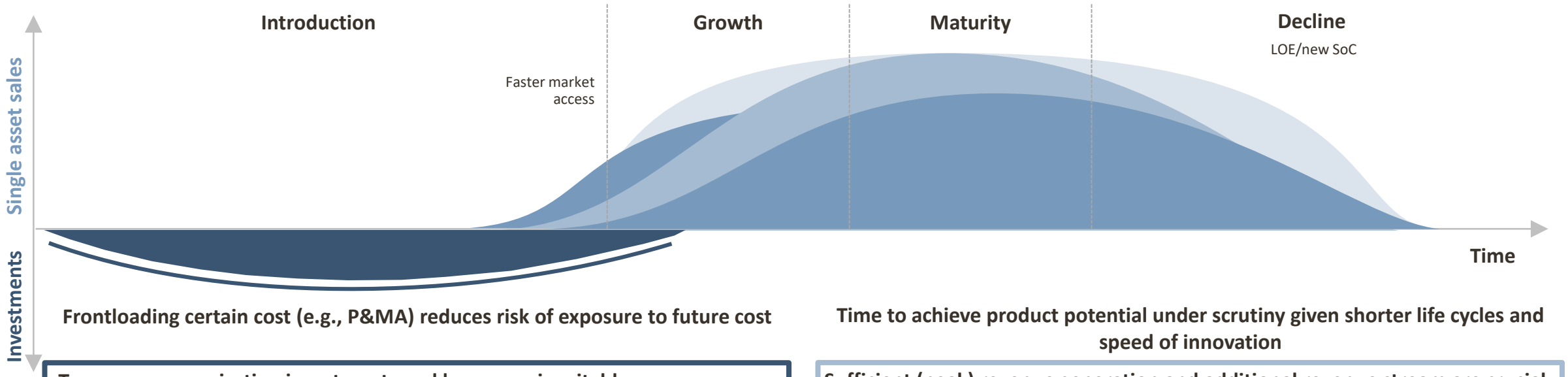
-- SVP Commercial, US-based biotech

Source: Simon-Kucher & Partners; Expert interviews (n =18).

To set up your operating model, first year losses are inevitable - long-term success is only possible with a robust pipeline (or decreasing presence)

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Investment/sales cycle for commercialization



Frontloading certain cost (e.g., P&MA) reduces risk of exposure to future cost

To ramp up organization investments and losses are inevitable:

- Rule of thumbs to assess whether investment cost are bearable
  - Can you achieve positive operating income (w/o cost allocation) within 3 years after launch?
  - 1m in sales per every FTE
  - Relatively: Investments of 15%-30% of peak revenues
  - Absolute: €60m to €120m per year operating cost (incl. non-FTE spending)

Rule of thumbs help to initially scan for potentials
For an informed decision, a robust commercial DD is mandatory

Time to achieve product potential under scrutiny given shorter life cycles and speed of innovation

Sufficient (peak) revenue generation and additional revenue stream are crucial in the long-term:

- Target to achieve peak revenues of €200m-€400m to have a viable start of the European organization
- Increasingly shortening product lifecycles: While competition increases (or shift in SoC), operating cost remain high
- Pipeline or indication expansion must offset declines
  - European labor laws hinder flexible hiring / cutting back

Plan to launch a new product or expand indications every 2-4 years in order to sufficiently use the organization to capacity

Source: Simon-Kucher & Partners; Expert interviews (n =18).

The seven secret ingredients for successfully launching and commercializing a company's first drug in Europe

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Source: Simon-Kucher & Partners.

Our expert panel believes, launching a drug in an orphan / rare disease space requires significant market shaping and education approaches

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Frequently mentioned areas to excel in to create awareness and access to patients.

High

Frequency of mentions

Low

"***Patient advocacies*** *are key, regulators, payers often do not know or understand the disease. They will ask for help."*
- Chief Operating Officer, US-based biotech

"***Patient advocacies*** *are different, they are not staffed by medical experts but often by parents of spouses. Hence, they need to be approached differently."*
- SVP Medical, US-based biotech

"Clinicians look up to ***lighthouse KOLs****, hence, ensure to engage with them early enough. I always engage regional MSLs to do so."*
SVP Medical, US-based biotech

"I am concerned about the trend to overemphasize ***MSLs****. They are not sales reps and may not act as such. Hence, you must utilize them carefully to unlock their potential."*
- Head of Market Access Europe, US-based biotech

*"****MSLs*** *become more and more important. In the orphan space treatment is often limited to few centers who execute trials and treat full patient population. Often the* ***KOLs*** *are situated there."*
- Chief Operating Officer, US-based biotech

"The classical ***sales rep*** *does not exist in such disease areas. They must become the partner of the treating facilities in all aspects beyond purely selling the drug."*
- Vice President Commercial Planning, US-based biotech

"Once you have created awareness among treating physicians, you also must ensure that the ***patients' journey brings them to treatment****."*
- VP Market Access And Pricing , US-based biotech

"To give you an example of the ***multiple stakeholders*** *involved. In SMA, the physiotherapist often is involved in evaluating treatment results. Hence you also want to engage with them."*
- Chief of Staff, US-based biotech

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Our expert panel believes, launching a drug in an orphan / rare disease space requires significant market shaping and education approaches

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Pathway to medical excellence

Starting point: Drug to serve an identified unmet medical need

Objective to unlock patient benefits

Understand to differentiate beyond offering just a treatment

- **Patient journey**: Who see patients see first? Who diagnoses? Who treats? Who decides on treatment success?
- **Patient needs**: What are pain points beyond the obvious?

Understanding patient reality – being patient-centric

Create awareness and ensure support of patient-related stakeholders

- **Patient advocacy**: Advising regulators and payers
- **KOLs**: Guiding prescribers

Engaging and advocating

Educate and have buy-in at all inflection points of the patient journey

- Diagnosis → Treatment → After care

Ensuring diagnosis & treatment

Offering comprehensive solutions to patients / physicians for disease management

Offering support and a treatment solution throughout

iStock/sbayram

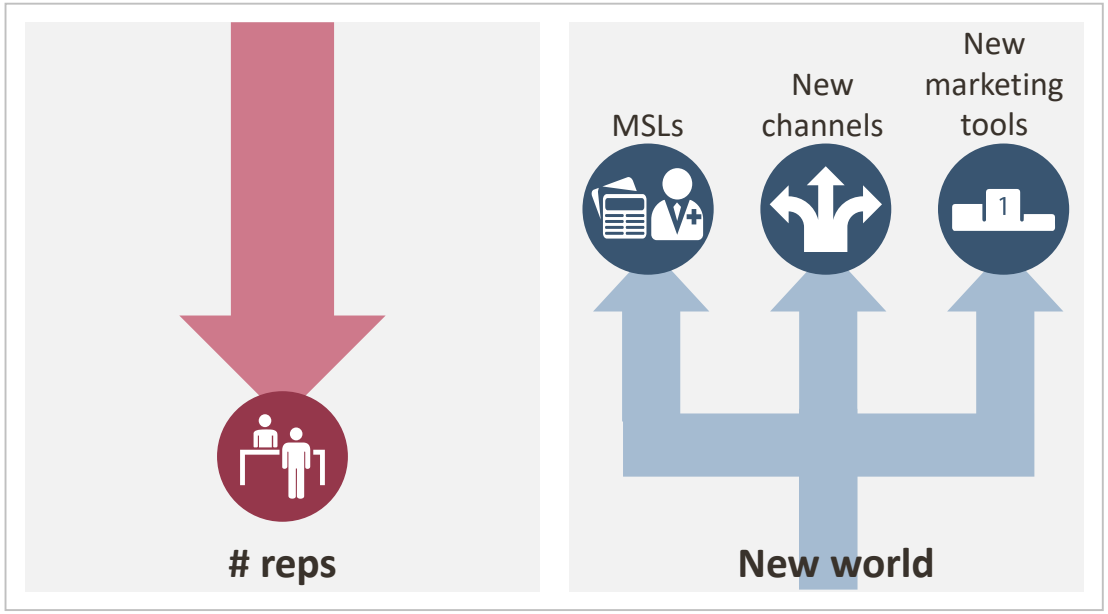
Source: Simon-Kucher & Partners; Expert interviews (n =18).

To address targeted needs, conventional sales models do not work in the orphan / rare disease space

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Conventional sales model in pharma

Alternative models in pharma



Key drivers for change

- Traditional set-up is not considered applicable to market orphan / highly specialized drugs
- To improve sales force effectiveness 'hybrid' routes-to-market and new specialized roles are considered a key success factor by our experts (MSLs shaping the market, sales reps acting as Key Account Managers)
- Digitalization will allow for new modes of interactions with customers (from webinars to augmented reality)

Source: Simon-Kucher & Partners; Expert interviews (n =18).

From personal to multi-channel customer interaction

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

New sales approaches

- Multi-channel engagement and information access to intensify customer relationship and reach
- Transfer to full remote / digital interactions for low priority accounts / products
- Usage of digital channels to expand reach to non-core market segments (incl. direct-to-patient)
- Usage of agile tools to monitor sales success and dynamically adapt sales approach

New marketing and customer service tools

Digital value-added services:

- Communicate (technical) medical information through interactive education and coaching tools

Social media applications:

- Engage with doctors (and patients) and encourage peer-to-peer communication

Mobile health solutions:

- Support disease monitoring and physician / patient interaction with remote monitoring tools

Source: Simon-Kucher & Partners; Expert interviews (n =18).

MSLs are considered to have more impact on the success of a drug launch than just relying on classical sales reps

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

MSLs

Key tasks: Communicate complex topics to external stakeholders

- Establish and maintain peer-peer relationships with KOLs
- Set-up early access programs
- Facilitate patient engagement
- Educate payers and regulatory bodies

Profile / skills:

- Advanced scientific training + generally a doctorate degree + **certain business acumen**

Size and relation of MSLs depend on disease area and country-specific characteristic

SALES

Key tasks: From marketing to key account management

- Complex, center-focused treatments require different sales rep management
- Holistic and multi-stakeholder support required: From prescriber management to support of order management at center

Profile / skills:

- Can do attitude
- Sales driven relationship manager

"KOL and patient advocacy is top priority. At the end of the day it comes down to physicians being able to prescribe, KOLs and patient advocacy can push forward on reimbursement hurdles if needed…."

– Vice President Marketing, US-based biotech

"In the orphan space, centers are very important. In the UK, most centers are in London. In Germany it is much more dispersed. Hence, even though UK is larger in sales due to higher prevalence, the sales force is much smaller."

– Director Market Access, US-based biotech

"With potentially fewer patients being treated but with a very high unmet need you cannot only deploy sales reps, you need key account managers that support the whole center beyond selling your product."

– SVP Medical, US-based biotech

Source: Simon-Kucher & Partners; Expert interviews (n =18).

The seven secret ingredients for successfully launching and commercializing a company's first drug in Europe

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Source: Simon-Kucher & Partners.

While P&MA excellence is manifold, we would like to focus on three key areas that could undermine a successful commercialization

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

"P&MA is more than market research or a price tag. It is probably one of the key functions to excel in."

- SVP Medical Affairs, US-based biotech

Today's focus

"Launch excellence starts with P&MA excellence."

- SVP Commercial, US-based biotech

"I believe sooner or later we will have Chief Access Officers next to or instead of Commercial Officers."

- Global Head P&MA , US-based biotech

Today's focus

"Getting the price right is one thing, but you need to have a compelling story behind it … For payers, physicians, media, and patients."

-Chief Commercial Officer, EU-based biotech

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Monetizing innovation: In general, expect three types of key concerns which payers will try to leverage in P&MA discussions

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Overview of frequently raised concerns regarding high-cost, highly innovative drugs in rare disease / orphan space

Exemplary: Not Exhaustive

Clinical

Limited clinical evidence:

- Trial methodology weakness (Ph I/II and single arm)
- Limited trial population
- …

Lack of long-term data:

- **Either hinging on curative claim or**
- Too short long-term benefits in chronic disease
- Safety / tolerability concerns
- ….

Financial

High price tag:

- Especially for one time or chronic treatments
- Value vs. breaching psychological thresholds
- …

Budget impact / affordability:

- Payers' incentives mainly based on annual (or short-term) savings
- Willingness to pay the amount for a treatment that reflects potential (indirect) long-term cost savings
- …

Market readiness

Infrastructure requirements:

- Center accreditation: Set-up needed before launch with time constraints and unclear pathway
- Genetic testing: required to ensure appropriate therapy

Monitoring capabilities:

- RWE collection / registries
- Patient monitoring
- …

.

Alternative access agreements could be the door-opener to market access negotiations and success by proactively mitigating these concerns

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Monetizing innovation: Different forms of alternative access agreements aligning value & price are being discussed

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Traditional model of fixed price per unit and negotiated discount depending on volume is no longer viable for new high cost treatment options

Subscription models

Payment is based on calendar units instead of pill units (fixed even if higher dosage or more pills are needed)
e.g. Roche in Diabetes Care

Results based payment

Payments are contingent on the (independent) verification of results
e.g. Luxturna in the US

Indication agnostic payment agreement

At launch a price is agreed that covers all future indications
e.g. Opdivo

Indication – specific bundled payment

Payment based on indication for which product / service will be used
e.g. Kymriah in the US

Annuity payments

Payment is divided into several instalments covering a number of years
e.g. Luxturna in the US

Public – private partnerships

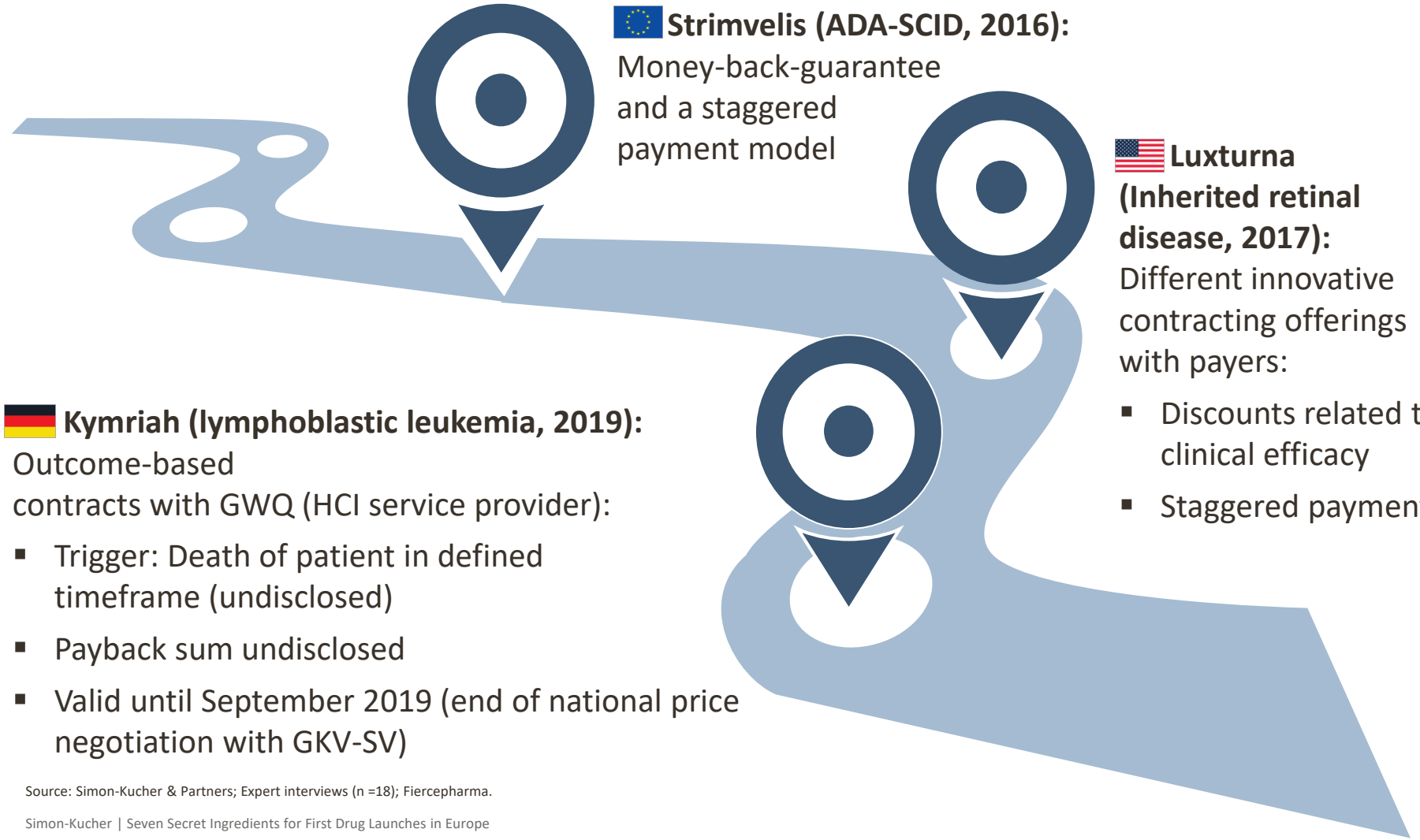
Agreement between manufacturer and (public) payers to provide goods, services, infrastructure, or investments in exchange for (exclusive) access
e.g. Bayer hemophilia in China

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Monetizing innovation: US and European members alike are trying to find new ways to make alternative access agreements work in reality

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Innovative contracting developments



Strimvelis (ADA-SCID, 2016):
Money-back-guarantee and a staggered payment model

Luxturna (Inherited retinal disease, 2017):
Different innovative contracting offerings with payers:

- Discounts related to clinical efficacy
- Staggered payments

Kymriah (lymphoblastic leukemia, 2019):
Outcome-based contracts with GWQ (HCI service provider):

- Trigger: Death of patient in defined timeframe (undisclosed)
- Payback sum undisclosed
- Valid until September 2019 (end of national price negotiation with GKV-SV)

Future outlook

- Increasing awareness for need of alternative access agreements
  - High importance of RWE to make access agreements work
- However, limited willingness to implement access agreements for any drugs
  - Limited to high priced drugs with high clinical uncertainty

Source: Simon-Kucher & Partners; Expert interviews (n =18); Fiercepharma.

International price referencing: Playing the game at launch

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

How to get from a country-specific price assessment…

… to a global launch strategy?

Over 50% of respondents mentioned IPR and launch sequence planning to be an important consideration in excelling in European launches

"I had never expected IPR to have an actual impact on my revenue potential until I was responsible for the whole EU launch of Product X."

- Chief Commercial Officer, US-based biotech

"You need to plan ahead, but you also need to be able to execute on your strategy. Hence it is key to have a clear understanding how each market is related to each other."

- Chief of Staff, US-based biotech

Source: Simon-Kucher & Partners, Expert interviews (n =18).

International price referencing: IPR assessment is required to transform a country-specific analysis of P&R potential into a launch strategy

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Optimal product launch strategy

Time

Country-specific price and volume potential in **key** markets

Launch study

Development of launch strategy for **key** markets

?

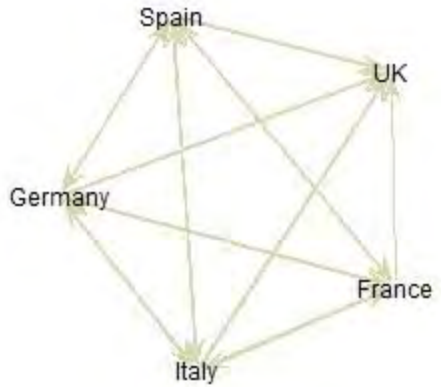
Development of launch and country sequencing strategy for **all** future markets (e.g. EU-15 or EU-28)

Launch preparation

Implementation of launch and country sequencing strategy

Complexity of IPR

Referencing relationships between countries



…an optimal launch strategy however, requires explicit and sophisticated consideration of IPR

Source: Simon-Kucher & Partners; Expert interviews (n =18).

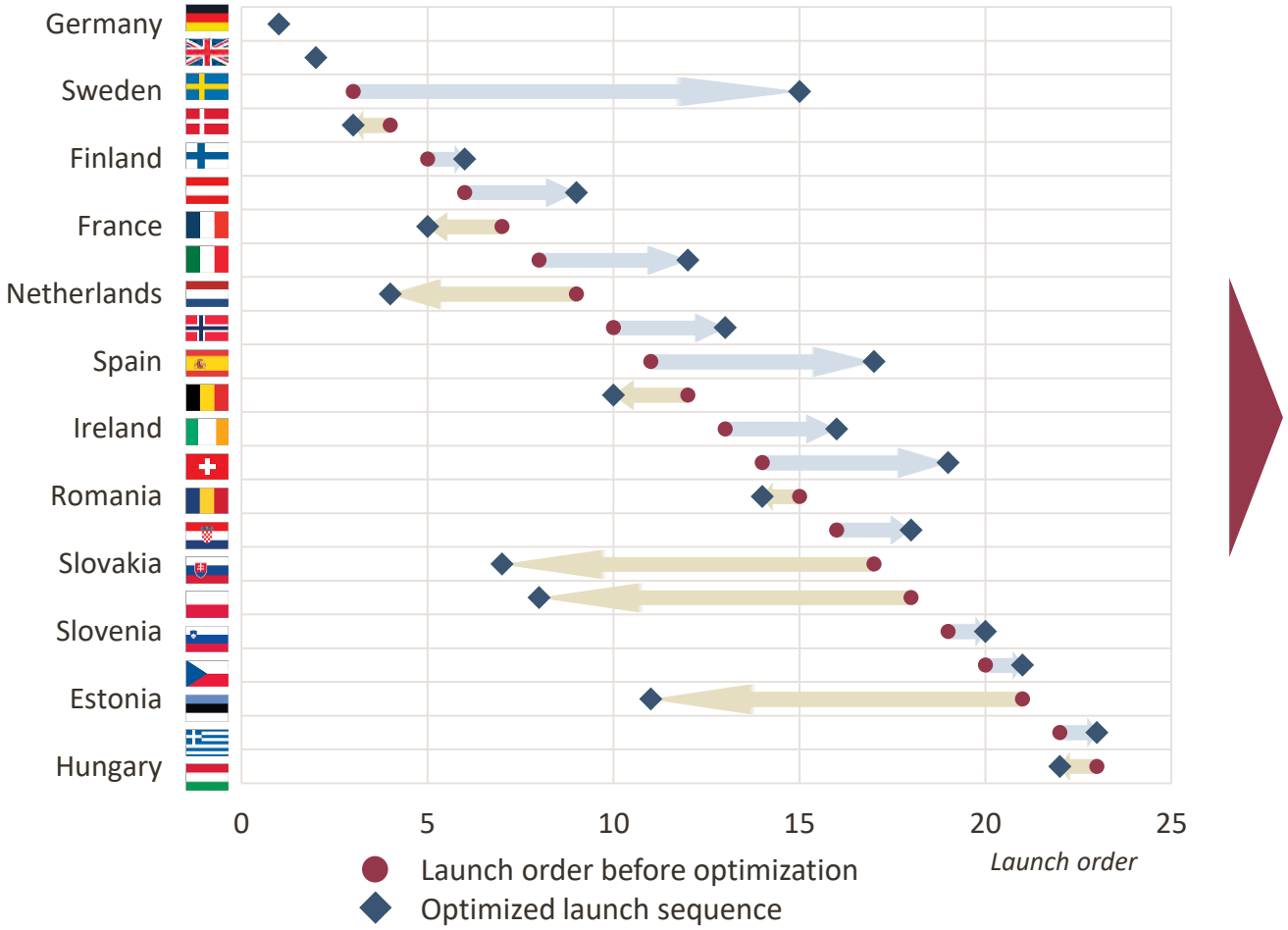
International price referencing: An comprehensive launch strategy allows to extract the optimal value from an innovative product

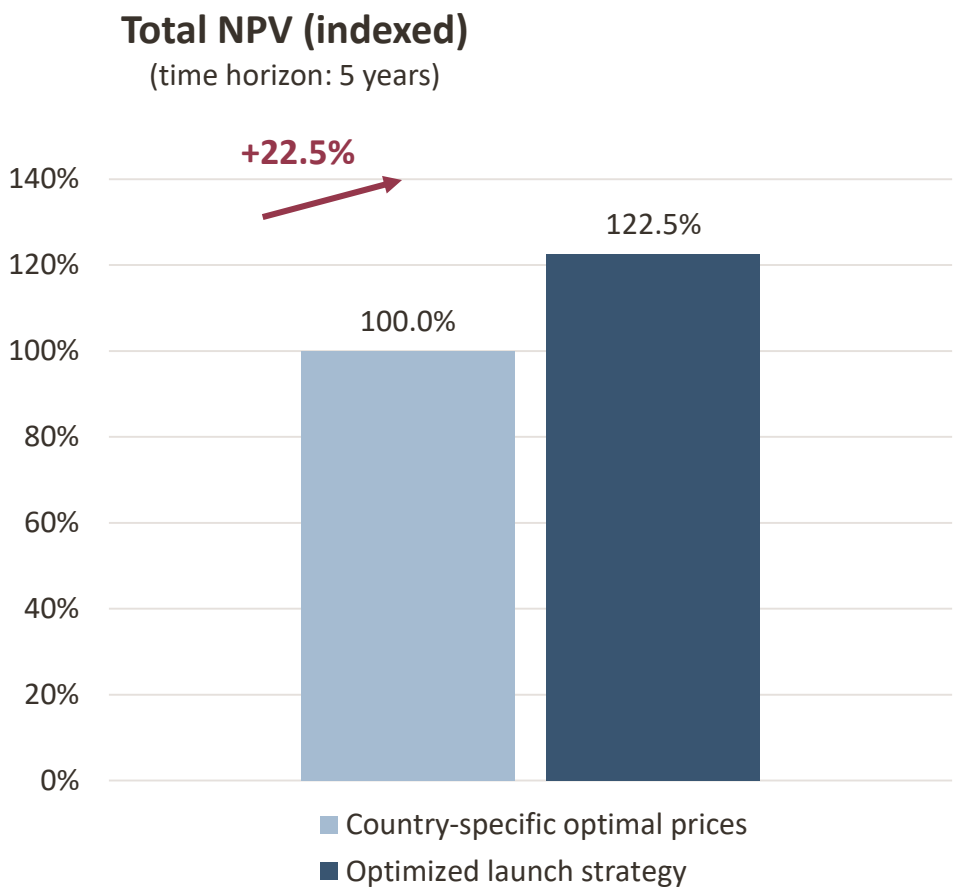
SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Example: The optimized price corridor and launch sequence increases the total NPV over 5 years by 22.5%.

Project example

Optimization of launch sequence





Source: Simon-Kucher & Partners; Expert interviews (n =18).

Negotiation excellence: P&MA negotiations with payers are inherently difficult as their experience and goals differ from those of an emerging biopharma company

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Common characteristics impeding a successful negation as reported by our expert panel:

Payers

Governance / process

- Tried and tested procedures
- Have the law and public opinion in their favor
- Don't mind delays

Skills

- Professional negotiators
- Experienced negotiators – "been there – seen it"
- Know approaches of your competitors

Tools / analytics

- Centralized data collection
- Data analytics departments

Emerging pharma company

Governance / process

- Overlapping workflows
- Lack of systematic approach
- Ad-hoc decision making
- Under time pressure

Skills

- Inconsistent across countries
- Lack of role clarity and experience
- Insufficient preparation, lack of knowledge of precedents
- Afraid to be assertive

Tools / analytics

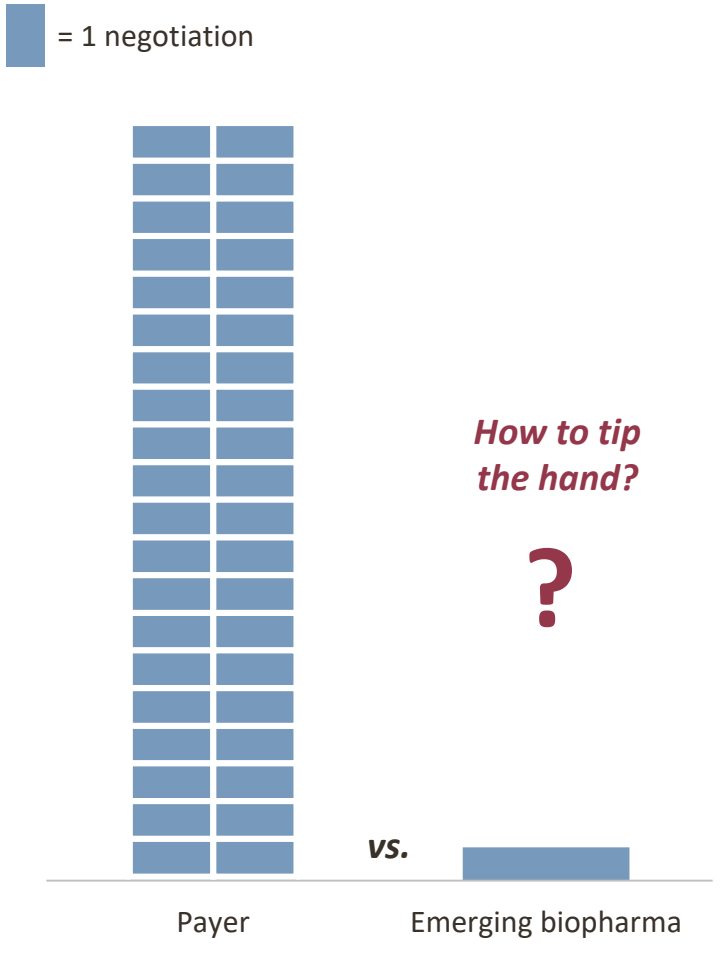
- Ad-hoc spreadsheets
- No after-action review

Simon-Kucher & Partners, Expert interviews (n=18).

Negotiation excellence: Only sufficient long-term planning, strategy development, and practice can tip the hand over experienced payer negotiators

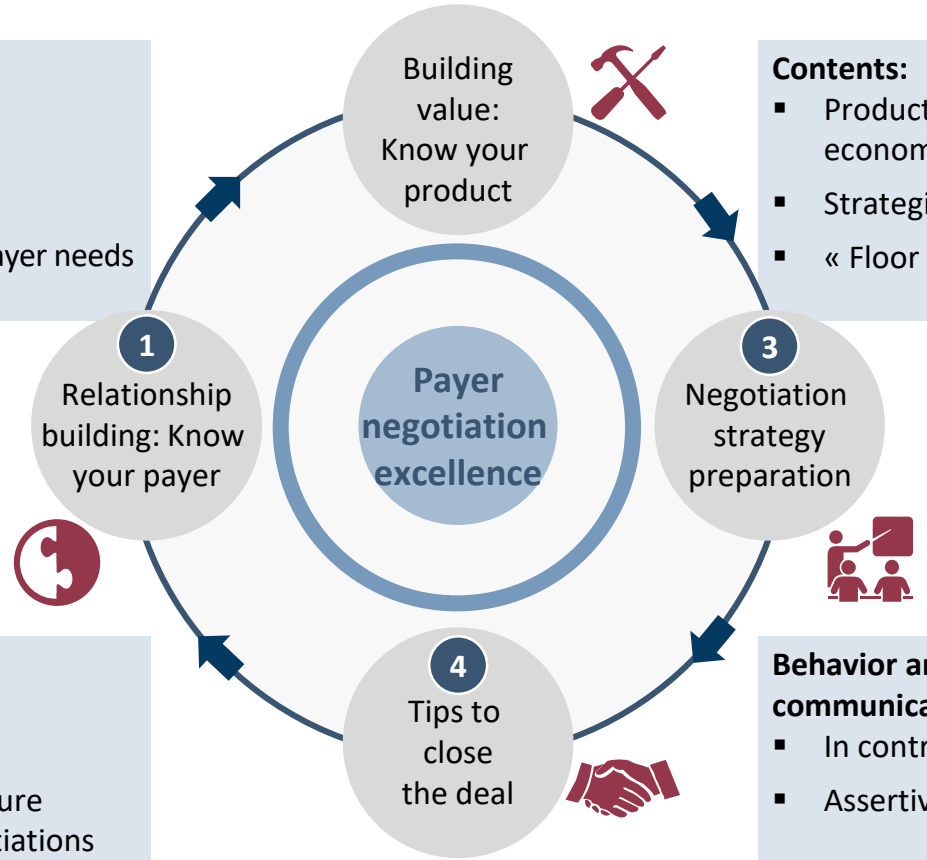
SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Hence, the development and training of a payer negotiation strategy guide, applicable to different payer archetypes and situations specific for the to be launched drug is an important pillar in excelling in P&MA.



Relationship:
- Open-minded
- Provide timely information
- Understand payer needs

Contents:
- Product clinical and economic value
- Strategic options
- « Floor »



Relationship:
- Reliable and trustworthy
- Protecting future product negotiations

Behavior and communication:
- In control, balanced
- Assertive, friendly

Source: Simon-Kucher & Partners; Expert interviews (n =18).

The seven secret ingredients for successfully launching and commercializing a company's first drug in Europe

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

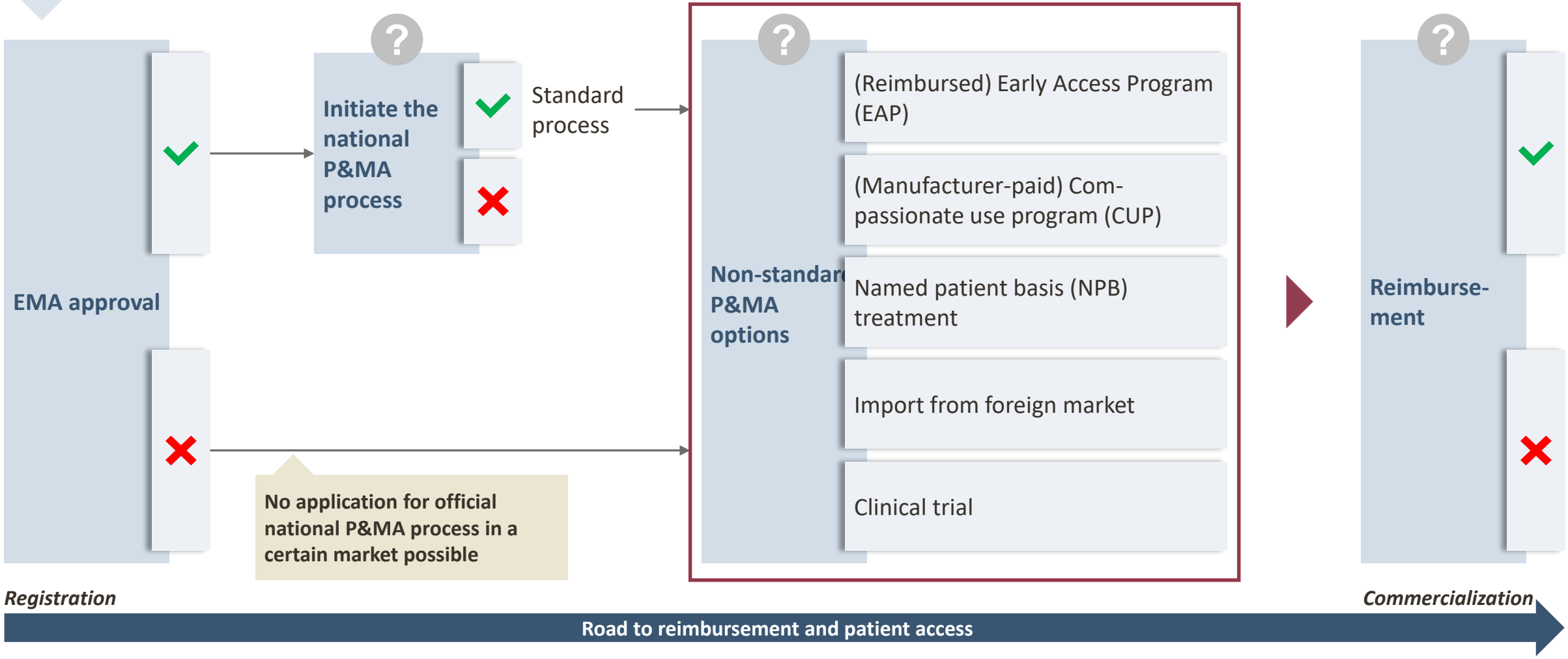
Source: Simon-Kucher & Partners.

Overview: There are several pathways outside the regular national P&MA process

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

"Early engagement and early access programs are the most important and most valuable tools one can leverage in the orphan space."
- SVP Medical, US-based biotech

Conceptual



Source: Simon-Kucher & Partners; Expert interviews (n =18).

Overview of all alternative access pathways in EU-5

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Pathway						Backup
Early access program (reimbursed)	Cohort/named patient ATU	Not available	Law 648	Not available	Not available	
Compassionate use program (not reimbursed)	*[Covered by cohort ATU]*	Cohort compassionate use	Decree 08/05/2003	Decree 1015/2009	Early Access to Medicines	
Named patient basis treatment (usually not reimbursed)	*[Covered by named ATU]*	Named patient basis treatment	Fondo AIFA 5%	Not available	Supply of "Specials"[1]	
Import from foreign market (reimbursed)	*[Only under ATU]*	Nominative import program	Decree 11/02/1997	Decree 1015/2009	*[Covered by "Specials"]*	
Clinical trial (usually not reimbursed)	Possible	Possible	Possible	Possible	CtE	
Other	Not available	Not available	Exceptional rare disease program (Law 326)	Hospital funding Managed Entry Agreements	CCU/IFR process/MEA[2]	

Most promising option

Identification requires individual assessment per case (Unmet need, perceived incremental value, etc.)

Source: Simon-Kucher & Partners; [1]Unlicensed medicinal products; 2Managed Entry Agreements

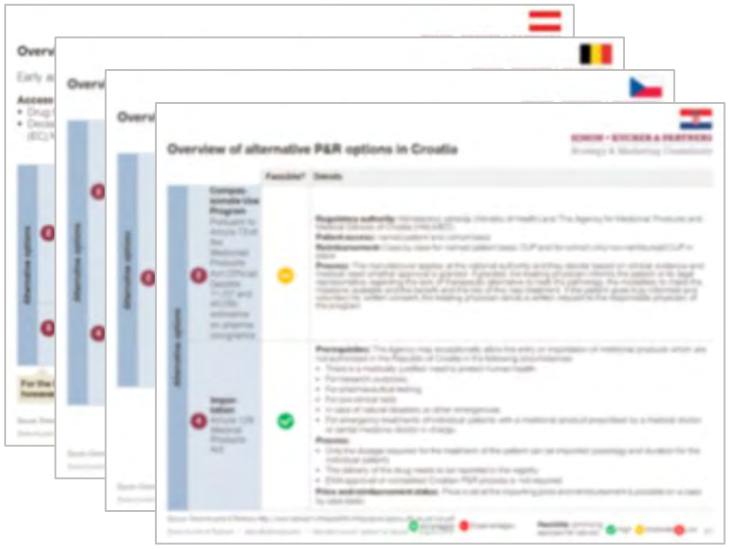
Alternative access pathways (AAP) can expedite commercial take-up

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

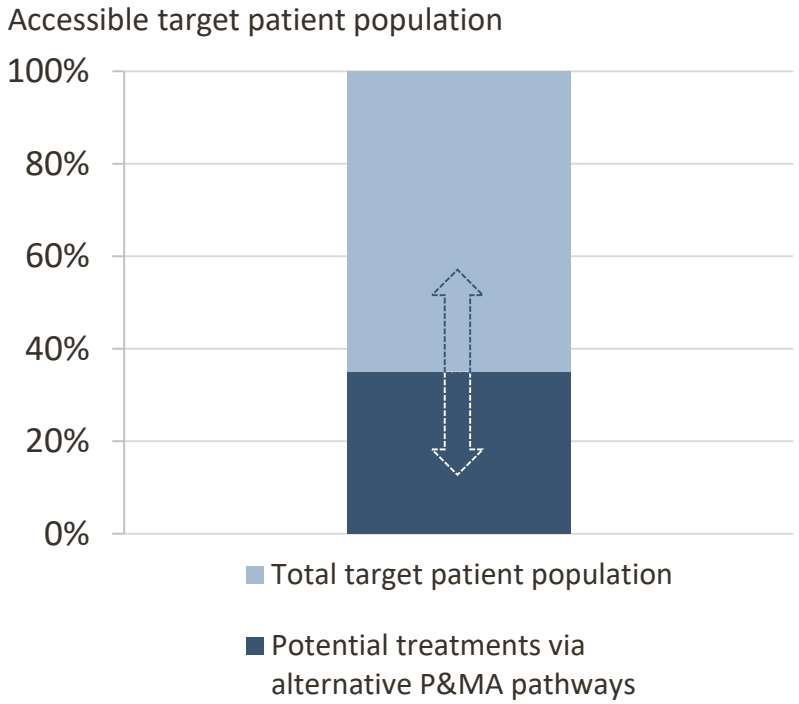
Experts recommend utilizing AAP to target patients as early as possible and, in turn, achieve quicker and steeper commercial uptake.

Conceptual

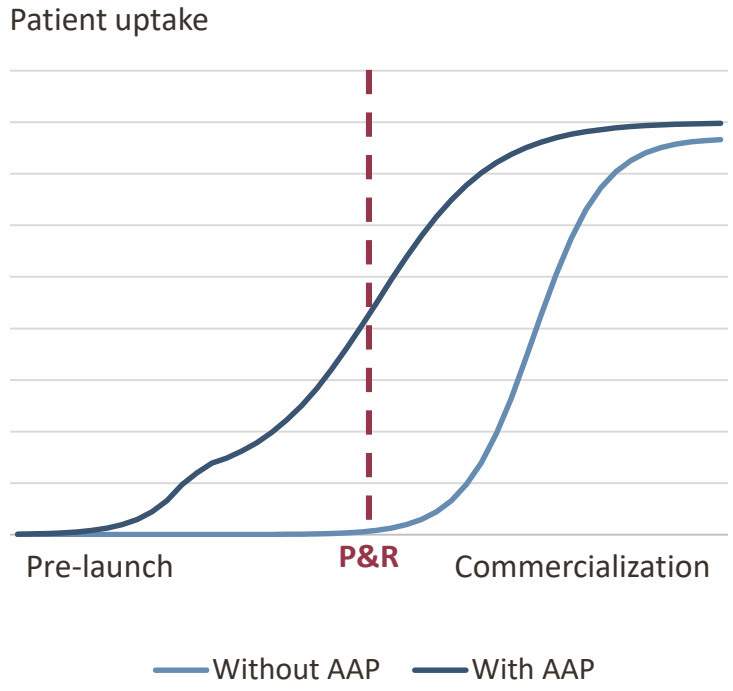
Alternative access pathways exist beyond the EU-5



Potential to access patients earlier and create buzz about new treatment



Quicker and steeper commercial uptake



Achieving alternative access with a significant share of accessible target patient population requires strong support by KOLs, physicians, and patients/patient associations, and, thus considerable efforts by the manufacturer

Source: Simon-Kucher & Partners; Analog research (n=20); Expert interviews (n=18).

Alternative access programs allow collecting RWE early and gain valuable commercial and operational experience

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

- **RWE will influence future therapy management and algorithms will become key decision drivers**
- **Increased availability / importance of RWE for assessment of:**
  - P&MA decisions and re-assessment
  - Especially relevant for orphan drugs given their (often) very limited data package

Independent RWE / data collection to:

- Validate treatment pathways
- Analyze cost-benefit of different treatments / pathways
- Improve safety or adverse event monitoring
- Implement payment-by-results schemes / flexible pricing agreements
- Perform post-launch studies in sub-groups

Further upsides for emerging bio-pharmas

- Create goodwill among patients, physicians, and KOLs
- Create own experience in serving patients in a non-trial setting without operating directly at full commercial scale (e.g., distribution)

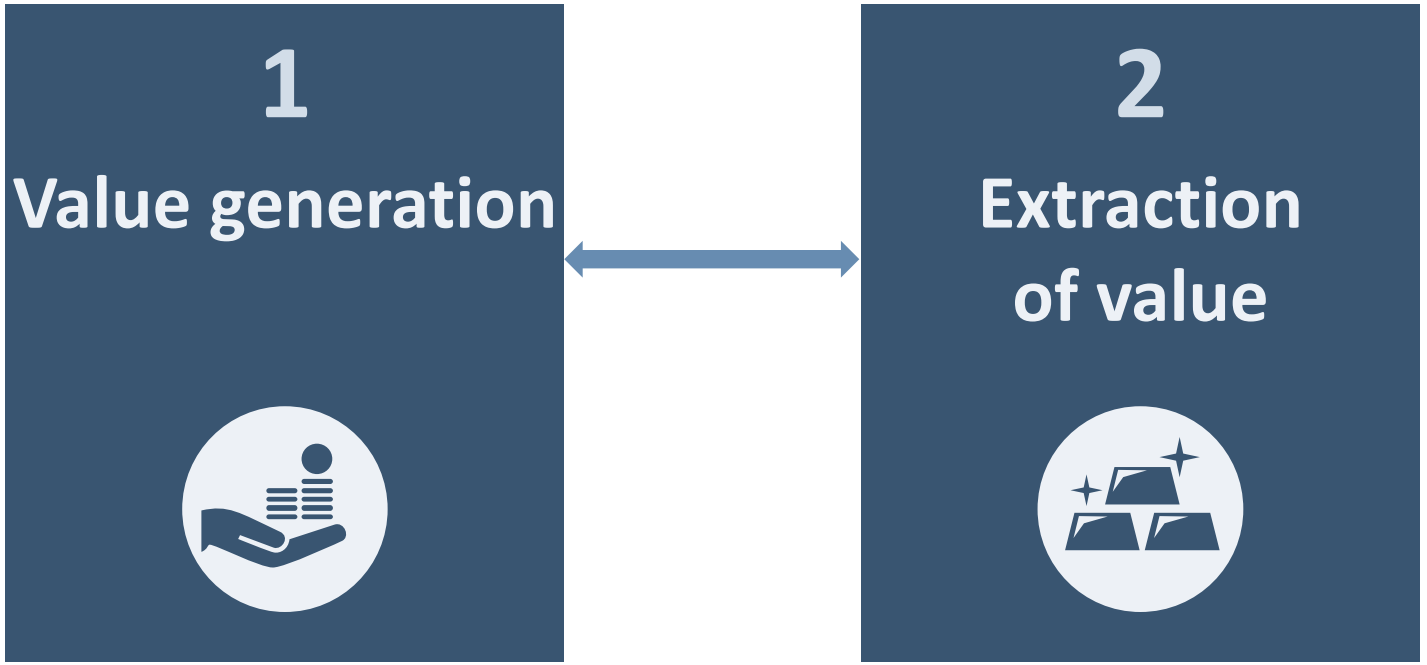
"Yes, there are many upsides for the patient and you can even earn money quicker. But it is also a great chance to acid test your operations and learn under real conditions."

-Country GM, US-based biotech

Source: Simon-Kucher & Partners; Expert interviews (n=18).

Bringing it all together

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants



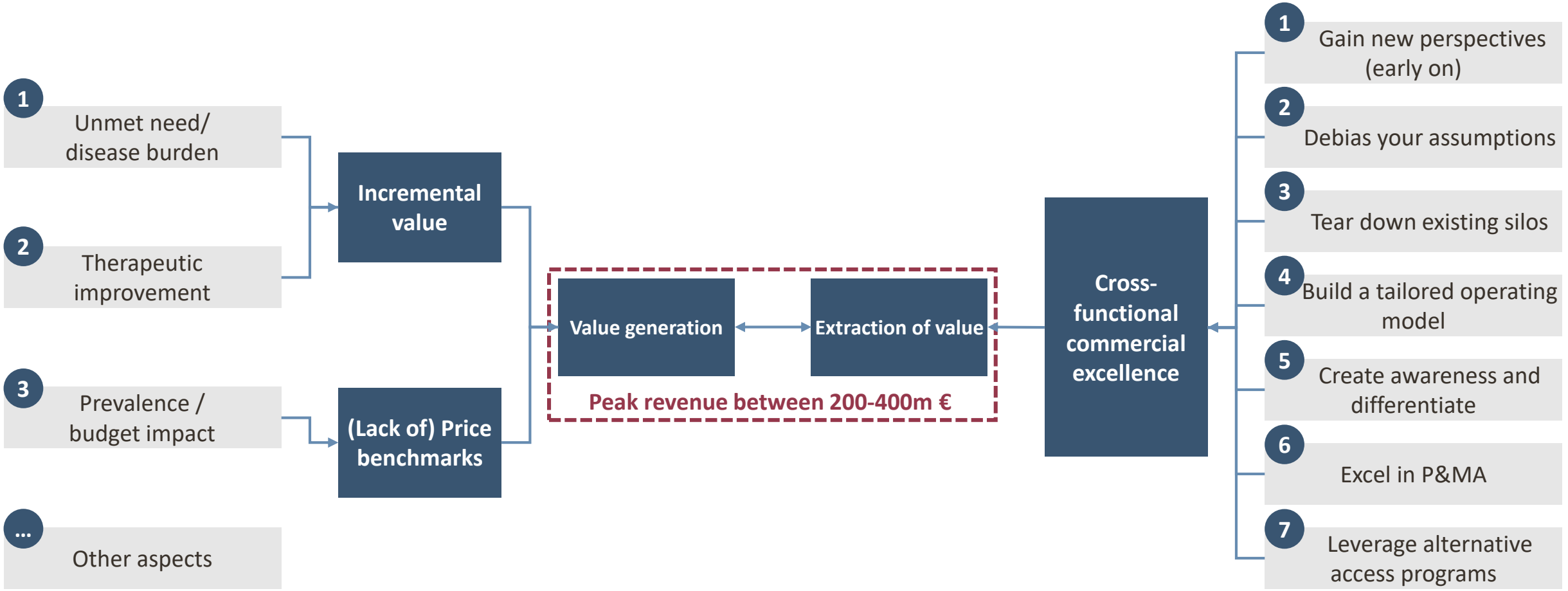
Willingness-to-pay + volume assessment

7 secret ingredients for success

Source: Simon-Kucher & Partners.

In summary, you must not only understand the value potential of your drug, but also consider the seven secret ingredients to extract properly

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants



Source: Simon-Kucher & Partners; Analog research (n=20); Expert interviews (n=18); * Theoretical value for an orphan drug with high therapeutic value and a medium fledged EU organization.

Despite every new commercialization considerations being unique, a few managerial implications hold true in general

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Take-aways

The dos

1 **Assess and incorporate the implications** of European commercialization **early** on

2 **Understand your product's pricing and commercial value**, potential hurdles, and key stakeholders to address in Europe

3 **Understand the importance of finding and empowering the right talent**; be willing to relinquish some control in order to enable the tailored execution of your strategy

4 **Plan ahead** and ask yourself **how** you can leverage your future commercial organization

The don'ts

5 **Don't rely on experience** and old assumptions; challenge them and allow them to be challenged**; seek expert help from a trusted advisor**, if needed

6 **Don't underestimate** the **operational** and **financial requirements** for making the leap to Europe

7 **Don't overestimate your drug's potential** or your European **capabilities**; make reasonable, fact-based decisions

8 **Don't copy and paste** other companies' approaches; design a unique commercialization strategy tailored to your venture

9 **Don't commercialize at all cost**; certain markets are better left to third parties

Source: Simon-Kucher & Partners; Expert interviews (n =18).

Q&A

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

… any questions?

Photo: www.colourbox.com

Source: Simon-Kucher & Partners.

SIMON • KUCHER & PARTNERS
Strategy & Marketing Consultants

Thank you!

Munich office
Luise-Ullrich-Str. 14
80636 Munich, Germany
Tel. +49 89 544793 0

Zurich office
Loewenstrasse 1
8001 Zurich, Switzerland
Tel. +41 44 22650 40

www.simon-kucher.com

IV.
EU-Proposal on Joint HTA

Stephen Norton, MAP BioPharma

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

EU Joint HTA

– Priorities for the Introduction of a European HTA System

After AMS GmBH presentation of 10 September 2019

Priority 1: The Comparator

- Company choice
- Clinical practice is the main factor, above other considerations
- Scientific advice can answer simple yes/no questions on comparators

- Committee is free to choose alternative comparator(s)
- Clinical practice may include off-label products

- Consideration of clinical practice and upcoming therapies
- All WP6 partners can give input for the choice of comparator(s) in order to achieve “European relevance“
- Relevant area i.e. clinical practice guidelines, routine use in clinical practice, evidence

- No guidance which guidelines are (more) relevant
- Exclusion of comparators even if approved in some countries
- Comparator may be a compound available at the time of report publication -> may be relevant for national uptake of the joint assessment in some countries
- Orphan drugs: Comparator for orphan drug assessments

Priority 1: The Comparator

- Company choice
- Most clinically-relevant (in practice, the product most likely to be replaced by the new product), licensed or not
- Acceptable to cite several comparators, the new product adding to patient choice
- "wrong" choice of comparator is often cited as a reason for negative guidance

- Consideration of clinical practice and upcoming therapies
- All WP6 partners can give input for the choice of comparator(s) in order to achieve "European relevance"
- Relevant area i.e. clinical practice guidelines, routine use in clinical practice, evidence
- No guidance which guidelines are (more) relevant
- Exclusion of comparators even if approved in some countries
- Comparator may be a compound available at the time of report publication -> may be relevant for national uptake of the joint assessment in some countries
- Orphan drugs: Comparator for orphan drug assessments

Priority 1: The Comparator

ASMR rating (Amélioration du Service Médical Rendu, Improvement in Medical Benefit) depends on choice of comparator

- ➕ Range of clinically-relevant comparators can be considered

- ➖ CT may choose different comparators
- ➖ Products must show additional benefit before qualifying for more favourable pricing
- ➖ Head-to-head studies must be conducted to demonstrate superiority

- ➕ Consideration of clinical practice and upcoming therapies
- ➕ All WP6 partners can give input for the choice of comparator(s) in order to achieve “European relevance“
- ➕ Relevant area i.e. clinical practice guidelines, routine use in clinical practice, evidence

- ➖ No guidance which guidelines are (more) relevant
- ➖ Exclusion of comparators even if approved in some countries
- ➖ Comparator may be a compound available at the time of report publication -> may be relevant for national uptake of the joint assessment in some countries
- ➖ Orphan drugs: Comparator for orphan drug assessments

Priority 1: The Comparator

Recommendations

- Definition of a consistent process for the derivation of comparator(s) by the coordination group, taking into account national requirements *and* scientific state of the art
  - Needs to account for different comparators in different countries
- Guidance on accounting for different indications
- Comparators identified during the scientific advice process should be consistent in the joint assessment

Priority 2: Relevant Studies

- RCTs remain gold standard
- NICE demonstrates willingness to consider other forms of data, especially for rare diseases:
  - Single-arm studies
  - Managed entry data collection
- Patients able to contribute to process (submissions, meetings)
- Not yet highly trusting of real-world evidence
- Patient contributions hold different influence in different assessments (e.g. HST vs STA)

- Inclusion of studies with different evidence level
- Tendency towards a broader body of evidence
- So far no definition of “relevant studies”

Priority 2: Relevant Studies

- Indirect comparisons may be used in rare cases
- Allowance of lower levels of evidence certainty for orphan/ultra-orphan products
  - Especially in economic evidence
- SMC favours simple submissions, may not be able to fully describe the data
- Data gathering requirement for ultra-orphan medicines could be burdensome

- Inclusion of studies with different evidence level
- Tendency towards a broader body of evidence
- So far no definition of “relevant studies”

Priority 2: Relevant Studies

- ➕ SMR/ASMR system allows innovative products to show significant benefit over current practice
- ➕ Published and unpublished evidence is submissible
- ➖ No exemptions or different requirements for orphan medicines
- ➖ Post-marketing real life studies may be required to gather further data

- ➕ Inclusion of studies with different evidence level
- ➕ Tendency towards a broader body of evidence
- ➖ So far no definition of “relevant studies”

Priority 2: Relevant Studies

Recommendations

- Definitions of categories of evidence levels and their significance to final recommendation
- Definition of situations or indications where “weaker” evidence (e.g. single-arm studies) may be most relevant and the highest available standard of data
- Outcomes from scientific advice should be very clear on required evidence and its likely influence in assessment

Priority 3: Patient Relevance

- Several patient-relevant values are used:
  - HRQoL
  - End-of-life
  - Degree of need
- Patient submissions and engagement at meeting welcomed in HST process
- Differences between processes: patient role not as significant in STA process
- Invited representatives' views not always factored into decisions

- Patient input to inform the scope of the assessment, e.g. on patient relevant outcomes or possible neglected outcomes
- More consistency with the endpoints in the registration trials
- Recommendation only: Comprehensively defined and justified in protocol and report
- Numerous different terms are used when endpoint issues are described at various places in the documents

Priority 3: Patient Relevance

- Detailed written submissions invited on lived experience of disease (patients and carers), quality of current treatments, knowledge of new medicine
- Patient and clinician engagement (PACE) meetings for orphan drugs allow more data to be gathered
- Patient representatives attend committee meeting

- Patient input to inform the scope of the assessment, e.g. on patient relevant outcomes or possible neglected outcomes
- More consistency with the endpoints in the registration trials

- Recommendation only: Comprehensively defined and justified in protocol and report
- Numerous different terms are used when endpoint issues are described at various places in the documents

Priority 3: Patient Relevance

- Patient-relevant measurements given highest priority
- Published and non-published data is welcomed if relevant
- Intermediate endpoints (with less patient-relevance) are deprioritised

- Patient input to inform the scope of the assessment, e.g. on patient relevant outcomes or possible neglected outcomes
- More consistency with the endpoints in the registration trials
- Recommendation only: Comprehensively defined and justified in protocol and report
- Numerous different terms are used when endpoint issues are described at various places in the documents

Priority 3: Patient Relevance

Recommendation:

- Definition of patient-relevant endpoints: What is important for the patient in clinical care, in particular the achievement of clinically relevant therapy targets
- Exact definition and consistent use of terms for endpoints
- Joint definition by EMA & EUnetHTA/EU HTA cooperation on relevant endpoints
- Endpoints accepted for marketing authorisation should also be accepted in the joint assessment

Priority 4: Subgroup Analysis

- Subgroups identified at NICE scoping specifically required
- Implied need to analyse any subgroups relevant to value proposition

- Insufficient subgroup analysis causes uncertainty, opening routes for decision makers to challenge
- Payers may choose to restrict reimbursement to groups with sufficient analysis and lower uncertainty

- No distinct EUnetHTA guideline on subgroups, no standardized procedure

Priority 4: Subgroup Analysis

- Implied need to analyse any subgroups relevant to value proposition

- Insufficient subgroup analysis causes uncertainty, opening routes for decision makers to challenge
- Payers may choose to restrict reimbursement to groups with sufficient analysis and lower uncertainty

- No distinct EUnetHTA guideline on subgroups, no standardized procedure

Priority 4: Subgroup Analysis

- Clear request: Subgroup analysis for all patient-relevant endpoints required

- Necessity of post-hoc analyses, study not powered for subgroup analysis
- Reimbursement can be rejected for subgroups with uncertainty
- No distinct EUnetHTA guideline on subgroups, no standardized procedure

Priority 4: Subgroup Analysis

Recommendation:

- Use of same subgroups for registration and HTA, standardisation of criteria to form subgroups
- Fixed definitions/wording of indications
- A feasible approach for subgroup evaluation may consider the stability of the subgroup effects across different endpoints, the biomedical plausibility, the pharmacological aspects and the appropriateness of the methods

Priority 5: National Uptake and (no) Duplication of Work

- Conclusion of joint clinical assessment limited to analysis of the relative effects of the technology based on patient-relevant outcomes and the degree of certainty
- Conclusion on added therapeutic value or cost-effectiveness remain on national level
- Further context-specific considerations on national level (e.g. number of patients affected in member states, how patients are currently treated in the healthcare system, costs), ethical, organisational and legal considerations

Recommendation:

- Definition of the process in between the European assessment and the subsequent national appraisal: Requirements (e.g. further analyses) need to be clear early in the HTA process

Priority 6: Early Dialogues and the Parallel Consultation Process

- Chapter II proposed regulation: “The Coordination Group will carry out an annual number of joint scientific consultations based on its annual work program, taking into account the resources available to it.”

Recommendation:

- The proposed scientific advice process must be adequately resourced in order to ensure that advice and joint clinical evaluation are properly linked
- Definition of requirements so that studies can be adequately planned by the MAH

Priority 7: Mandatory Data & Confidentiality

- ➕ Clear definition what data must be submitted, and in what form
- ➕ Confidentiality respected throughout assessment:
  - "Commercial-in-confidence"
  - "Academic-in-confidence"
- ➕ Early-stage safe harbour meetings where issues can be shared
- ➖ Confidentiality relies on whole system behaving as expected, flaws could emerge later

- ➖ Definition of "incomplete" submission files and consequences?
- ➖ No guidance for the submission of documents or publications cited (copyright on European level?)
- ➖ No different requirements for orphan drugs
- ➖ No clear rules on confidentiality of data submitted

Priority 7: Mandatory Data & Confidentiality

- ➕ Clear definition what data must be submitted, and in what form
- ➕ Private sessions held at meetings for confidential information, AIC and CIC both accepted

- ➖ Confidentiality relies on whole system behaving as expected, flaws could emerge later
- ➖ Company must justify each confidential item individually

- ➖ Definition of “incomplete” submission files and consequences?
- ➖ No guidance for the submission of documents or publications cited (copyright on European level?)
- ➖ No different requirements for orphan drugs
- ➖ No clear rules on confidentiality of data submitted

Priority 7: Mandatory Data & Confidentiality

- ➕ Clear data requirements at each stage of the process
- ➕ Once agreed, medicine pricing remains confidential

- ➖ Definition of „incomplete“ submission files and consequences?
- ➖ No guidance for the submission of documents or publications cited (copyright on European level?)
- ➖ No different requirements for orphan drugs
- ➖ No clear rules on confidentiality of data submitted

Priority 7: Mandatory Data & Confidentiality

Recommendations:

- Definition of specific submission requirements for companies (data & documents)
- Definition of AIC/CIC
- Clear process for inclusion of AIC/CIC data
- Provision of an adequate and secure data transfer system, guidance for handling of copyright issues on European level (e.g. provision of hyperlinks to references only instead of handing in copies)

MAP BioPharma
ACCELERATING PATIENT ACCESS

Accelerated Access Collaborative

AAR to AAP and AAC

- Accelerated Access Review (AAR): independent report conducted with the support of the Wellcome Trust, set up late 2014
- Aimed to improve uptake of new medicines into the NHS, final report published October 2016
- Called for improved horizon scanning, a pathway for strategically important innovations, and improved access routes across medtech, diagnostics and digital
- November 2017: UK Government set up the Accelerated Access Pathway (AAP) under the management of the Accelerated Access Collaborative (AAC)
- Aim: to promote widespread NHS uptake of proven, cost-neutral products
- AAC is led by an independent Chair, supported by NICE and NHS England, along with a wide range of other agencies (MHRA, NIHR, DHSC etc)

Accelerated Access Review final report

AAC – First Round products

A first round of 'rapid uptake' products was considered by the AAC in 2018, with successful technologies announced in October 2018:

- **Cladribine** – adult highly active relapsing-remitting multiple sclerosis
- **PCSK9 inhibitors**** – treatment of very high cholesterol
- **HeartFlow**** – coronary CT angiography technology
- **Urolift*** – minimally invasive procedure for prostatic hyperplasia symptoms
- **Placental growth factor (PlGF)-based tests*** to predict pre-eclampsia risk
- **High sensitivity troponin tests*** to exclude myocardial infarction
- **Quantitative faecal immunochemical tests (FIT)** for risk assessment in colorectal cancer

**Supported in Phase I*

***Supported in Phase II*

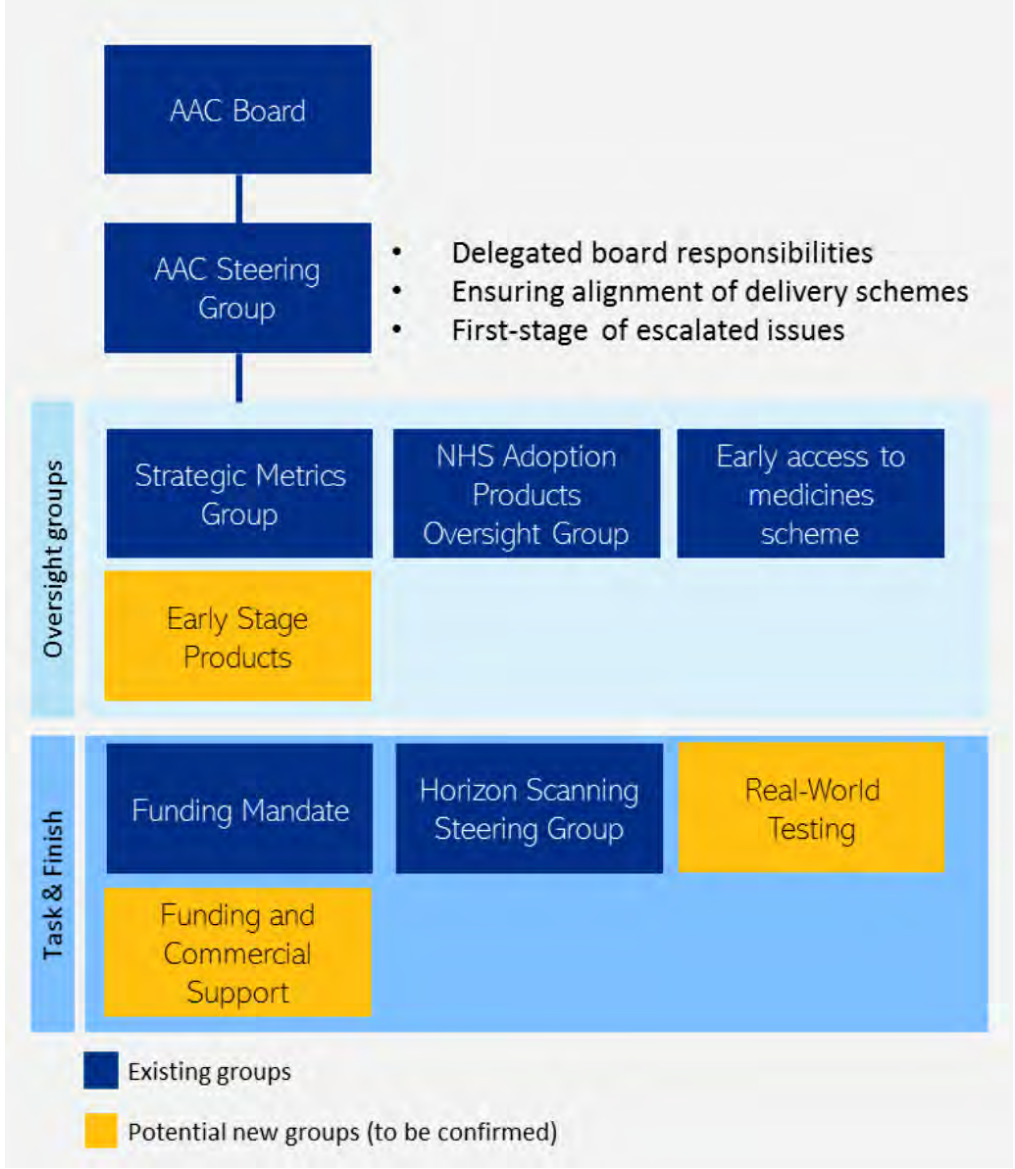
From 2019, AAC is now the umbrella body for health innovation in the UK – more strategic role

AAC to become umbrella organisation for UK health innovation
Current NHS England information on the Accelerated Access Collaborative

AAC – Next steps

At present there are few details on how the expansion of the AAC will be implemented. However, the AAC has committed six priority areas:

- Create a “single front door” to the innovation ecosystem
- Bring together horizon scanning for the best new innovations
- Develop an approach to local and national demand signaling
- Establish globally leading testing infrastructure
- Improve the quality of adoption and spread support for the best new innovations
- Deliver better practical innovation support funding



AAC to become umbrella organisation for UK health innovation
AAC July 2019 board papers published

Thank you!
Any questions?

V.

New Italian Decree on P&R Procedures: upcoming changes

Claudia Garimberti, Regulatory Pharma Net

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

New Italian Decree on P&R Procedures: upcoming changes

EUCOPE - Market Access / Pricing and Reimbursement working group meeting
21st November 2019

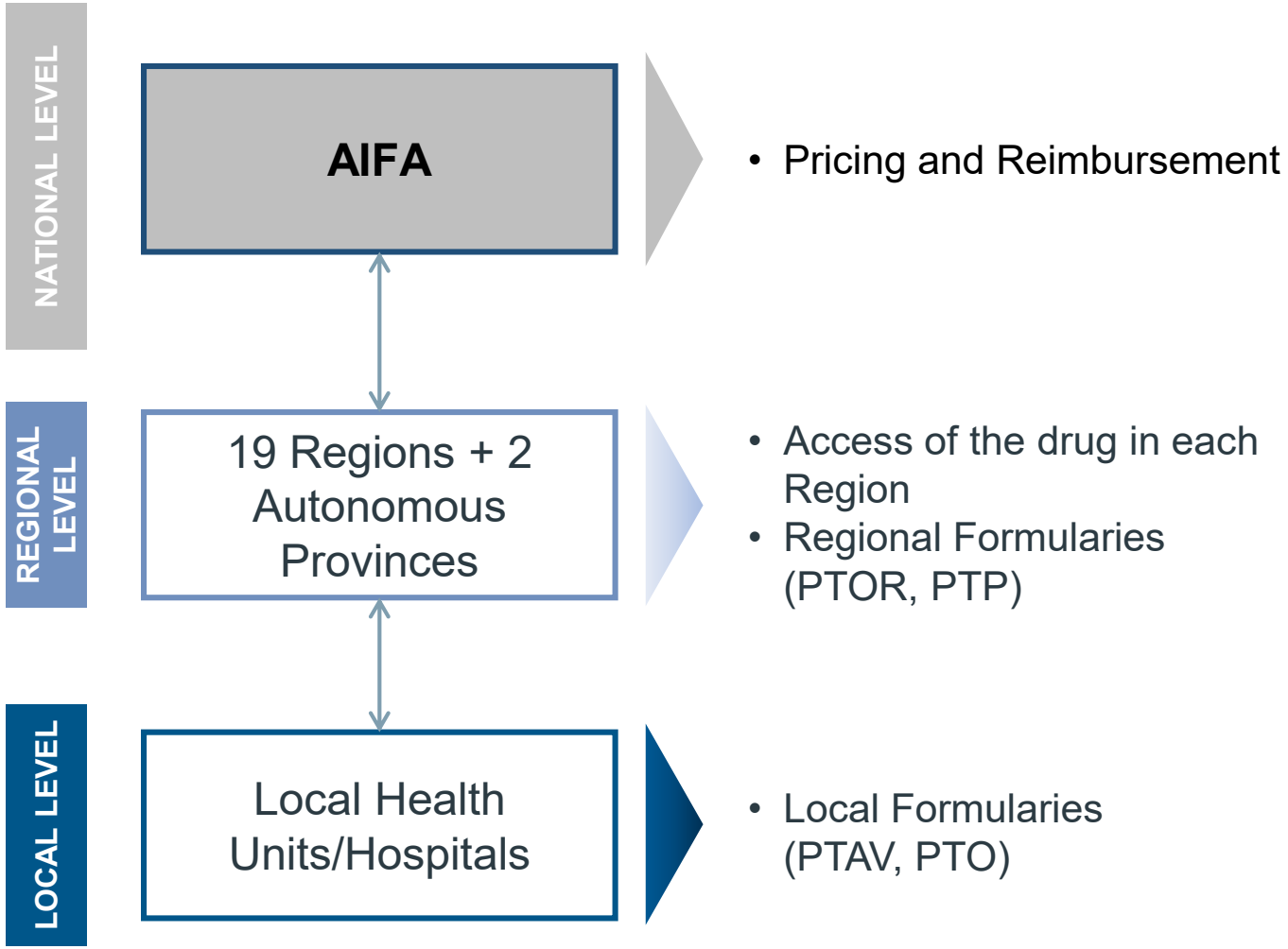
Claudia Garimberti, MSc
Market Access Consultant & Project Manager
Regulatory Pharma Net srl – Italy
Member of Pharos Healthcare Consulting network

Regulatory Pharma Net

PHAROS
YOUR KEY TO EUROPEAN MARKETS

Brief overview of current P&R environment in Italy

Market access in Italy



- Pricing and Reimbursement

- Access of the drug in each Region
- Regional Formularies (PTOR, PTP)

- Local Formularies (PTAV, PTO)

Pricing & Reimbursement dossier in Italy

(Delibera CIPE 2001)

- In Italian language
- Pre-defined structure (template defined in CIPE 2001) as follows

1. DRUG DESCRIPTION
2. CHARACTERISTICS & CLASSIFICATION
3. THERAPEUTIC SPECIFICATIONS
4. PLACE IN THERAPY
5. CLINICAL TRIALS TO SUPPO… …URSEMENT
6. AVAILABLE PHARMA…
7. PRICES IN OT… …HICH THE DRUG IS MARKETED
8. PROP… …R THE ITALIAN HEALTH SYSTEM
9. PHARM… …STUDIES (Budget Impact Analysis)
10. CONCL…
11. REFERENCES

Delibera CIPE is being superseded by a new Decree (text approved on August 1st, 2019 but still to be published).
P&R template is going to change.

National negotiation process

COMPANY
Submission of P&R application

AIFA

HTA Office: Preparation of the report with clinical and economic aspects of the concerned product

Technical-Scientific Commission (CTS) assessment
The CTS evaluates if the reimbursability premises are met and issues an opinion on:
- Place in therapy
- Innovation (if requested by the company)
- Legal status (dispensing condition)

Price & Reimbursement Commission (CPR) assessment
The CPR discusses the application and defines:
- Price
- Other negotiation conditions

AIFA Board of directors (CDA)
Final acknowledgment

AIFA P&R decree publication

Average (**HIGHLY VARIABLE***) timelines on the basis of experience

HTA Office	1-2 months
Technical-Scientific Commission (CTS) assessment	3 months
Price & Reimbursement Commission (CPR) assessment	4 months
AIFA Board of directors (CDA)	1 month
AIFA P&R decree publication	2 months

* timelines of P&R procedures are highly variable, can take from 6 months to even 2 years in some cases

Highlights of P&R in Italy

- There are currently no fixed rules/criteria for deciding the price of drugs or entity of discounts, AIFA will perform an assessment on a case-by-case basis.
- Price references for AIFA usually are:
  - Price of competitors/similar drugs in Italy (AIFA will aim at least for parity price unless it can be demonstrated that the product provides a significant benefit)
  - Price of the concerned drug in the other EU countries (AIFA usually aim for the lowest price in EU)
- On the basis of practical experience, during the price negotiation AIFA always ask for a discount on the proposed price, ranging from 30% up to 70%.
- Pre-submission meeting with AIFA/Commissions not allowed
- Face-to-face meetings with AIFA Commissions are possible and usually are the best opportunity to come to a quick agreement. They are held in Italian language and KOLs can participate with company representatives
- CTS can consult external experts (list of AIFA experts publicly available)
- So far, it has always been possible to keep the amount of the negotiated discount confidential (i.e. not published on the Italian OJ), despite recent discussion on the need for transparency.

Overview of upcoming expected changes

Proposed changes

New decree

- New Decree from the Italian Ministry of Health (represented by Giulia Grillo) and the Ministry of Economy and Finance (represented by Giovanni Tria), concerning the **negotiation of price and reimbursement of medicinal products** was approved by the Italian State-Regions Conference on **1st August 2019**. It will become effective only after the publication on the Italian Official Journal.

- The dispositions of the decree apply to:
  - The negotiation of price and reimbursement of medicinal products authorized through centralized, mutual recognition, decentralized and national procedures;
  - The inclusion of medicinal products in the list provided for by law 648/1996;
  - Some specific categories of C/Cnn medicinal products purchased by NHS facilities for public health needs.

Proposed changes

P&R application

- Scientific documentation showing the **added therapeutic value** in relation with the identified comparator(s) and considering the available therapeutic options
- Economic evaluation
- Commercialisation, reimbursement and sales in other Countries
- Estimated market shares for the following 36 months
- → Self-declaration stating the company's manufacturing capability and ability to manage possible unexpected events that could jeopardise manufacturing and supply
- Cost estimates for the NHS
- Quantification of any public contributions/incentives received for R&D activities
- → Quantification of the economic impact for the NHS consequent to the inclusion of the product in early access schemes as per law 648/96 or law 326/2003
- Quantification of the economic impact consequent to the commercialization of the product in Cnn class
- Information on patent

Proposed changes

Negotiation procedure

- Initiated by the company, but it can also be initiated by AIFA:
  - In case of drugs whose reimbursement leads to a significant impact on the NHS budget
  - In case of drugs that have never been object of previous negotiation
  - In case of drugs whose previous negotiation ended with collocation in C class (not reimbursed)
- The CTS issues an opinion on the clinical value of the product and on the added therapeutic value in relation with the identified comparator(s)
- The CTS may restrict reimbursement. If this causes a significant change to the expected treatable population, the company must submit updated documentation on the basis of the introducted limitations
- Possibility to suspend the procedure only once for a maximum of 90 days
- **The negotiation is negatively concluded if no clinical superiority on the comparator(s) is identified and the company does not provide an updated proposal with a therapy cost equal to or lower than that of the comparator(s)**
- If there is no comparator, the company needs to support the price proposal according to the R&D and manufacturing costs
- As part of the agreement with AIFA, companies are asked to communicate sales data, revenues and patent status every year to AIFA and highlight any changes to what previously defined
- Possibility to agree on new, innovative negotiation models
- The negotiated, agreed price will be the MAXIMUM price for sales to the NHS facilities
- In case of non-reimbursement, AIFA will publish the reasons of the decision

Proposed changes

Negotiation agreement

- Duration: 24 months with automatic renewal if none of the parties asks for a review of the conditions at least 60 days before the natural expiry date of the contract.

- AIFA can start renegotiation at any time:
  - In case of market changes leading to an increased use of the drug or an unfavourable cost/therapy ratio compared to other alternatives
  - In case new efficacy/safety evidence has become available that changes the drug's place in therapy or that significantly resizes the drug's estimatedclinical benefits
  - In case of shortage of the product in the Italian market

NEW

What is going on in Italy?

New Italian government

- 8th August 2019– After some weeks of tension, the Government crisis is triggered
- 29th August 2019 - Law professor Giuseppe Conte got a NEW mandate as Prime Minister from the President of the Italian Republic Sergio Mattarella
- 5th September 2019 - Ministers of the new “Conte” government swear in front of the President of the Italian Republic
- The government rests on an alliance between the 5-Star Movement (M5S) and the Democratic Party (PD)
- New minister of Health: Roberto Speranza (Art 1 party, previously part of the Democratic Party)
- New minister of Economy and Finance: Roberto Gualtieri (Democratic Party)

Changes within AIFA

- 7th November 2019: the new President of AIFA, Domenico Mantoan, took up his position

- New General Director of AIFA:

  By 9th December 2019 a new General Director of AIFA should be appointed, replacing former Director Luca Li Bassi, whose position has NOT been confirmed by new Minister of Health

And the new decree?

- So far, the text of the new decree has not been published in the Italian Official Journal, yet

- After the publication of the decree, new AIFA guidelines should be issued

- Due to the many recent/ongoing changes, delays are expected

There is still uncertainty regarding the future of pharmaceutical governance, but changes are forthcoming, let's talk about it again in a few EUCOPE meetings!

Grazie!

Regulatory Pharma Net srl

Corso Italia, 116 - 56125 Pisa Italy
Phone: +39 050 9134
Fax: +39 050 220 4315

Member of Pharos Healthcare Consulting network

https://pharos-healthcare-consulting.com/

Claudia Garimberti, MSc
Market Access Consultant & Project Manager

c.garimberti@regulatorypharmanet.com

- Phone: +39 050 9134 43

VI.

France: The PLFSS 2020 – implications for the pharmaceutical sector

Alexandre Regniault, FranceBiotech

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Market Access, Pricing & Reimbursement Meeting

Overview of the French bill on the financing of the social security ("PLFSS") for 2020

Brussels, 21 November 2019

Alexandre Regniault

France Biotech, VP / Simmons & Simmons, Partner

Summary

1. Introduction
2. Provisions relating to medicinal products
3. Provisions relating to medical devices

1. Introduction

- Every year in the autumn, the French Parliament discusses a bill on the financing of social security *("PLFSS").* Purpose = to control social and health expenditures
  - **October 29th** : adoption of the PLFSS for 2020 by the French **National Assembly**
  - Discussions before the French Senate initially scheduled between November 12th and 19th
    - ✓ The **French Senate rejected the bill on November 14th** (unanimity) further to declarations of President Emmanuel Macron concerning a "massive emergency plan" for French hospitals
  - Convocation of a joint committee on November 15th – **proposition of a common text discussed:**
    - ✓ before the French National Assembly as of November 25;
    - ✓ before the French Senate on November 30 and December 1st.
- Some of the measures of the PLFSS for 2020 relate to health products (medicinal products and medical devices) and have an impact on pharmaceutical and MD companies

2. Provisions relating to medicinal products

- ❑ Relevance of medicinal products prescriptions – ***Art. 43***
- ❑ Revision of framework for Temporary Authorizations for Use *("ATUs")* – ***Art 30***
- ❑ Strengthening the system for preventing medicinal products stockouts – ***Art. 34***
- ❑ Safeguard clause – ***Art. 4 and 16***
- ❑ Reimbursement of medicinal products from parallel import or distribution – ***Art. 29***
- ❑ Other measures – ***Art. 29***

2. Provisions relating to medicinal products

Relevance of the prescriptions of medicinal products – *Art. 43*

- **Softening of the conditions applicable to the Temporary Recommendations of Use ("RTUs") - deletion of the condition** under which the physician should consider the use of the therapeutic alternative with a RTU as essential to improve the patent's clinical condition
  - Even though a medicinal product with a MA exists in the concerned indication, the medicinal product with a RTU can be prescribed if the medicinal product with a RTU meets the patient's needs
- **New financial penalty for companies in the event the packaging of the medicinal product is not "adapted to the conditions of prescription or therapeutic use"**
  - Purpose = to limit waste and the risk of self-medication or overdose
  - Amount of the penalty = cannot exceed 10% of turnover (excl. taxes) achieved in France for the last financial year concerning the medicinal product
- **Encouraging the prescription of (cost-)efficient products (including biosimilars) during hospital stays**
  - Creation of a specific financial incentive for healthcare establishments provided by health insurance

2. Provisions relating to medicinal products

Revision of the framework for *Temporary Authorization of Use ("ATU")* – *Art 30*

- **Amendment of the conditions for granting a nominative ATU**:
  - A "*clinically relevant efficacy and a significant effect*" for the patient and "*serious consequences are highly likely in the current state of available therapies*" + the drug's efficacy and safety "*are strongly* [added word] *presumed*"
  - Deletion of the condition relating to filing for a clinical trial authorisation
  - Addition of a new condition – requesting an ATU is legitimate if "the patient status, due to his/her vital emergency, requires an immediate treatment by the medicinal product"
- **New set of cumulative conditions for the admissibility** of an application for a nominative ATU
- **Price for a nominative ATU**:
  - No longer freely fixed by the pharmaceutical company → replaced by a compensation determined by the Government
- **Better predictability of clawbacks to be paid by a pharmaceutical company**
  - CEPS *(the French Economic Committee for Health Products)* will be able to negotiate a schedule for the payment of clawbacks covering a period of more than 1 year
  - Minister responsible for social security will communicate the estimated amount at which the health insurance could cover the indication on leaving the ATU

2. Provisions relating to medicinal products

Strengthening the system for preventing stockouts of medicinal products – *Art. 34*

- **Obligation for the MA holder / "*exploitant*" to build up a maximum 4 months safety stock of medicinal products for the French market**
  - The stock must be located on the European territory
- **ANSM may request MAH and *"exploitants"* of "*medicinal products with a major therapeutic interest*" to import any therapeutic alternative in proportion to its share of the needs coverage during the 6 months preceding the stockout**
- **Several new breaches subject to financial penalties**:
  - For example → failure to build up a safety stock of medicinal product
  - Financial penalties ordered by ANSM. The amount may not exceed:
    - For an individual : € 150,000
    - For a legal entity: 30% of the turnover generated during the last financial year, with a maximum limit of € 1 million

2. Provisions relating to medicinal products

Safeguard clause – *Art. 4 and 16*

- **Safeguard clause** = a contribution paid by pharmaceutical companies to “safeguard” the Social Security budget when the turnover (excl. taxes) relating to reimbursable medicinal products in France increases quicker than a rate defined by the law
  - **For the year 2019**: retroactively fixing at 1% of the trigger threshold of the clause *(art. 4)*
  - **For the year 2020**: fixing at 0,5% of the trigger threshold of the clause *(art. 16)*

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

2. Provisions relating to medicinal products

Medicinal products in a context of a parallel import or distribution – *Art. 29*

- **Adding definition of a medicinal product in a context of parallel distribution**
  - A medicinal product (i) with an EU marketing authorization and (ii) imported from another country member or part of the European Economic Area by a pharmaceutical company which is not the MAH, in order to be sold on the French market
- **Parallel distributors exposed to several pharmaceutical taxes** – for example :
  - Safeguard clause
  - Contribution on turnover (excl. taxes) achieved in France and additional contribution for reimbursable medicinal products
  - Contribution on promotional expenses for reimbursable medicinal products
- **Obligations binding on parallel distributors and conditions of marketing in France** specified by Decree
- **Agreement between CEPS and the parallel distributor** to determine the selling price to the public and sales limit prices

2. Provisions relating to medicinal products

Other measures – *Art. 29*

- **Setting a maximum selling price for some medicinal products prescribed within an homogeneous stay group** *("GHS")* (equivalent of DRG)
  - Limitation occurs in 2 situations: *(which can be combined)*
    - In the event of a risk of unjustified expenditure, in particular with regards to a significant increase in the selling prices observed;
    - If the product is particularly costly for some establishments in a predictable way (at a unit price or in view of their overall global)
- **Pharmacies will no longer be able to substitute biosimilars**
- **Pharmaceutical companies will be entitled to file a marketing authorization application for a biosimilar** before the expiry of the patent of the reference biological medicinal product

3. Provisions relating to medical devices

- Creation of a “safeguard” clause – ***Art. 15***
- Expansion of the early access system *(“dispositif d’accès précoce”)* for innovative medical devices – ***Art. 28 bis***
- Strengthening competition in the medical devices sector *(various measures)* – ***Art. 28***

3. Provisions relating to medical devices

Creation of a safeguard clause – *Art. 15*

- ❑ For medical devices covered by the "list in addition" *("liste en sus")* at hospital
  - According to the Government → more than 90% of these expenditures are made up of orthopedic or implantable cardiovascular devices

- ❑ Applicable if the evolution of the expenditure actually reimbursed exceeds **3%** in 2020

- ❑ **Contribution** = pro rata to the amount reimbursed for the products and services that *"exploitant"* operates
  - Contribution cannot exceed 10% of the pre-tax turnover achieved in France

3. Provisions relating to medical devices

Expansion of the early access system – *Art. 28 bis*

- **Where the MD has a CE marking in the considered indication** → companies can apply for transitional reimbursement
  - If no application for inclusion in the list of products and services qualifying for reimbursement *("LPPR")* has been submitted within 12 months following the request: reimbursement is suspended
- **Companies propose the maximum amount of the compensation**
  - MoH can object and submit a counter-proposal to fix the amount of the compensation
  - If this counter-proposal is rejected → the request for transitional reimbursement is deemed to have been abandoned
- **In exchange of transitional reimbursement** → obligation for the companies to ensure the continuity of the treatments initiated
  - In case of breach: financial penalty pronounced the CEPS, which cannot exceed 30% of the turnover (excl. taxes) achieved for the MD during the 24 months before the breach

3. Provisions relating to medical devices

Reimbursement and strengthening competition – *Art. 28*

- **Introduction of a selective referencing procedure *(= a tendering mechanism)***
  - At the initiative of the MoH
  - Selection according to criteria: compliance with technical specifications; quality; proposed pricing conditions; volume of products needed to supply the national market
  - Referencing limited to 2 years *(extensible for 1 year)*
  - Cannot lead to placing a product in a monopoly situation
- **Reimbursement of "reconditioned" MDs if they meet safety conditions**
  - Only MDs for individual use on a list established by Decree *(for example: wheel chairs)*
  - Refurbishment for re-use by another patient
- **Obligation to report sales prices by calendar year and by product to CEPS** → for *"exploitants"* and suppliers to retail distributors
  - In the event of breach or inaccuracy: maximum annual financial penalty of 5% of the turnover (excl. taxes) of the sales of the product concerned

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Thank you

Do you have any question ?

alexandre.regniault@simmons-simmons.com

VII.
Further Country Updates

France

Sébastien Pradeau, Fieldfisher

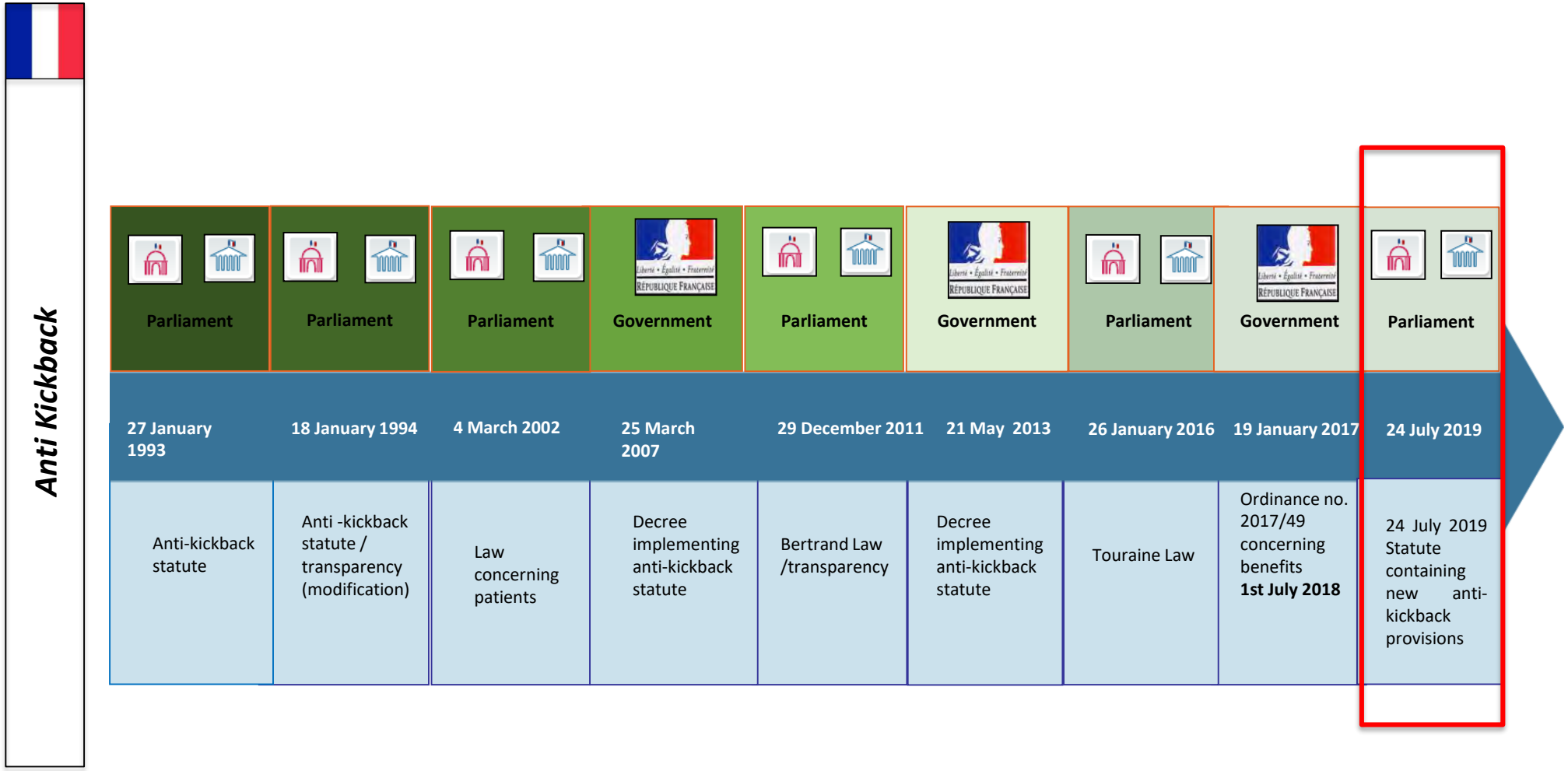
fieldfisher

Compliance & Life Sciences in Europe:

UPDAPE : main principles governing transparency and anti-kickback in France

Sébastien Pradeau, Of Counsel – Paris Office

1. On which basis does France regulate transparency and anti-kickback?



1. On which basis does France regulate transparency and anti-kickback?

Anti Kickback

Prohibited benefits:

- benefits in cash
- benefits in kind
- direct or indirect
- Students hospitality
- Hospitality to students associations (Grant)
- Hospitality to professional national councils

(24 July 2019 statute, art 77)

Are not considered as benefits in kind and are thus allowed:

- Fees
- Indemnities
- Expenses
- Royalties or sale of IP
- Commercial agreements (rebates, etc.)
- Minor benefits of negligible value
- Grant/donations of HCPs or students

1. On which basis does France regulate transparency and anti-kickback?

Anti Kickback

- Minor benefits of negligible value were defined in a draft decree of November 2019. Its implementation date is yet unknown. The thresholds are the following:
  - Non-scheduled meals and snacks related to the recipient's profession: €30 ; no more than twice a year per HCP
  - Book, manual or magazine, including subscription, relating to the practice of the recipient's profession: €20 ; up to a maximum of three per calendar year per HCP
  - Samples of health products for health purposes or demonstration copies: €20 ; up to a maximum of three per calendar year per HCP (exception when it is used for educational purposes for HCPs or patients)
  - Office supplies: €20 in total per calendar year per HCP
  - Other product or service that relates to the practice of the recipient's profession: €20 in total per calendar year per HCP

1. On which basis does France regulate transparency and anti-kickback?

Changes in France (Anti Kick Back)

Contract

Below a threshold (to define by the law)

Either declaration

To the relevant authority
(e.g.: medical council for doctors)
8 days ?

Issuing of possible recommendations by the authority concerning the contract

Above a threshold (to define by the law)

Or authorisation

To the relevant authority
(e.g.: medical council for doctors)
3 months ?

Authorisation or refusal

Challenging if refusal?

1. On which basis does France regulate transparency and anti-kickback?

Anti Kickback

Draft decree's authorisation thresholds for medical professions, medical auxiliaries, and other professions as mentioned 1° article L. 1453-4 of the FHPC

Net salary, compensation and expenses for research, scientific evaluation, advice, provision of services or commercial promotion activities	€200/hour up to a maximum of €800 per half-day and generally inferior to €2.000
Grants and donations intended exclusively to finance research or scientific evaluation activities	€5.000
Hospitality during professional or scientific events or products/services promotion	€150 per night, €50 per meal, €15 per snack. Up to a cumulated amount of €2.000 including travel costs to go to the meeting Registration fees can be assumed in addition to these threshold and must be declared when higher than €1.000
Financing or participation in the financing of professional training or development	€1.000

1. On which basis does France regulate transparency and anti-kickback?

Anti Kickback

Draft decree's authorisation thresholds for students as defined in 2° art. L. 1453-4 FPHC

Net salary, compensation and expenses for research, scientific evaluation, advice, provision of services or commercial promotion activities	€80/hour up to a maximum of €320 per half-day and generally inferior to €800
Grants and donations intended exclusively to finance research or scientific evaluation activities	€1.000
Financing or participation in the financing of professional training or development	€1.000

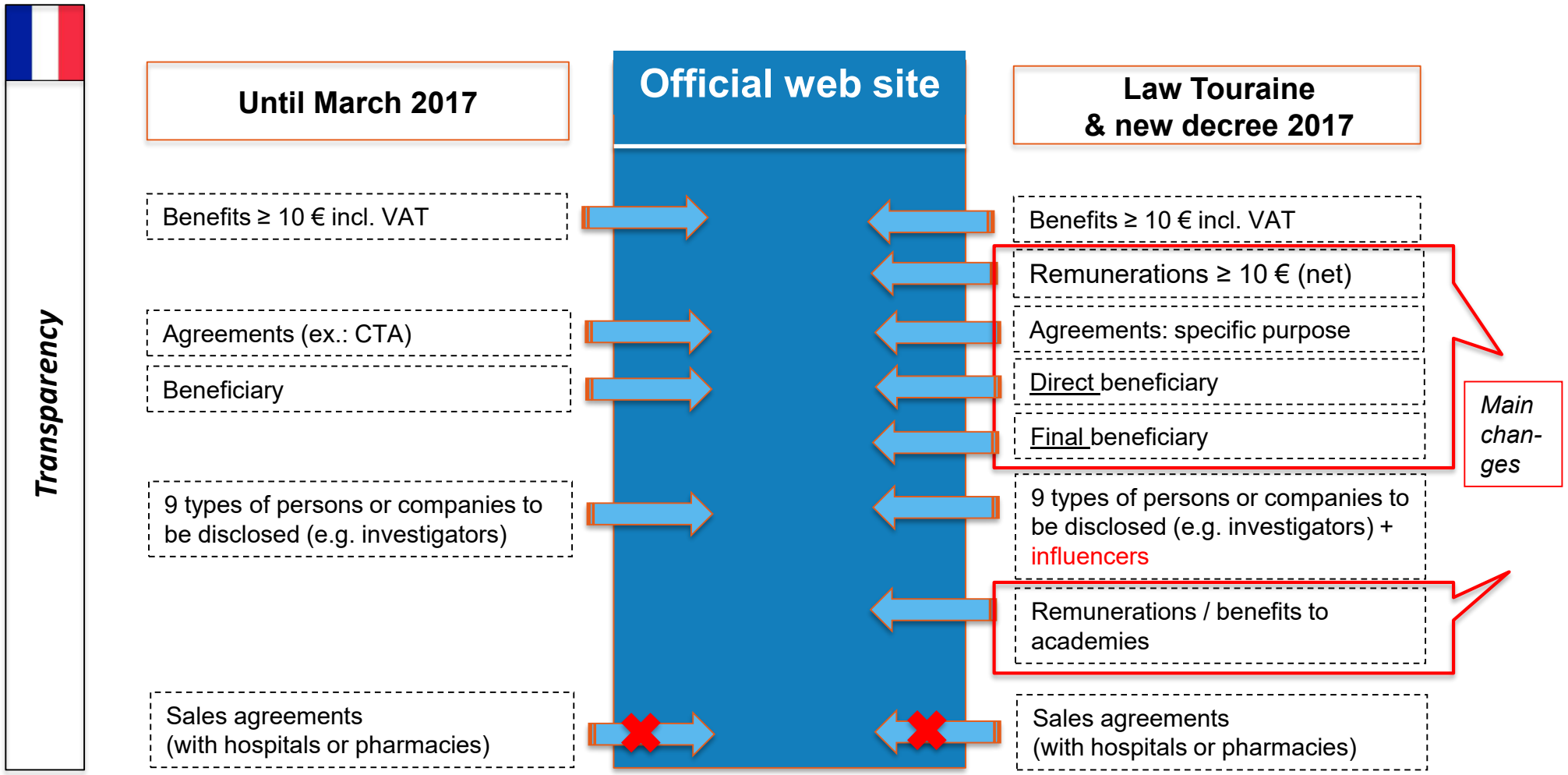
1. On which basis does France regulate transparency and anti-kickback?

Anti Kickback

Draft decree's <u>authorisation thresholds</u> for grants and donations to associations as defined in 3° art. L. 1453-4 FPHC

Grants and donations intended exclusively to finance research or scientific evaluation activities	**€8.000**
Grants and donations with another aim related to health	**€1.000**
Grants and donations to associations declared to be of public utility, including those intended to exclusively finance research or scientific evaluation activities	**€10.000**

1. On which basis does France regulate transparency and anti-kickback?



Do you have any questions?

fieldfisher

Sébastien Pradeau, Of-Counsel

Sebastien.Pradeau@fieldfisher.com
+33 1 70 37 81 29

COCIR

VIII.
AOB / End of Meeting

Chairs

Thank you for your attention!