Refueling the innovation engine in vaccines

NVAC Discussion
7 June 2016

McKinsey&Company

McKinsey is currently undertaking an effort to understand the challenges and solutions to vaccine innovation

Questions:

Are we **progressing to address unmet needs** in vaccination globally?

If not, **what are the challenges**?

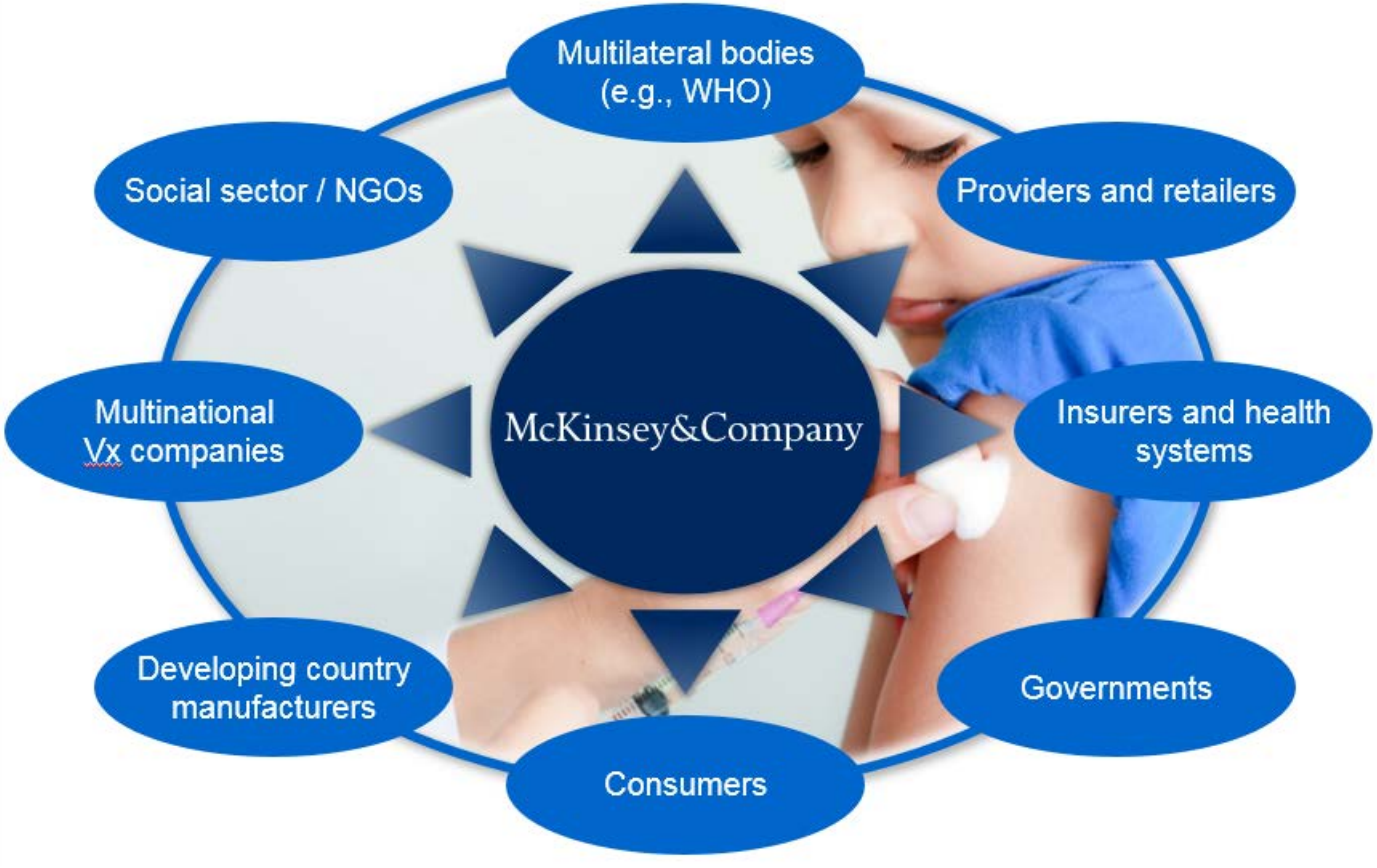
What are the **solutions to accelerate** needed innovations and create a sustainable industry?

Early insights:

- **Unmet needs in vaccine-preventable disease persist**
- **On the surface, the industry looks to be thriving**
- **However, a closer look suggests challenges**
- **Three barriers are limiting innovation**
- **Targeted economic and technical solutions are needed**

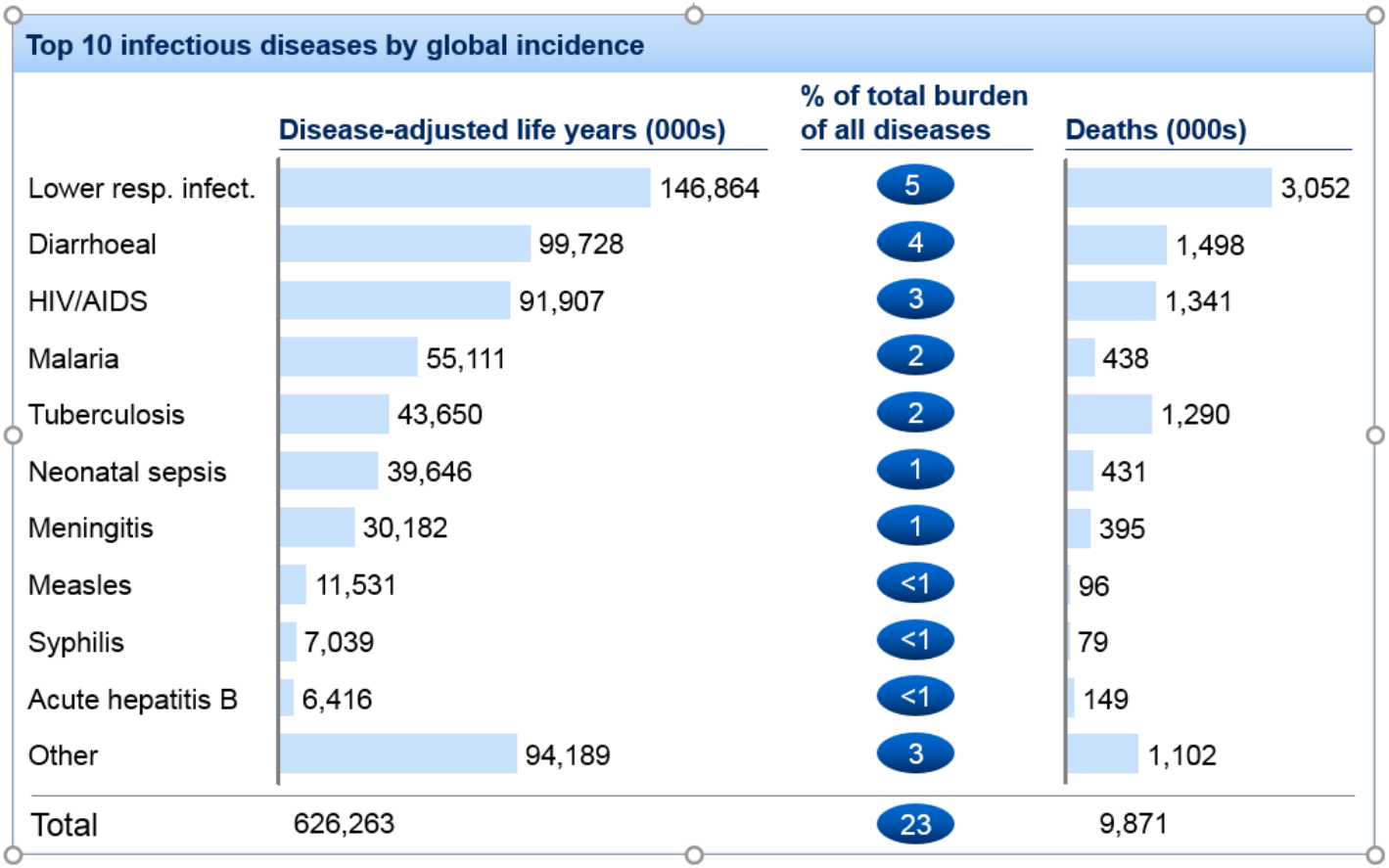
SOURCE: McKinsey

These perspectives informed by interactions across vaccine space



There are persisting unmet needs in vaccine-preventable disease that call for improved and new product innovations

Vaccine-preventable diseases today cause >600 million DALYs and make up ~23% of the burden across all diseases



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SOURCE: WHO; 2012 DALYs

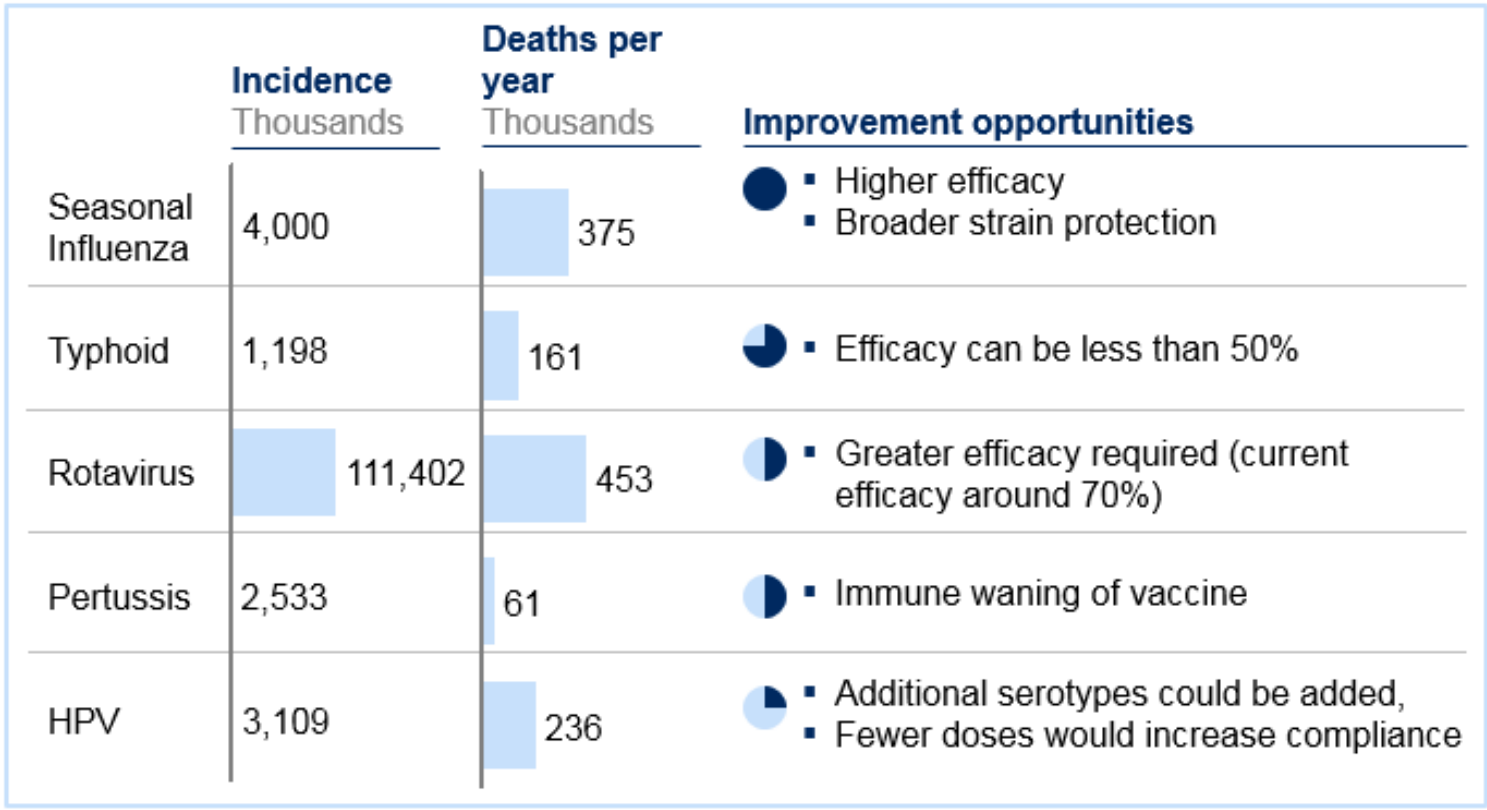
These unmet needs call for innovations on both existing vaccines and new products

	Examples
1 **Improve existing vaccines** to address unmet needs e.g. in efficacy, duration of protection, ease of use	▪ Improved antigens e.g. – Pertussis – Flu – Measles ▪ Combination vaccines ▪ Delivery technologies
2 **Create new vaccines** to address diseases for which burdens persist and prophylaxis can play an important role	▪ HIV ▪ RSV ▪ Ebola

SOURCE: McKinsey

1 Several existing vaccines still fall short on fully addressing public health needs

High Low



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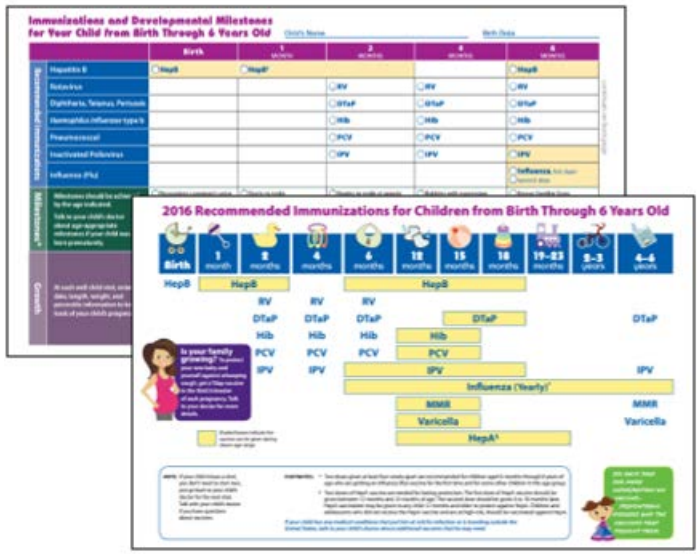
1 Vaccines where there is a need to improve overall efficacy/effectiveness of the vaccine
2 Vaccines which are only against a subset of serotypes/strains, or where the pathogen mutates frequently
3 Vaccines where the formulation needs to be changed or the doses need to be reduced (e.g., moving from 3 to 1 doses)

SOURCE: IHME; WHO

1 Increasing complexity in patient diversity and program delivery also raises the need for product improvements

Pediatrics

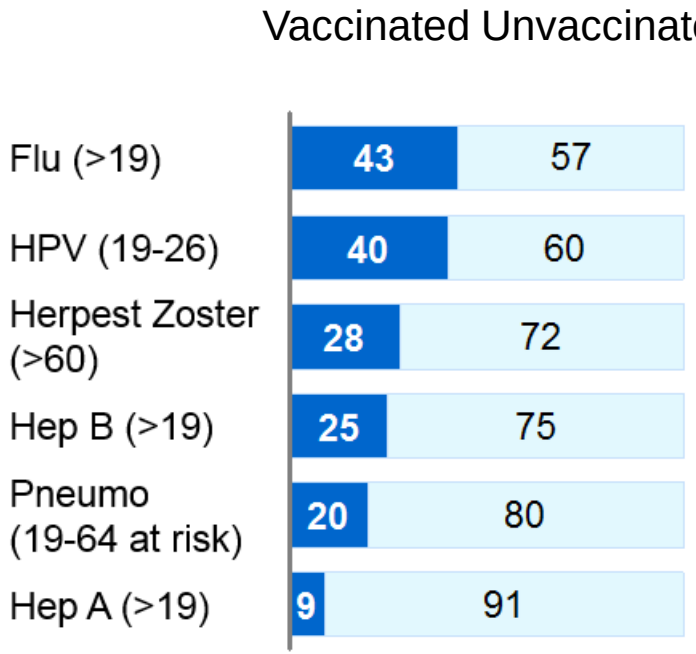
Extensive immunization schedule



How can innovations make the schedule simpler and more efficient for parents? E.g. through more combination vaccines?

Adult

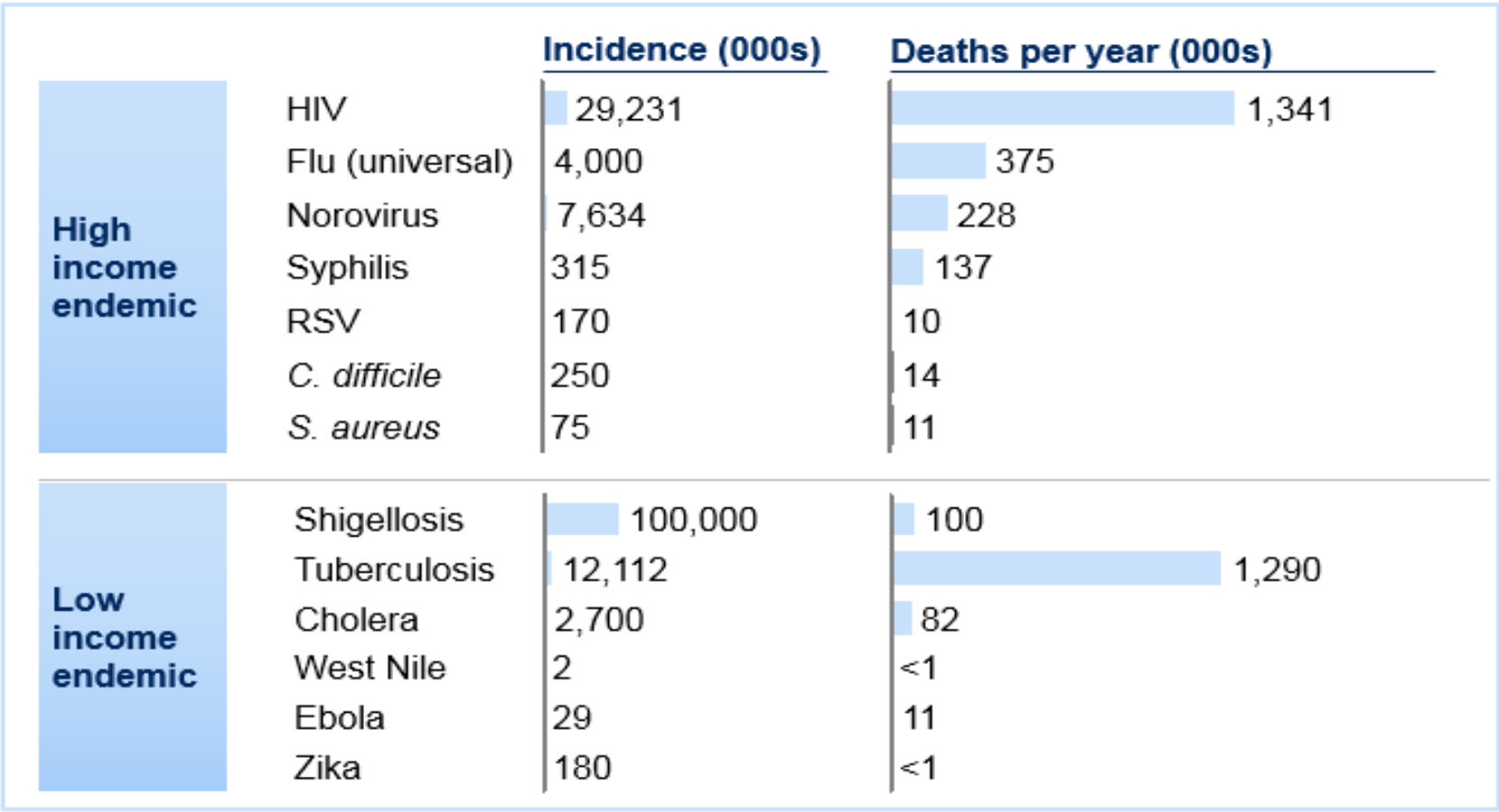
Limited penetration and uptake



What innovations can get vaccines to more adolescents, adults, expecting mothers, and elderly? E.g. new delivery devices?

SOURCE: CDC

2 There are several high-burden and high-priority diseases for which we do not yet have vaccines on the market



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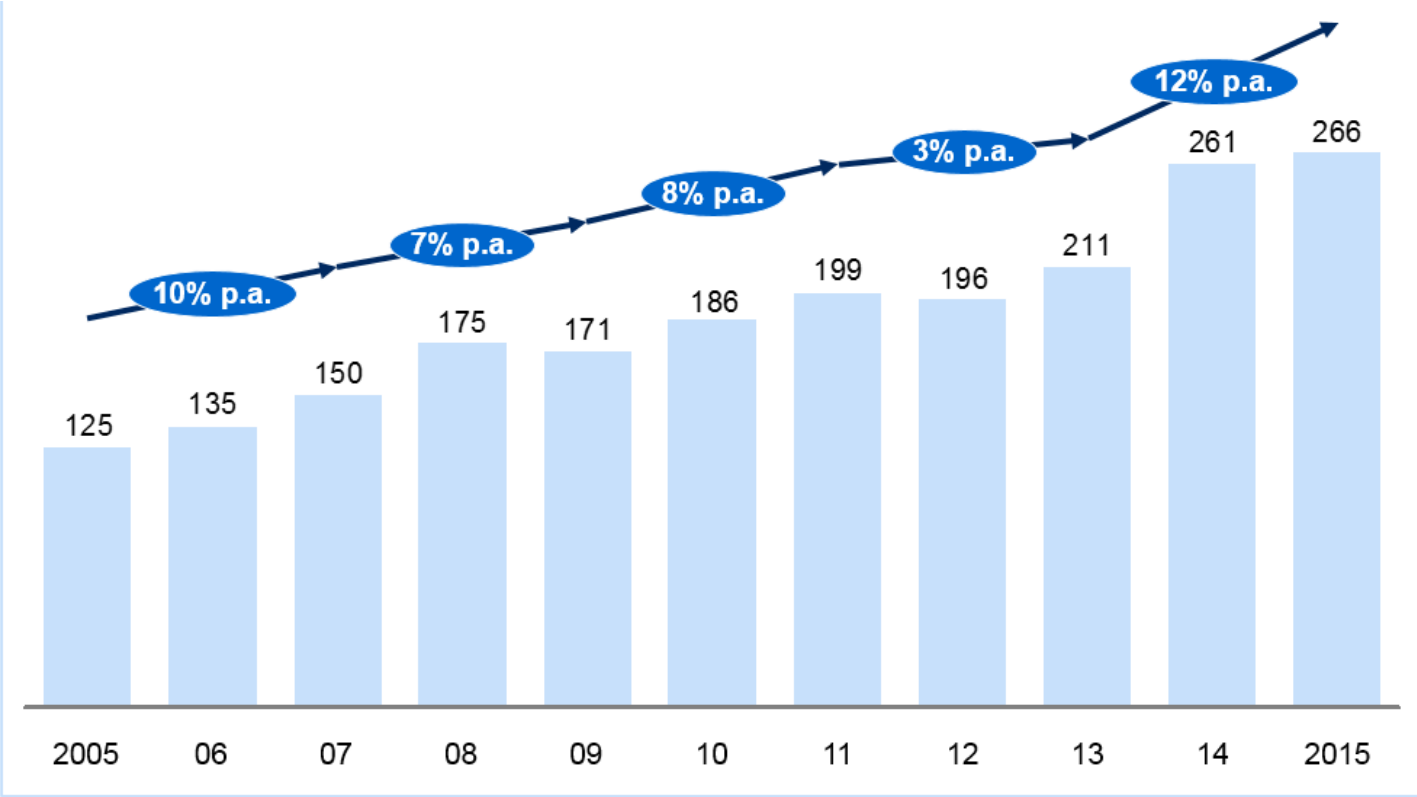
SOURCE: IHME; WHO, CDC

At first glance, the industry looks to be thriving – pipelines are robust, and revenues are growing

The vaccine product pipeline has been growing at a healthy rate over the last decade

Number of vaccines in development globally (phase I to pre-registration), 2005-15



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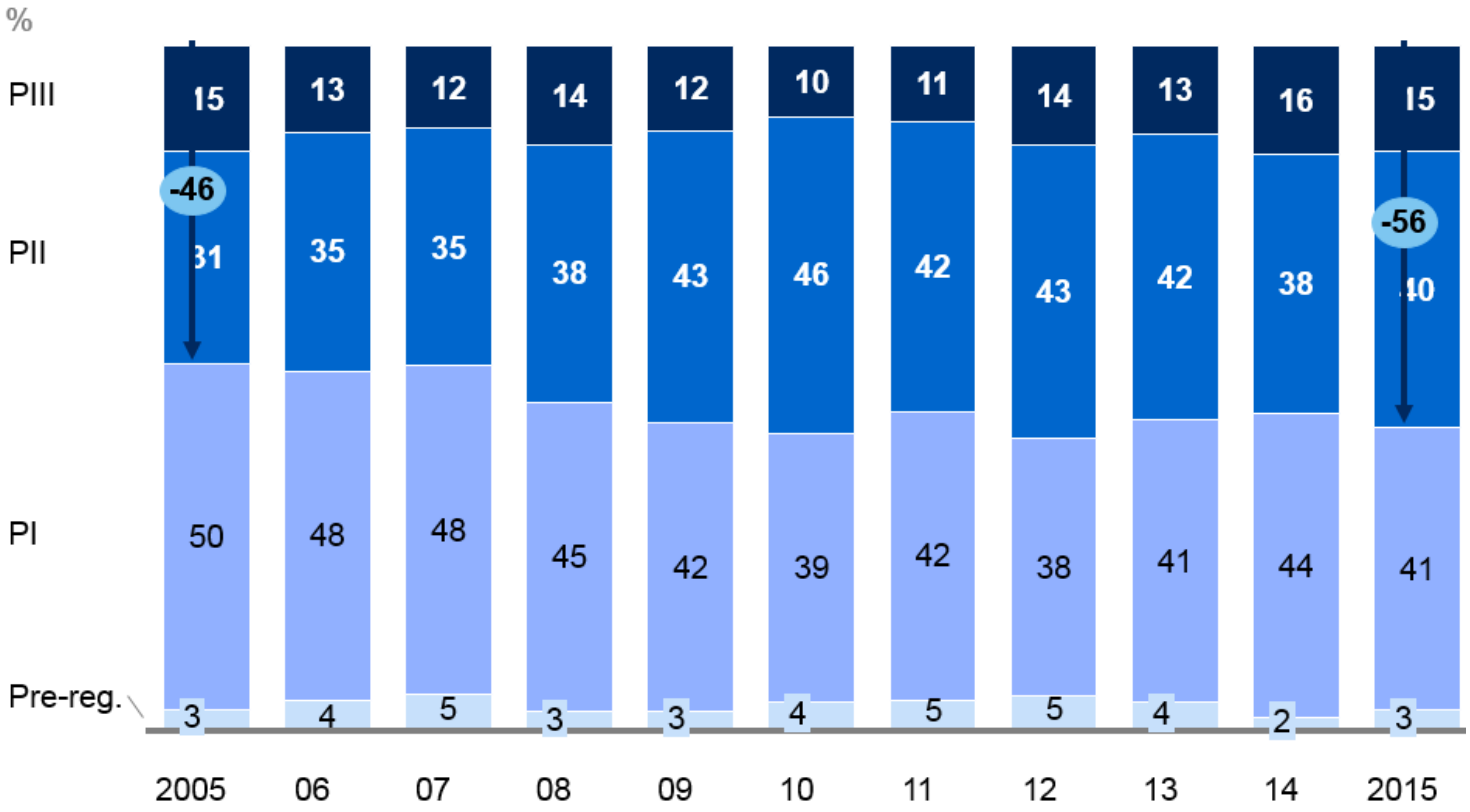
SOURCE: Pharmaproject2015

We have a higher proportion of late stage vaccine candidates now than we did in 2005

Share of candidates in each stage of development 2005-15



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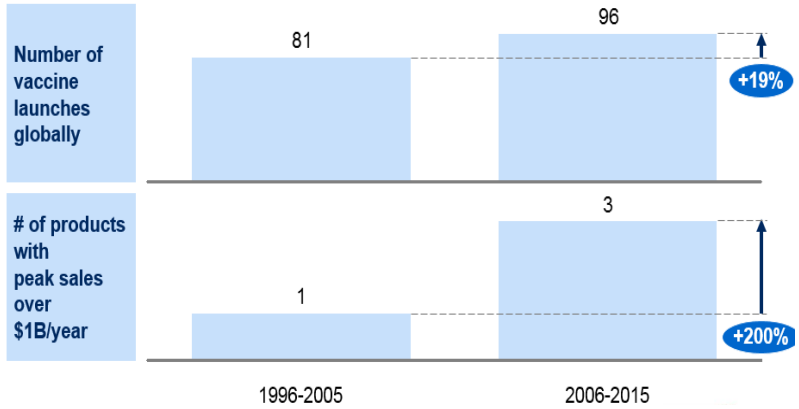
SOURCE: Pharmaproject2015

As the pipeline has continued to grow, so have the number of new product launches worldwide

Year	Number of vaccine launches globally	# of products with peak sales over $1B/year	Percentage
1996-2005	81	96	+19%
2006-2015	1	3	+200%



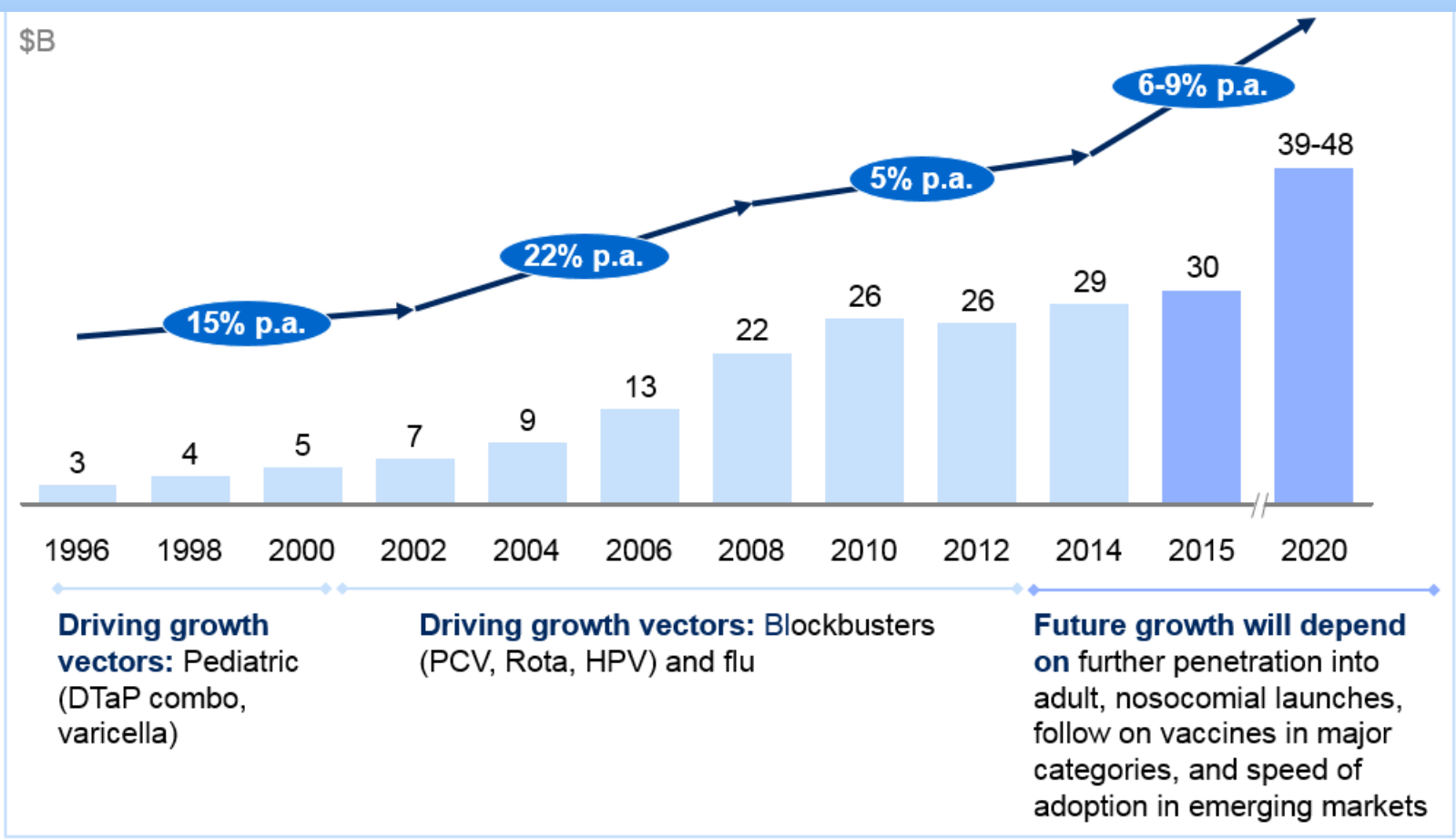
SII RABIVAX
VAQTA
Prevnar
Every Dose Matters.
MENINGITEC
Shanvac - B
重组(CHO细胞)乙型肝炎疫苗
True Pentavalent vaccine
Easyfive
Easy solution for 5-in-1 protection
Menactra

GARDASIL
ZOSTAVAX
Zoster Vaccine Live
ZOSTER PREVENTION MADE POSSIBLE
Prevenar 13
BEXSERO
IXIARO
RotaTeq
Rotarix
Cervarix
Human Papillomavirus Bivalent (Types 16 and 18) Vaccine, Recombinant
Trumenba
Meningococcal Group B Vaccine
MENVEO

SOURCE: Evaluatepharma, Company websites

Global industry growth has also kept pace, and is expected to continue to grow at close to double-digits through 2020

Global vaccine sales, 1996-2020



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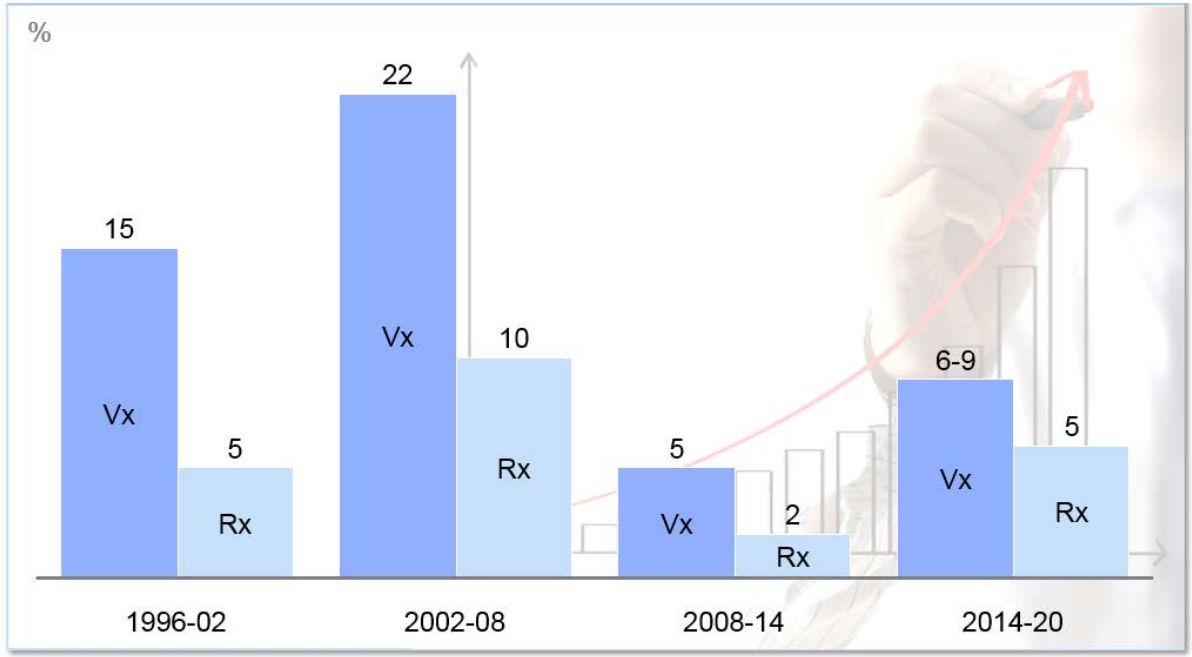
SOURCE: Evaluatepharma February 2016

Growth in the global vaccine market has and will continue to out-pace that of the rest of the pharma industry

Annual growth rates

Year	RX	VX
1996-02	5	15
2002-08	10	22
2008-14	2	5
2014-20	5	6-9

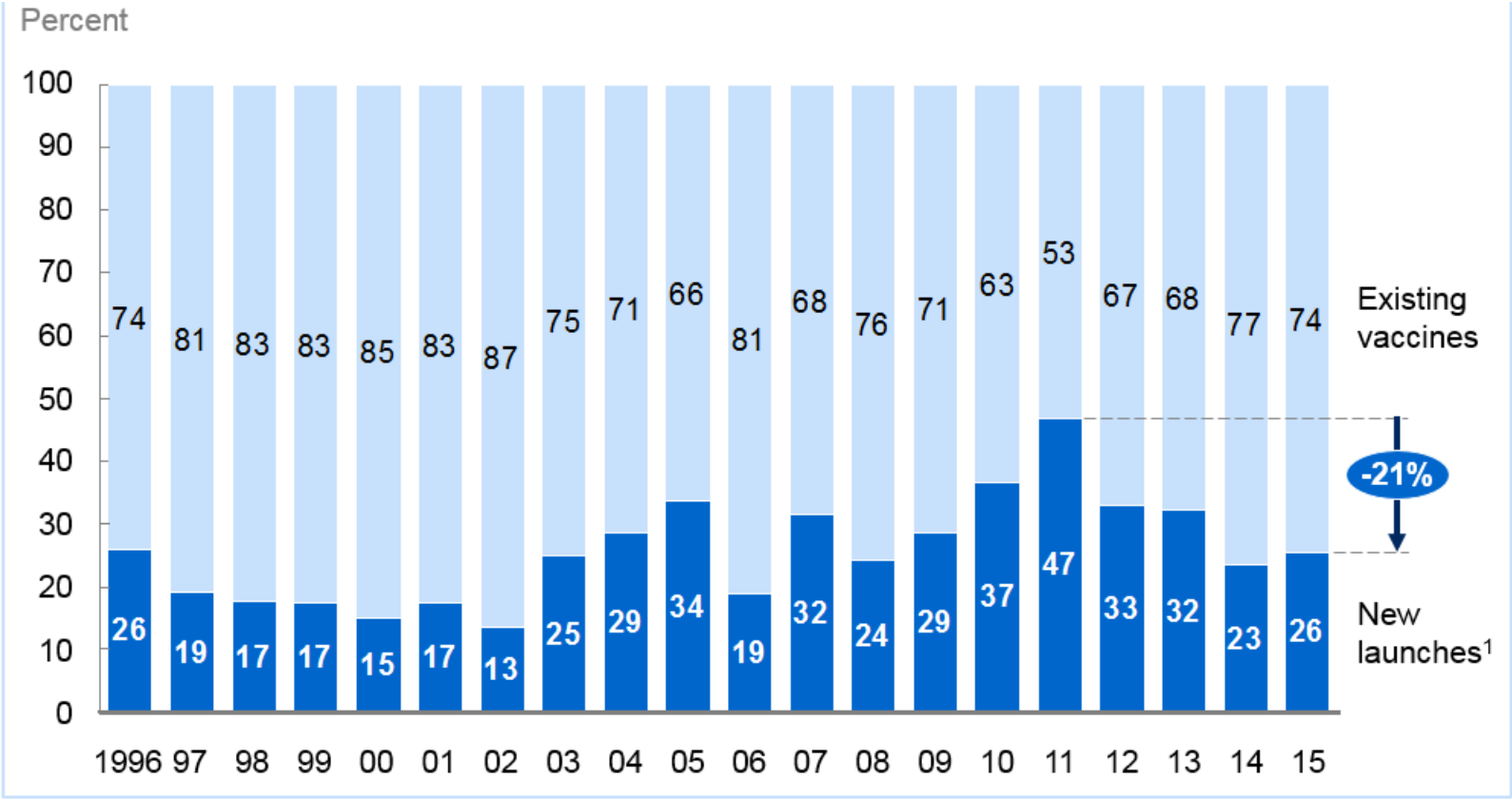


SOURCE: Evaluate Pharma February 2016

However, looking closer, signals suggest that there are real challenges to innovation

The majority of the market growth has come from existing vaccines rather than new launches

Global vaccine sales, 1996-2015



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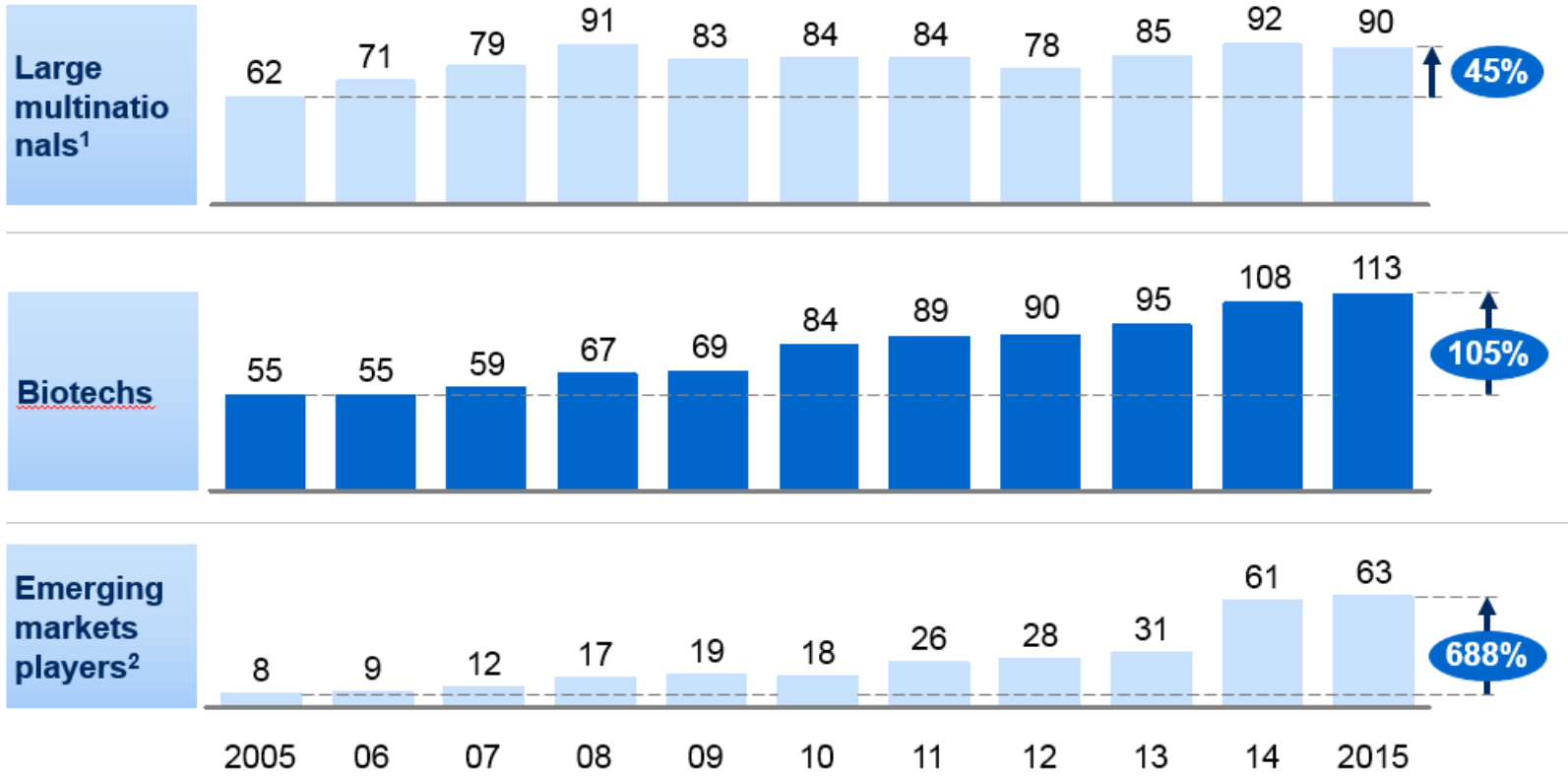
1 Defined as any vaccine that received FDA approval in the proceeding five years

SOURCE: Evaluatepharma Feb 2016

Biotechs are driving most early stage programs, but facing limitations in the absorptive capacity of big pharma to take innovations to market

Number of vaccine development programs globally



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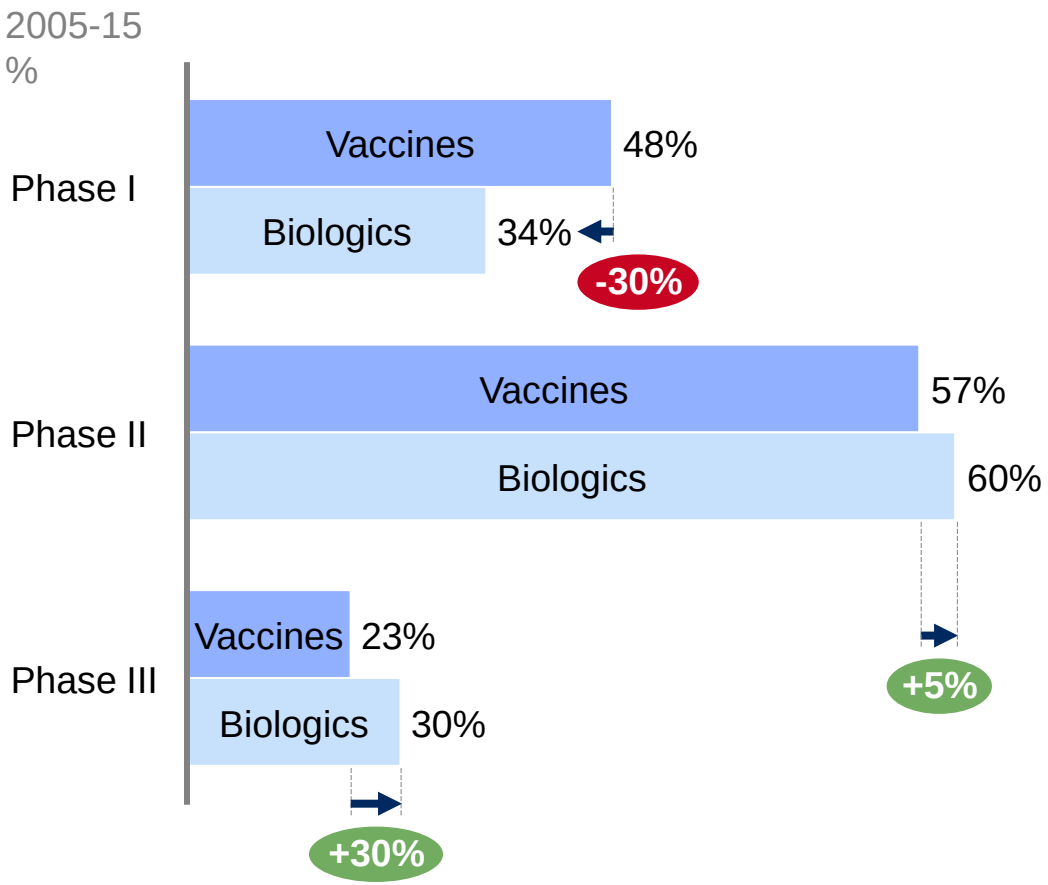
1 Referring to Pfizer, Merck, Sanofi, GSK and Novartis (pre-2014), Takeda, CSL, Abbott, J&J, AZ, Baxter, including in-licensed products
2 Including Japan

SOURCE: Pharmaproject 2015

Vaccine candidates are killed earlier than biologics, and we get fewer shots on goal

Attrition rate of programs



Examples of discontinued programs

GSK stops genital program after PhIII failure due to no efficacy to HSV-2, only to HSV-1

Genocea Bio stops GEN-004 program at PIIa (efficacy is not statistically significant)

NIAID discontinues HIV candidate after HVTN505 trial (PIIb) because of no efficacy

AERES discontinues MVA85A, a TB candidate, due to low efficacy at PII/III trial

Attrition in Phase I drive by 3 factors: (1) Limited funding, especially for Phase II (2) biologic complexity of candidates (3) evidence that identifies unviable candidates earlier than for biologics

SOURCE: Pharmaproject, McKinsey analysis

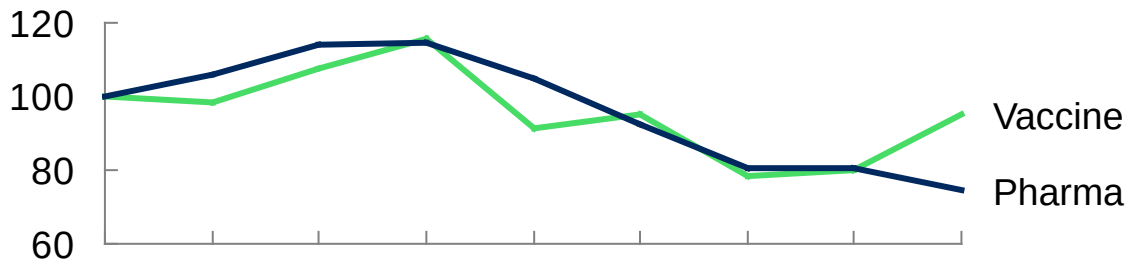
Three factors are challenging the underlying business model for vaccines innovation

Vaccines businesses are on a trend of declining profitability, placing increasing pressure on the economics

Indexed BU-level operating margin, 2007-15 2007 margin as 100

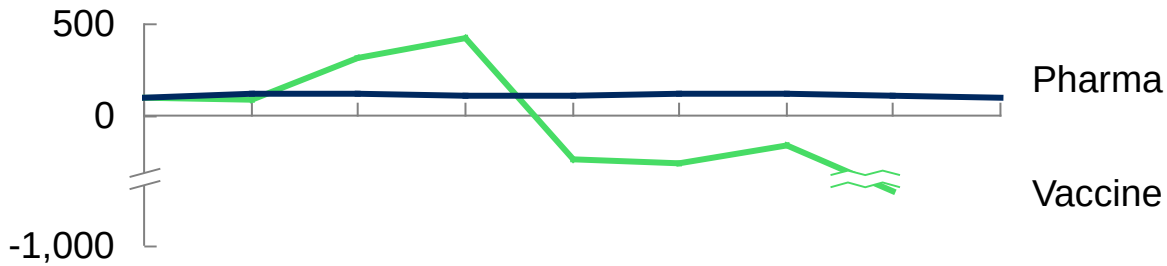
Pharmaco 1

- Both vaccines and pharma margins declining



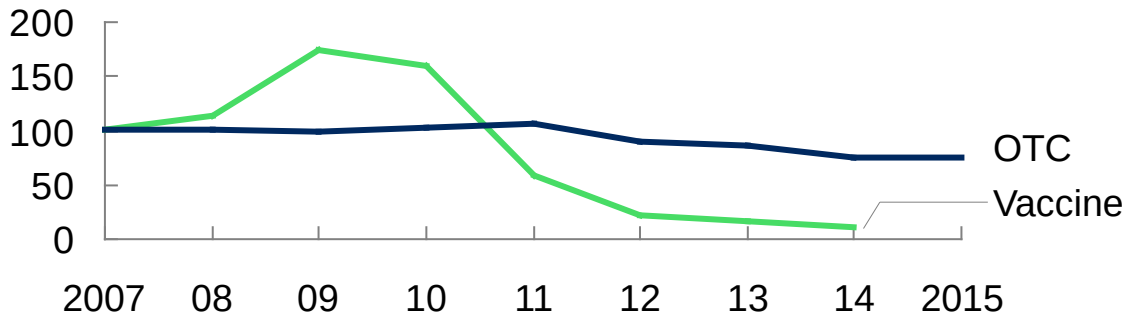
Pharmaco 2

- Pharma remained stable, while vaccines fell of cliff



Pharmaco 3

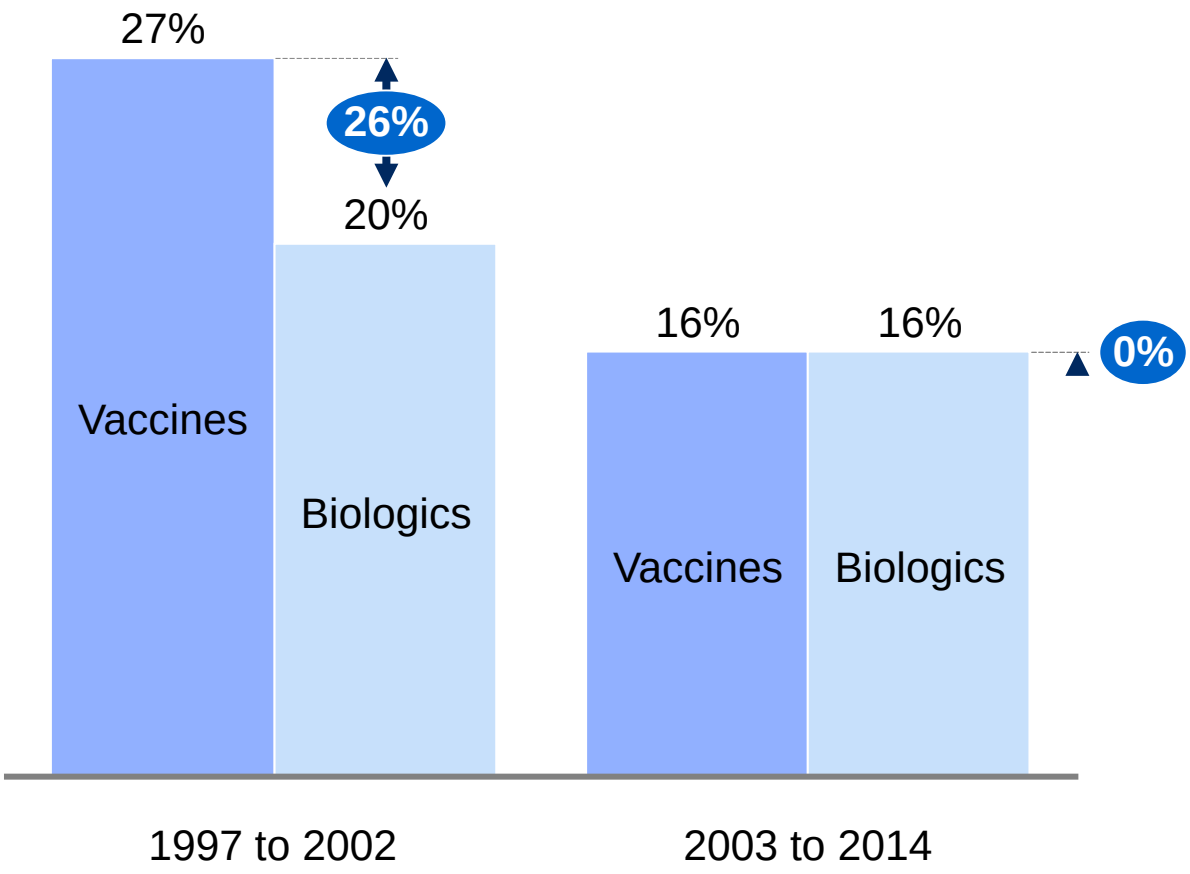
- Pharma remained stable, while vaccines declined significantly



SOURCE: Company annual reports

Relative vaccine economics have been changing, with lower returns on investment as success rates converge with biologics

Success rate of products from Phase I to launch



- Vaccines have peak revenues of up to low digit billion (e.g. the blockbuster Prevnar13 - $6B, Gardasil - $2B)
- Biologics conversely can have peak revenues of up to double digit billion (e.g. Humira $19B, Enbrel $13B)
- The convergence of success rates in vaccines and biologics makes vaccines less attractive for investment

SOURCE: Pharmaprojects 2013

We see three potential drivers challenging the business model

1 **Underlying R&D and manufacturing requirements** for vaccines are becoming more demanding and creating a higher hurdle rate for innovations

2 **Commercial potential of new innovations** is uncertain, given open questions on commercial models, regulatory and policy approvals, and patient accessibility

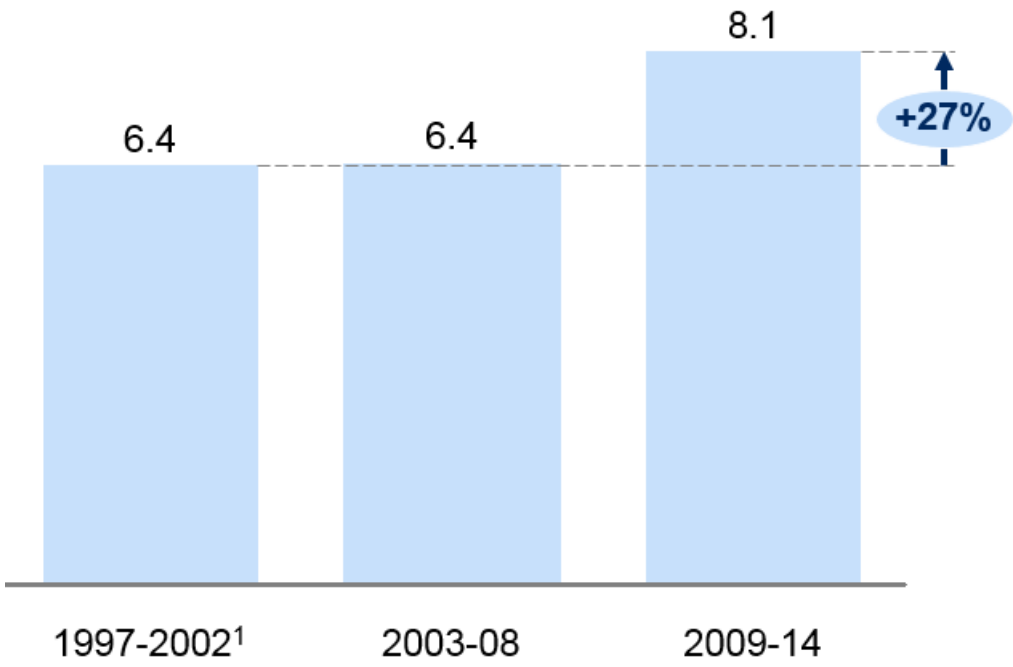
3 **Technical challenges are reducing the probability of success and elevating the investment risks** associated with product innovations

SOURCE: McKinsey

1 Time to market for vaccines is increasing, implying increasing costs and creating potential economic uncertainty

Time from Phase I to launch

Average time in phase for successful phases, years



- Vaccine trials are getting longer. This driven both by more advanced technology, and increased Regulatory hurdles
- Recruiting participants is becoming more difficult, especially as trials grow larger (e.g., from variable prevalence of diseases or going head to head) which increases the time to launch

1 Anti-infective vaccine products including prophylactic vaccines and recombinant vaccines as defined by Pharmaprojects. Note that recombinant vaccine group may contain some therapeutic vaccines.

SOURCE: Pharmaprojects 2013

1 Shortages, recalls and other manufacturing challenges and required investments add additional risks to the economics

Selected examples

SANOFI PASTEUR	Pentacel shortage	2012 – ongoing
gsk GlaxoSmithKline	Varicella recall and shortage	2014
MERCK	West Point compliance (MMR, varicella, HepB)	2008 - 12
SHANTHA A SANOFI COMPANY	PQ withdrawal (penta, cholera)	2012 – 14
Panacea Biotec Innovation in support of life	Pentavalent PQ withdrawal	2011 - 13

SOURCE: Press search

2-3 Commercial attractiveness and technical feasibility vary by vaccine and vaccine archetype

Commercial attractiveness

	Assessment of commercial attractiveness
Volume	▪ Is there a large population at risk? Does the disease have a high incidence?
Price	▪ Are people or payors willing to pay for the vaccine? ▪ Are there other vaccines or treatments on the market?
Ability to access market	▪ Are there existing commercial channels? ▪ If not, is there a way to make the commercial access work?

Technical Feasibility

	Assessment of technical feasibility	Example of *challenging* vaccine
Natural immunity	▪ Does the pathogen trigger antibody response and confer immunity post-infection?	▪ HIV
Adaptability of pathogen	▪ Is there high antigenic variability or does the pathogen mutate/ evolve quickly?	▪ Universal flu
Strength of immune response	▪ Can an adequate immune response be achieved? Are adjuvants necessary and do they work?	▪ Pertussis
Clinical trials	▪ How easy are clinical trials (i.e., finding population at risk, diagnosing, prevalence of disease)? Is there a correlate of protection?	▪ C. Diff

SOURCE: McKinsey

The low-hanging fruit no longer exists – needed innovations will be less commercially attractive and less technically feasible than in the past

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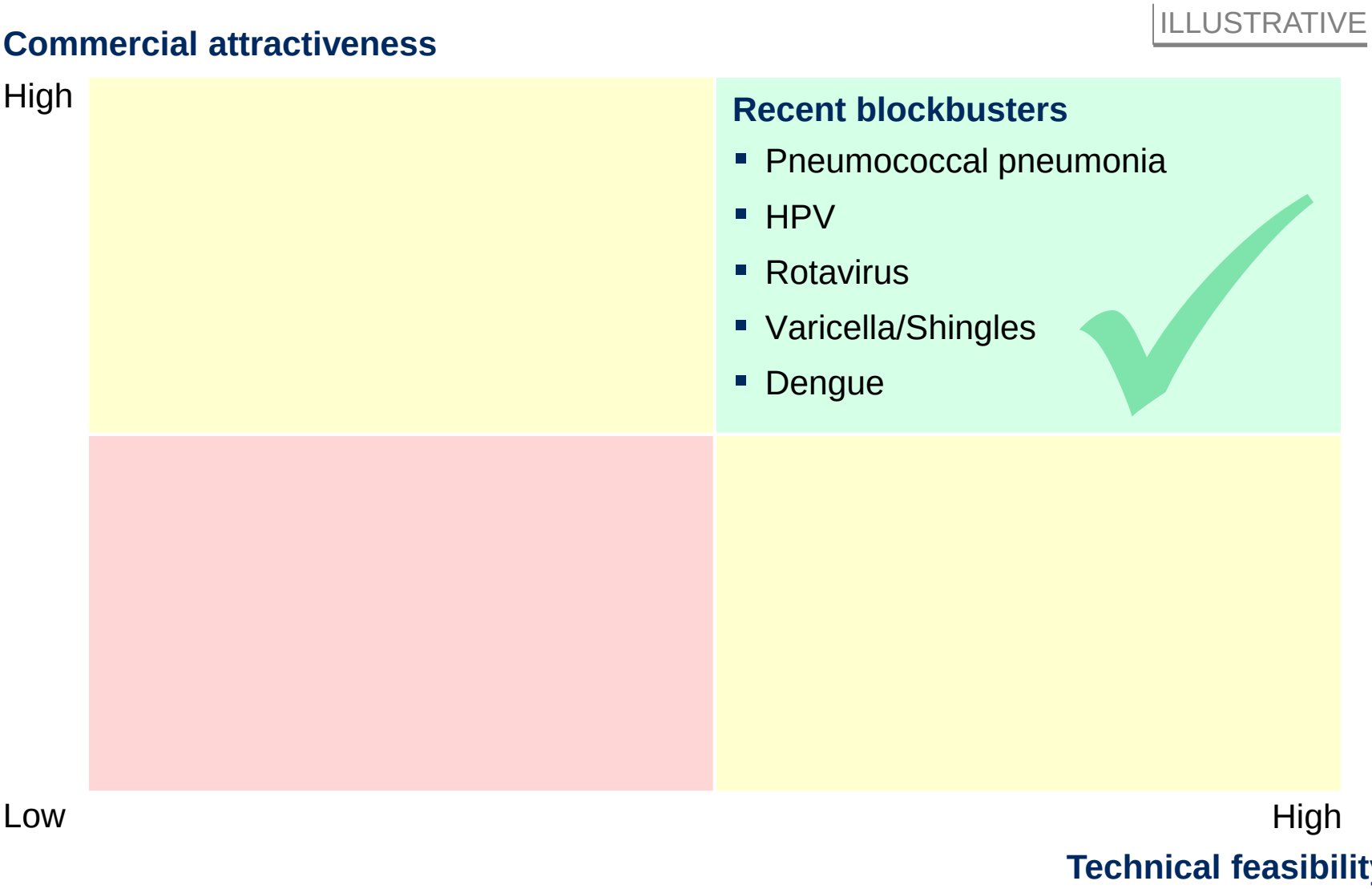

SOURCE: McKinsey

Five vaccine archetypes carry distinct profiles for commercial potential and technical feasibility

Archetype	Description	Examples
1 **High income + nosocomial**	▪ Moderate technical feasibility ▪ Nosocomial: market potential high, but commercial model/indication unclear ▪ Others: Moderate commercial potential and mix of commercial models	▪ C Diff ▪ Staph ▪ Norovirus
2 **Incremental improvements**	▪ Uncertain commercial value for incremental improvements, especially on price ▪ Moderate-high technical feasibility	▪ Pertussis ▪ Typhoid ▪ Measles
3 **Emerging threats**	▪ Limited reliable and large-scale commercial potential e.g. vaccine only stockpiled ▪ Moderate technical feasibility	▪ Ebola ▪ Zika ▪ MERS
4 **Potential blockbusters**	▪ High commercial potential – large burden of disease and large potential patient pools ▪ Low-moderate technical feasibility	▪ HIV ▪ Improved/universal Flu ▪ RSV ▪ Hep C
5 **Low income**	▪ Moderate commercial potential and mix of commercial models ▪ Low-moderate technical feasibility	▪ Malaria ▪ TB

SOURCE: McKinsey

There are several potential solutions to re-fuel the vaccines innovation engine

Initial thoughts on potential solutions

1 **High income and nosocomial**	▪ Earlier **clarity on market demand** – published TPPs on desired product profiles and pricing? ▪ Greater **certainty on use case and potential recommendation** – ACIP "advance recommendation"? ▪ Further investment in infrastructure and information systems to **track adult immunizations**
2 **Incremental improvements**	▪ Clear, aligned articulation **of value placed on antigen improvements** -- Clearer pricing and market signals? ▪ More specific **guidance on formulation, presentation and delivery innovations** desired – TPPs?
3 **Emerging threats**	▪ Improve **economic incentives** – push investments to create a development fund for emerging threats? ▪ Develop **technology platforms** that can flexibly accelerate innovation – e.g. shared emergency platform?
4 **Potential blockbusters**	▪ Improve **openness and data-sharing** to overcome technical challenges – New models of partnerships on early stage work?
5 **Low income**	▪ Greater clarity on **value of longer-term product innovations** – TPPs and pricing signals?

NVAC could play a lead role in some of these potential solutions

1 High income and nosocomial	▪ Earlier **clarity on market demand** – published TPPs on desired product profiles and pricing? ▪ Greater **certainty on use case and potential recommendation** – ACIP "advance recommendation"? ▪ Further investment in infrastructure and information systems to **track adult immunizations**
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4 Potential blockbusters	▪ Improve **openness and data-sharing** to overcome technical challenges – New models of partnerships on early stage work?
5 Low income	▪ Greater clarity on **value of longer-term product innovations** – TPPs and pricing signals?

Questions for discussion

- What are the most salient challenges to solve across vaccine types? Within specific archetypes?
- What solutions will help us accelerate needed innovations?
- What are the roles of industry, government and policymakers, and research and academia in accelerating innovation? In particular, what is the relevant role for NVAC?

Top 10 infectious diseases by global incidence

Diseases	Top 10 infectious diseases by global incidence	% of total burden of all diseases	Deaths (000s)
Lower resp. infect.	146,864	5	3,052
Diarrhoeal	99,728	4	1,498
HIV/AIDS	91,907	3	1,341
Malaria	55,111	2	438
Tuberculosis	43,650	2	1,290
Neonatal sepsis	39,646	1	431
Meningitis	30,182	1	395
Measles	11,531	<1	96
Syphilis	7,039	<1	79
Acute hepatitis B	6,416	<1	149
Other	94,189	3	1,102
Total	626,263	23	9,871

Several existing vaccines still fall short on fully addressing public health needs

Vaccines	**Incidence** Thousands	**Deaths per year** Thousands	**Improvement opportunities**
Seasonal Influenza	4,000	375	• Higher efficacy • Broader strain protection
Typhoid	1,198	161	• Efficacy can be less than 50%
Rotavirus	11,402	453	• Greater efficacy required (current efficacy around 70%)
Pertussis	2,533	61	• Immune waning of vaccine
HIV	3,109	236	• Additional serotypes could be added, • Fewer doses would increase compliance

High and Low Endemic Diseases

	Diseases	Incidence (000s)	Deaths Per Year (000s)
High Income Endemic			
	HIV	29,231	1,341
	Flu (universal)	4,000	375
	Norovirus	7,634	228
	Syphilis	315	137
	RSV	170	10
	C. difficile	250	14
	S. aureus	75	11
Low Income Endemic			
	Shigellosis	100,000	100
	Tuberculosis	12,112	1,290
	Cholera	2,700	82
	West Nile	2	<1
	Ebola	29	11
	Zika	180	<1

Number of vaccines in development globally (phase I to pre-registration), 2005-15

Year 2005-15	Number of Vaccines in development globally	phase I to pre-registration
2005	125	10% p.a
2006	135	10% p.a
2007	150	10% p.a
2008	175	7% p.a
2009	171	7% p.a
2010	186	8% p.a
2011	199	8% p.a
2012	196	3% p.a
2013	211	3% p.a
2014	261	12% p.a
2015	266	12% p.a

Share of candidates in each stage of development 2005-15

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
PII	15	13	12	14	12	10	11	14	13	16	15
PII	31	35	35	38	43	46	42	43	42	38	40
PI	50	48	48	45	42	39	42	39	41	44	41
Pre-reg	3	4	5	3	3	4	5	5	4	2	3

Note:

There was a -46 drop from PIII to PII in 2005

There was a -56 drop from PII to PII in 2015

Global vaccine sales, 1996-2020

Year	Global vaccine sales	P.A
1996	3	15% p.a
1998	4	15% p.a
2000	5	15% p.a
2002	7	15% p.a
2004	9	22% p.a
2006	13	22% p.a
2008	22	22% p.a
2010	26	5% p.a
2012	26	5% p.a
2014	29	5% p.a
2015	30	6-9% p.a
2020	39-48	6-9% p.a

1996 -2000

Driving growth vectors: Pediatric (DTaP combo, varicella)

2002-2012

Driving growth vectors: Blockbusters (PCV, Rota, HPV) and flu

2014-2020

Future growth will depend on further penetration into adult, nosocomial launches, follow on vaccines in major categories, and speed of adoption in emerging markets

Global vaccine sales, 1996-2015

	1996	1997	1998	1999	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
New launches[1]	26	19	17	17	15	17	13	25	29	34	19	32	24	29	37	47	33	32	23
Existing vaccines	74	81	83	83	85	83	87	75	71	66	81	68	76	71	63	53	67	68	77

Number of vaccine development programs globally

Programs	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Large multinationals[1]	62	71	79	91	83	84	84	78	85	92	90
Biotechs	55	55	59	67	69	84	89	90	95	108	113
Emerging markets players[2]	8	9	12	17	19	18	26	28	31	61	63