POLIO GLOBAL ERADICATION INITIATIVE

EVERY LAST CHILD

Medium and long term IPV product development strategies

DCVMN meeting, Mexico City
10&11 July 2013

World Health Organization

CDC Centers for Disease Control and Prevention

unicef

Bill & Melinda Gates foundation

Presentation overview

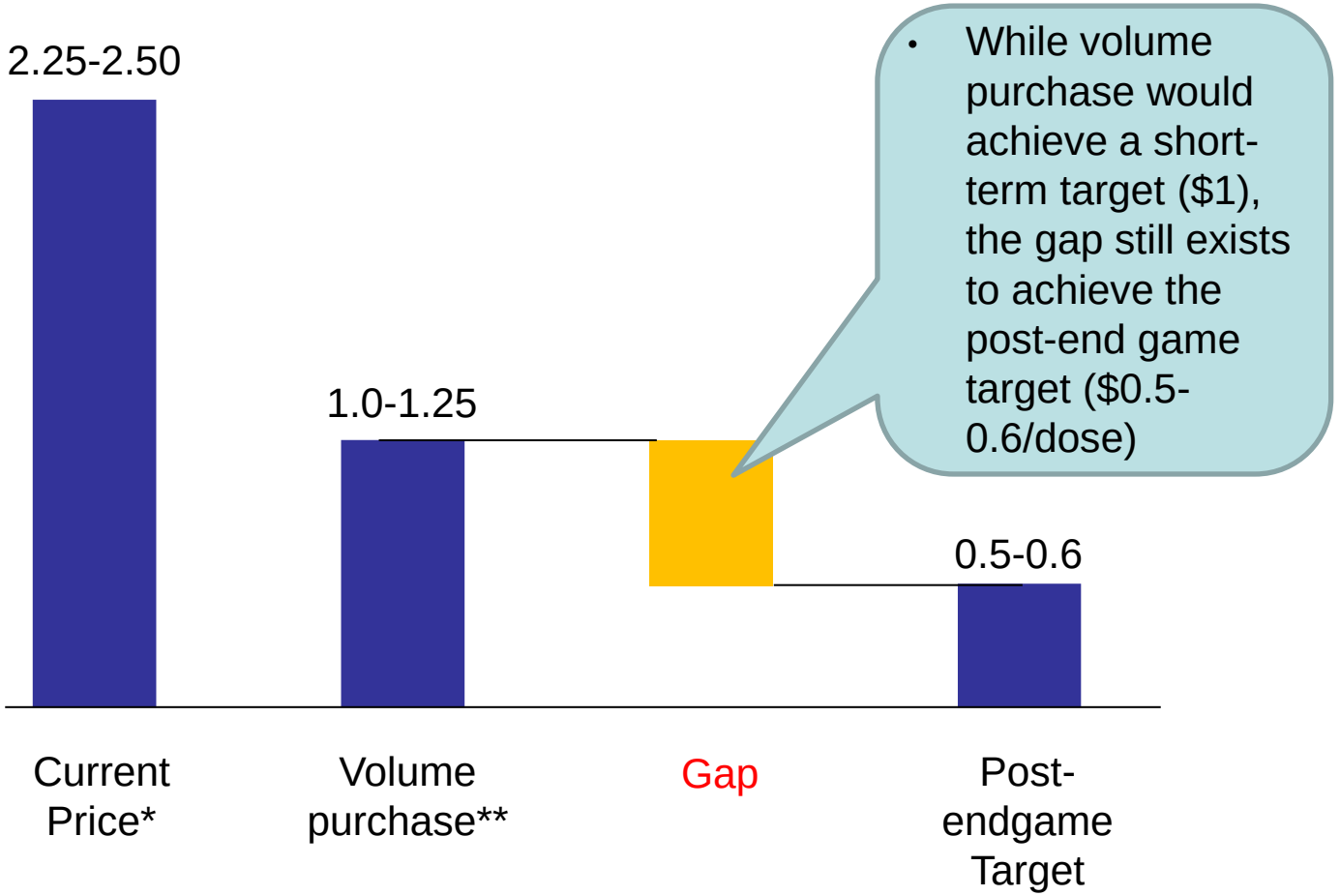
- Current status of prequalified IPV
- Target price of affordable IPV
- IPV development roadmap
- Conclusion

Status of prequalified IPV

Bilthoven Biologicals (NVI), Netherlands	6 December 2010
GSK, Belgium	5 August 2010
Sanofi Pasteur, France	9 December 2005
Statens Serum Institut, Denmark	23 December 2010
Fillers of inactivated trivalent bulks	In the pipeline

Development of Affordable IPV : Context

IPV price per dose (USD)



* UNICEF tender price (November 2012).

IPV Development Roadmap

Approach	Current	Mid-term (~2016)	Long-term (~2020)

1 Adjuvant		• IM, Adjuvant (1)
		  • Aluminum hydroxide
			• IM, Adjuvant (others)
			  • Aluminum hydroxide
			  • Novel adjuvant

2 Fractional dose		• ID, fractional dose (3)	• ID, fractional dose (others)
3 Combination	• IM, aP-hexa (2)	• IM, aP-hexa	• IM, aP-hexa • IM, wP-Hexa
4 IPV Strain	• Salk (4) • Sabin (Japan)	• Salk (2) • Sabin (China/Indonesia)	• Salk (others) • Sabin (Others) • Alternate IPV strain • Virus-Like Particle
5 Production technology	• Serum containing media with Vero cell	• Serum containing media with Vero cell	• Serum-containing media • Animal Component Free (ACF) media • New cell line (e.g., PER. C6)

1 Middle-/Long-Term Strategy: Adjuvant

	Aluminum	Novel Adjuvant
Description	• Aluminum hydroxide may enable 2-4 fold dose reduction of IPV	• Animal studies showed novel adjuvant (e.g., o/w emulsion, Lipid-A, IStP) may enable higher (5~10 fold) dose reduction
Progress to date	• Two fold dose reduction was confirmed with Sabin-IPV, through two rat potency studies and Phase I/IIa infant study in Poland (Intravacc/WHO) • Rat studies showed a similar (or higher) effect (2-4 fold) with Salk-IPV but there is no human study yet • Ongoing work to optimize and develop aluminum adjuvant S-IPV (Preliminary results ~early 2014)	• BMGF supports work to explore different adjuvant options (~early 2014) • Regulatory requirements for these adjuvants (esp. for pediatric use) need to be determined
First product available	• 2016-17	• 2018~

2 Middle-Term Strategy: Intradermal IPV

	Needle and syringe	Jet injectors and micro-needles (Patch)
Description	• Intradermal administration of IPV enables five fold dose reduction	• ID device and patch will significantly improve the ease of use
Progress to date	• Clinical trial requirements for IPV label change is being finalized with NRAs • Most likely, two non-inferiority trials will be conducted by WHO (late 2013)	• Device comparison study in Cuba ongoing (~Q4 2013) • CDC, WHO, and BMGF plan four studies with different schedules and devices • ID patch was shown to induce sufficient immunogenicity (to IM) in primates with full-dose • Other micro-needles technologies expected
First product available	• 2015~	• 2016-17

3 Long-Term Strategy: Low-Cost Hexavalent

	Hexavalent
Description	• Currently, two IPV-containing hexavalent vaccines on the market (GSK, Sanofi) with aP component • Multiple suppliers are developing wP-based, low cost hexavalent • No prequalified product yet
Progress to date	• Development is still ongoing for more affordable wP hexavalent vaccines
First product available	• 2018~

4 Middle-/Long-Term Strategy: Safer IPV

	sIPV Development	Alternate Strains	Virus Like Particle
Description	• IPV produced from Sabin strain • Safer to produce, less containment issues	• IPV produced from genetically modified strains ("safer than Sabin" strains)	• Stabilized poliovirus capsid • No containment required
Progress to date	• Japanese NRA licensed two products (Aug '12) • Kunming finished phase III trial • WHO/Intravacc completed phase I/IIa	• WHO selected candidate strain for evaluation of production feasibility (May '12)	• technical feasibility demonstrated • further evaluation ongoing
First product available	• 2013 (China) • 2016 (Indonesia) • 2017~ (Others)	• 2018~	• 2018~

sIPV Development: WHO/Intravacc (RIVM) Collaboration

- GMP production and pre-clinical tests completed

- Phase I/II in infants (Poland) showed 95-100% seroconversion rate against Salk and Sabin virus with high GMT

- Selected six partners* for the technology transfer
- Two partners (Panacea, SII) already started a tech. transfer project

* Panacea, SII (India), CNBG, Sinovac (China), LGLS (Korea), and Birmex (Mexico)

Phase I/IIa Study in Poland: Seroconversion rate

Selected by Advisory Panel for further development

Doses		Sabin			Salk		
		Type I	Type II	Type III	Type I	Type II	Type III
Salk IPV (40:8:32) n=20		100%	100%	100%	100%	100%	100%
Sabin IPV	Low (5:8:16) n=20	100%	100%	100%	100%	100%	100%
	Mid (10:16:32) n=20	95%*	100%	100%	100%	100%	100%
	High (20:32:64) n=20	100%	100%	100%	100%	100%	100%
Sabin IPV (adj)	Low (2.5:4:8) n=20	100%	100%	100%	95%	100%	100%
	Mid (5:8:16) n=20	100%	100%	100%	100%	100%	100%
	High (10:16:32) n=20	100%	100%	100%	100%	100%	100%

*One subject had very high prevaccination titer (>10.5) and intermediate post-vaccination titer (6.83 log2 titer)

5 Long-Term Strategy: Production Optimization

	Production Optimization	
	ACF media	**New Cell line**
Description	• Preliminary research showed the production process can be improved 2-3 fold with Animal Component Free (ACF) media, which increases the cell densities	• Production of IPV with PER. C6, a new cell line derived from human retina cells (by Crucell/J&J) • Potentially increase production yield 10-30 fold
Progress to date	• WHO/Intravacc are negotiating a new memorandum of understanding (MoU), including the further research on the production optimization	• Higher yield confirmed at a lab-scale production model • Commercial scale production and development is planned
First product available	• 2018~	• 2018~

Conclusions

- Major progress in supplying and developing affordable IPV:
  - The volume purchasing will reach a short-term target of $1/dose. However, further technological innovation is needed to achieve the ultimate GPEI target ($0.5-0.6/dose)
  - Sufficient evidence is now available for technical feasibility of ID administration (earliest 2014) and adjuvant (earliest 2016)
  - Preliminary results from other technologies suggests the feasibility of further technical innovation (such as VLP, and production optimization) . They may enable more IPV supply options, facilitate containment and likely reduce the IPV price in the long run (around 2020)

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THANK YOU

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