



# **Championing a Smoke-Free World**

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September 28, 2023

# Forward-Looking and Cautionary Statements

- This presentation contains projections of future results and goals and other forward-looking statements, including statements regarding business and
  regulatory plans, expectations, opportunities, ambitions, targets, and strategies. These forward-looking statements and anticipated results reflect the
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- PMI is further subject to other risks detailed from time to time in its publicly filed documents, including PMI's Annual Report on Form 10-K for the fourth
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## **Glossary and Key Terms and Definitions**

- A glossary of terms, including the definition for smoke-free products as well as adjustments, other calculations and reconciliations to the most directly comparable U.S. GAAP measures for non-GAAP financial measures cited in this presentation are available on our <u>Investor Relations website</u>
- Growth rates presented on an organic basis reflect currency-neutral adjusted results, excluding acquisitions and disposals. As such, figures and comparisons presented on an organic basis exclude Swedish Match up until November 11, 2023

## About Me



### Education: MD and PhD

### Medical Training:

Internal Medicine, Wayne State University School of Medicine and the Detroit Medical Center, Detroit, Michigan, US

Allergy and Immunology, National Institute of Allergy and Infectious Disease, National Institutes of Health, Bethesda, Maryland, US

### Medical Licenses (active): States of Maryland, US District of Columbia, US

Work Experience (selected):

Director, Division of Pulmonary, Allergy, and Rheumatology Products, US Food and Drug Administration (1997 to 2018)

Senior Vice President and Chief Physician Scientist, Respiratory Inflammation and Autoimmunity, Astra Zeneca Pharmaceuticals

# The Scientific Basis for Tobacco Harm Reduction

- Many misperceptions on smoke-free products & nicotine
- The science from existing laboratory and clinical data is conclusive:
  - Heated tobacco products
  - E-vapor products
  - Oral products

ARE NOT equally or more harmful than cigarettes

- Nicotine is not the primary cause of smoking-related disease
- We expect future risk reduction studies to further support these facts



# Smoke-Free Product Portfolio



# **Cigarette Combustion Causes Harm to Health**



Note: HPHC stands for Harmful and Potentially Harmful Constituent. PAH stands for polycyclic aromatic hydrocarbons Source: Left chart: Cozzani, 2020 (DOI: 10.1016/j.tca.2019.178475); right chart: McGrath, 2007 (DOI: 10.1016/j.fct.2006.12.010)

## The Difference Between Cigarette Smoke & IQOS (THS) Aerosol Heated Tobacco Aerosol Chemistry & Physics





(a) Analysis of the 54 Harmful or Potentially Harmful Constituents as defined by FDA. Includes Health Canada, the WHO and the FDA-18 lists of HPHCs. Note: THS here stands for Tobacco Heating System. Health Canada's Intense Puffing Regime. Comparison on a per-stick basis (excluding nicotine). Reference Cigarette = 3R4F: University of Kentucky 10 Reference Cigarette





Source: Bottom: REXA-07-JP (NCT01970995) – Lüdicke et al. 2018 (DOI: 10.1093/ntr/ntx028); Top: REXA-08-US (NCT01989156) – Haziza, 2019 (DOI: 10.1093/ntr/ntz013)

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## Exposure Response Study: Biomarkers of Potential Harm (BoPH) Clinical Assessment HTP (in Smokers Who Would Otherwise Continue to Smoke)



Source: ZRHR-ERS-09-US (NCT02649556) – Lüdicke et al. 2019 (DOI: <u>10.1158/1055-9965.EPI-18-0915</u>)

# Exposure Response Study: Effects of IQOS (THS) Use on BoPH

Assess Changes Across a Set of 8 Primary BoPH Endpoints in Smokers Who Switch from Smoking Cigarettes to Using IQOS (THS), as Compared to Those Continuing to Smoke Cigarettes, for 6 Months



Significant reduction in exposure to Carbon monoxide and Tobacco Specific Nitrosamine. The other three biomarkers of potential of harm moved in the same direction observed when quitting cigarette smoking



Changes were statistically different between IQOS (THS) and cigarettes for five out of eight BoPH as per pre-specified analysis despite that dual-use of cigarettes for up to 30% of product use was allowed in IQOS (THS) study arm. Source: ZRHR-ERS-09-US (NCT02649556) – Lüdicke et al. 2019 (DOI: <u>10.1158/1055-9965.EPI-18-0915</u>)

## Reduced Toxicant Emission – VEEV E-Vapor Aerosol Chemistry & Physics

Average Reduction<sup>(a)</sup> in Emission of Harmful or Potentially Harmful Constituents

(HPHC) of VEEV Relative to the Reference Cigarette for Two Power Settings



- Significant reduction in HPHCs compared to reference cigarette
- Reduction in HPHCs were largely independent of power setting
- No carbon-based solid particles generated

(a) Average HPHC reduction (excluding nicotine) in 3 batches per product version when normalized to 100% of the 1R6F combustible reference cigarette smoke levels. The average HPHC reduction refers to 16 HPHCs measured in the emissions, (15 HPHCs in common between FDA ENDS (33) list of analytes (for e-vapor products) and Health Canada & WHO (46) (for tobacco products) and benzo[a]pyrene). Reduction was calculated comparing data on a per puff basis based on standard puffing regime ISO-20768:2018.

# Mouse Toxicology Study – Findings in the Lung After E-Vapor Aerosol Exposure



Note: PG stands for Propylene Glycol, VG stands for Vegetable Glycerin. N stands for Nicotine. F stands for Flavor. Reference Cigarette = 3R4F: University of Kentucky Reference Cigarette. Source: Wong et. al. Archives of Toxicology (2021) 95:1805–1829, https://doi.org/10.1007/s00204-021-03020-4: https://pubmed.ncbi.nlm.nih.gov/33963423/



# Comparison of Exposure to HPHCs in Cigarettes, Swedish Snus and Nicotine Pouches







Usage Rates of Snus and Cigarettes in Swedish Men Correlate With a Reduction in Tobacco Related Diseases



# Sweden: Lowest Male Smoking Prevalence in the EU

Product Use and Health Harm Reduction



## One of Lowest Tobacco-Attributable Male Mortality in EU Product Use and Health Harm Reduction



# Epidemiology Supports Snus Reduced Risk Claim for Major Smoking Related Diseases

Lung Cancer		
Boffetta et al. 2008		0.8 (0.6-1)
Lee & Hamling 2009; Lee 2011		0.82 (0.52-1.28)
Mouth Cancer		
Boffetta et al. 2008	<b>_</b> _	1 (0.7-1.3)
Lee & Hamling 2009; Lee 2011	<b>—</b>	1.01 (0.71-1.45)
Emphysema and Chronic Bronchitis		
Roosaar et al. 2008 (< 80 years old)		0.8 (0.2-3)
Roosaar et al. 2008 (80+ years old)		2 (1.2-3.4)
Heart Disease		
Rostron et al. 2018	+	1.04 (0.93-1.16)
Boffetta & Straif 2009 (any MI)	-	0.87 (0.75-1.02)
Boffetta & Straif 2009 (fatal MI)	-	1.27 (1.07-1.52)
Stroke		
Rostron et al. 2018	+	1.04 (0.92-1.17)
Boffetta & Straif 2009 (any stroke)	+	1.02 (0.93-1.13)
Boffetta & Straif 2009 (fatal stroke)		1.25 (0.91-1.7)
0.1	1 2 5 10 15	20
AC Meeting Materials and Information presented in tabular format	Relative Risk (95% CD)	

## Health Effects of Oral Nicotine Products (e.g., ZYN) Long-term Data from Oral Tobacco Product (e.g., Snus) Provides a Basis

- The chemical composition of nicotine pouches contain the same or less amount of harmful and potential harmful constituents compared to Snus
- No additional harmful or potentially harmful constituents are added to the nicotine pouch compared to the constituents in Snus

Source: Based

- Nicotine exposure for users of nicotine pouches is comparable to that of a Snus user
- The nicotine pouch is used in a similar way as Snus



The oral nicotine category is new but the long-term health effects can be predicted based on oral Snus data given some fundamental assumptions are met



# Nicotine is Not the Primary Cause of Smoking-Related Diseases

### What we know

Tobacco smoke contains thousands of chemicals. This mix of chemicals – not nicotine – is the primary cause of serious disease and death in tobacco users, including fatal lung diseases ... like chronic obstructive pulmonary disease (COPD), and cancer. [emphasis added]

US FDA Website (Accessed: May 2023)

Nicotine is addictive, but not intoxicating and not functionally impairing<sup>(a)</sup>

### What needs to be better understood

- **1. Understand the health risks** of nicotine per-se in different forms of administration
- 2. Understand potential benefits of nicotine that consumers report, and investigate nicotine levels showing such benefits:
  - Concentration, short-term memory, etc.,

#### 3. Understand therapeutic applications of nicotine

• Therapeutic benefit of nicotine as NRT – inhaled NRT likely giving similar nicotine kinetics and experience to cigarettes

# Nicotine – Potential Medical or Therapeutic Benefits

Potential Benefit	Source/Citation		
Chronic Cough	Chest, 2016; 149 (1): 161-5		
Anxiety, Depression	Neuroreport, 2002; 13 (9): 1097-1106		
Schizophrenia	Neuropsychophamacology, 2004; 29(7): 1378-85		
Ulcerative colitis	Alimentary Pharmacology and therapeutics, 2012; 36 (11-12): 997-1008		
Attention deficit hyperactive disorder	Psychopharmacology, 1996; 123 (1): 55-63		
Parkinson's disease	Movement disorders, 2012; 27 (8): 947-57		
Mild Cognitive impairment	Neurology, 2012; 78 (2): 91-101		
Alzheimer's disease	Psychopharmacology, 1992; 108 (4): 485-94		
With funding from the US National Institutes of Health (NIH), the MIND (Memory Improvement through Nicotine Dosing) Study is testing whether nicotine can safely improve memory and functioning in people with mild memory loss and mild cognitive impairment www.mindstudy.org			
Developing nicotine products for treating human diseases may not be practical, except for high unmet need where the demonstrated benefits would justify the risks			

Note: The list of potential benefits was created from a review of third-party studies. PMI has not independently assessed whether the existing evidence is sufficient to support a conclusion that nicotine has a beneficial effect on each of the conditions listed

# **Cost of Regulatory Inaction**

### Encouraging progress being made in many countries - however:

- A failure to acknowledge the role that harm reduction can play in bringing about the end of cigarettes seriously hinders the ability of adult-smokers to switch to better alternatives
- The science is clear it is no longer a case of *IF* smoke-free alternatives are better than cigarette smoking, but *BY HOW MUCH* they are better
- Many policymakers perceive it as safer to abstain from the debate rather than be seen as "siding" with the industry by adopting risk reduction policies
- Not making a decision on smoke-free products today is a decision in and of itself and it's a
  decision with consequences
- Governments and public health authorities must act quickly and decisively rather than remaining tied to outdated approaches that have failed to solve the problem of smoking

## Embracing harm reduction will accelerate the end of smoking

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