PMI INVESTOR DAY – SEPTEMBER 29-30
RRP Highlights from the presentations include:

iQOS
The iQOS heated tobacco system continues to show strong potential as a non-combustible alternative to cigarettes. Nearly 1 million adult smokers have quit smoking and switched to iQOS since its launch less than two years ago.

- Furthermore, 60% to 70% of adult smokers who purchase iQOS either fully or predominantly switch to it – i.e. they stop smoking (full = 95% or more of total consumption; predominant = 70%-95% of total consumption).
- Outside of Japan, iQOS share of market has grown quickly in all launch markets, showing that adult smokers find it an acceptable substitute to cigarettes.
    - iQOS will be available in cities in 20 markets by the end of the year and an additional 10-15 markets in 2017.

Management recapped on the status of the scientific assessment of iQOS and re-stated that the evidence generated to-date supports our conclusion that iQOS has the potential to reduce the risk of smoking-related diseases in adult smokers who switch to it completely.

- In summary, the results to-date show that:
    - iQOS reduces the formation of Harmful and Potentially Harmful Constituents (HPHCs), excluding nicotine, by 90% on average compared with cigarette smoke.
    - This leads to a concomitant, greater than 90%, reduction in toxicity compared with cigarette smoke in standard laboratory toxicity tests that measure cytotoxicity and genotoxicity in vitro.
    - Randomized 3-month clinical trials, showed significant reductions in fifteen biomarkers of exposure to HPHCs in adult smokers who switched to iQOS, which approached the reductions seen in smokers who quit smoking for the duration of the study.
- An application for authorization from the US FDA to market iQOS as a reduced risk or reduced exposure product will be filed by the end of 2016.
- To establish a "gold standard" of cessation for assessing Reduced-Risk Products, PMI is conducting a Smoking Cessation Response study to measure the reversal of clinical risk markers when adult smokers quit smoking for 12 months. A 6-month interim report is expected by the third quarter of 2017, while the full 12-month results with be available by the first quarter of 2018.
- In parallel, PMI is conducting an Exposure Response study to measure clinical risk markers when adult smokers switch to iQOS over a 12-month period. Top line results of the first 6-month phase are expected by the second quarter of 2017, while the full 12-month results are expected by the first quarter of 2018. These results will be benchmarked against those of the Smoking Cessation Response study.
- While the long-term effects of switching to Reduced-Risk products are clearly the most important for public health, adult consumers are also interested in short-term benefits such as dental hygiene. In this context, PMI has demonstrated that exposure to iQOS aerosol resulted in reduced tooth coloration in comparison to cigarette smoke exposure.

E-cigarettes

Demonstrating a strong commitment to the e-cigarette category, PMI will introduce next generation e-cigarette technology in the UK by the end of the year.

- The new Mesh e-cigarette employs a novel stainless steel mesh heating source as opposed to the traditional coil and wick design of current generation e-cigarettes. This new design allows for automated GMP compliant manufacturing in the EU.
- The Mesh product includes a low liquid level detection system and will automatically shut off if the temperature exceeds a certain level, addressing concerns with some current generation e-cigarette products.
- The new technology could allow for licensing by the UK MHRA in the future.

With regard to PMI's current e-cigarette product offerings, a number of pre-clinical studies have been completed to assess aerosol chemistry and in vitro and in vivo toxicity.

- In a 90-day inhalation study, no respiratory toxicity was observed in rats exposed to e-cigarette aerosols generated from mixtures of the aerosol formers propylene glycol and glycerin with and without nicotine.
- Studies on the impact of using our e-vapor products Solaris, Nicolites, and Vivid on indoor air quality indicate that the use of these products did not negatively affect indoor air quality.

Platform 2

Initial results of the scientific assessment of Platform 2, a second heated tobacco product that heats tobacco via a pressed carbon heat source, are also promising.

- Consistent with iQOS the levels of HPHCs in the aerosol from platform 2 were reduced on average by more than 90% compared to the levels seem in 3R4F reference cigarette smoke and translated into significant reductions in toxicity *in vitro*.
- A five-day clinical trial showed that reductions in 15 biomarkers of exposure to HPHCs approached the reductions seen in those seen in adult smokers who quit for five days. The clinical phase of a 90-day reduced exposure study has been completed and the results will be available in mid-2017.
- Platform 2 is expected to be commercialized in early 2017.

Platform 3

Research on Platform 3, which creates an aerosol of nicotine salt via a chemical reaction of a nicotine solution and a weak acid, is also progressing. A pharmacokinetic study conducted jointly with external researchers in New Zealand showed nicotine uptake levels in line with the levels seen with cigarette smoking, showing Platform 3's potential as an alternative to cigarettes.

- Further research, such as a pharmacodynamics study in the US and a six month safety study are planned or ongoing.
- Platform 3 is expected to be commercialized in the second half of 2017.