This document discusses the clinical validity and utility of the HairDX genetic test for androgenetic alopecia.

INTRODUCTION: CLINICAL VALIDITY OF GENETIC SCREENING
The goal of genetic screening is to identify subjects for preventive treatment or extended surveillance prior to onset of symptoms; therefore, the sensitivity of the test should be high so most people that eventually will develop the condition will be identified early. Also, a high specificity is desired to increase the efficacy of the screening and minimize the number of subjects that will be treated unnecessarily.

STATISTICAL ANALYSIS
We will demonstrate the clinical validity of the HairDX genetic test using standard statistical methods.

We pooled data from 5 independent peer reviewed and published studies that demonstrated statistical significant association between the genetic variants measured by the HairDX genetic test and androgenetic alopecia in men. The studies examined European, Northern European, Australian, and Middle Eastern men. A total of 2078 men were genotyped.

Bald men consisted of men age 18 and above with a Hamilton grade III and above. Non-bald men consisted of men age 50 and above with a Hamilton grade II or below.

The pooled data reported by the studies is presented in the table below:

<table>
<thead>
<tr>
<th>SNP: rs6152</th>
<th>Bald</th>
<th>Non-Bald</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>TP = 1096</td>
<td>FP = 677</td>
<td>1773</td>
</tr>
<tr>
<td>A</td>
<td>FN = 81</td>
<td>TN = 224</td>
<td>305</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1177</td>
<td>901</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used: T = a positive test result i.e., G allele; ~T = a negative test result i.e., A allele; D = a person having the disease i.e., bald; ~D = a person not having the disease i.e., non bald; TP = True Positive; FN = False Negative; FP = False Positive; TN = True Negative

Based on the pooled data we calculated the following:

Sensitivity = the probability that a bald person will test positive = P(T|D) = 93%
Specificity = the probability that a non bald person will test negative = P(~T|~D) = 25%

The clinical value of the HairDX genetic screening test needs to be interpreted in relation to the population prevalence of baldness.

We selected a disease (baldness) prevalence = P(D) = 63%. This prevalence number is a lifetime estimate cited in several population surveys. For example, Desmond et al. found in an Australian population that by age 60, 63% of men were bald. DeMuro-Mercon et al. found in a Norwegian population that 63% of men ages 20-50 reported some degree of hair loss. Tang et al. found in a Singapore population of mixed ethnicity that 63% of the men ages 17-86 experienced some degree of androgenetic alopecia. The prevalence of baldness parameter be adjusted, but the resultant clinical validity of the test remains similar to the one presented in this document.

Of particular important to physicians is the probability that a person will become bald if he was tested positive as well as the probability that a person will not become bald if he was tested negative. Applying the Bayes formula to the pooled data we conclude:

Probability that a person that tested positive will become bald = P(D|T) = 68%

Probability that a person that tested negative will not become bald = P(~D|~T) = 68%

Finally, a measure that is important to a physician, is the probability that a subject will receive unnecessary treatment = P(~D|T) = 32%

**CLINICAL VALIDITY:**
A physician using the HairDX genetic screening test for hair loss, can reliably predict that a patient that tests positive has approximately a 70% chance of becoming bald; thus, the patient can benefit from early treatment.

Similarly, a physician can reliably predict that a patient that tests negative has approximately a 70% chance of not becoming bald; thus, the patient can avoid costly treatment.

As any screening test is not perfect, approximately 30% of the subjects that will be identified by the HairDX genetic screening test may be treated unnecessarily. Of course, screening tests should always be accompanied by a medical diagnostic to reduce unnecessary treatments.

While the statistical analysis is not provided in this letter, an expert in the field of hair loss can appreciate that the percent of subjects that will be treated unnecessarily can be significantly reduced by reviewing the subject’s family history in combination with a scalp examination.

**CONCLUSION:**
Currently there are only two FDA approved medications for the treatment of androgenetic alopecia in men. Both medications work best at retaining a men’s hair rather than re-growth of lost hair. A recent study has demonstrated that one of the medications, Finasteride, is effective at retaining hair for periods longer than a decade.

Given that the risks associated with the FDA approved treatments for hair loss are extremely low and the cost of the HairDX genetic screening test is minimal, the HairDX test in combination with a physician scalp examination and review of family history is a clinically valid and effective tool for early intervention in preventing androgenetic alopecia in men.

REFERENCES: