To: Sunny Balwani[sbalwani@theranos.com]
From: Mark Pandori[/O=THERANOS ORGANIZATION/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=MARK PANDORI16D]
Sent: Fri 5/30/2014 10:09:03 PM (UTC)
Subject: RE: HCV small volume thoughts,

Yes, I understand.

From: Sunny Balwani
Sent: Friday, May 30, 2014 3:01 PM
To: Mark Pandori
Subject: RE: HCV small volume thoughts,

Thanks for the summary.

I agree. This is precisely what we were expecting and planning to do so this in line with our estimates.

As you know, this is Theranos Trade Secret and something we intend to offer soon.

Thanks.

From: Mark Pandori
Sent: Friday, May 30, 2014 1:33 PM
To: Sunny Balwani
Subject: HCV small volume thoughts,

Sunny,

Wanted to make sure I gave you my HCV thoughts you asked for, in case they help:

I reviewed several pieces of peer reviewed literature on HCV and viral load to try and get an idea of how useful a small-volume HCV test would be for treatment monitoring.
I also reviewed FDA literature on recommended sensitivities for HCV viral load tests.

I conclude that there may be considerable value to a low volume test, until the load (if the load) of the patient dips below the predicted detectable limit of a 70ul assay.
Based on the dilution factor (below), I would predict that limit to be approximately 170 copies/ml (better than the HIV).

Essentially:

The average HCV viral load of people newly diagnosed (untreated) is approximately 3x10e6.
It varies slightly (and perhaps not significantly) by genotype:

Genotype: load

1a: 2.75x10e6
1b: 3.9x10e6
3a: 2.65x10e6
3b: 2.51x10e6

If we estimate that the number is 3x10e6:

A “Rapid Viral Response” to therapy is considered in much of the literature to be a 2-log drop within 4 weeks of therapy. That would be expected to bring the average infected individual to approximately 3x10e4. This is a number well Above the expected sensitivity threshold of a small-volume assay.

A “Sustained Viral Response” to therapy is considered in much of the literature to be, at 12 weeks, an additional 2-log decrease from
The 4-week measurement, which for our estimates would be 3x10e2. It is ESTIMATED that the small volume assay would be capable of a sensitivity of this level, just based on the dilution factors. It is also probably true that there would be measurements
at 6 or 8 weeks, which would fall into the range of such an assay:

1.0 ml of plasma or serum gives a sensitivity of 12 international units/ml on the M2000,
hence, 70ul might be expected to give a sensitivity of approximately 170 copies. (to be determined).
This is based on what is roughly a 1/14 dilution factor.

Under these “average” or estimated conditions, therefore, most people would benefit from viral load tests for quite a while. It is of course going to be variable, as some patients and HCV genotypes will respond more rapidly to therapy, particularly as the therapies change. However if someone came back as undetectable on the small volume assay, a redraw would not be particularly “bad” news for the patient, as it is being done to test with a more sensitive version of the test (perhaps a Theranos developed Real Time PCR).

These are some thoughts. Hope they help these efforts out, going forward.

Mark Pandori