

From: [Richard Chen](#)
To: [John West](#); [Carol Tillis](#); [Christian Haudenschild](#)
Subject: Final board slides
Date: Wednesday, December 12, 2012 4:52:53 PM
Attachments: [board.12.14.12.v5.roc.ppt](#)

My final board slides attached

R&D Update

Personalis, Inc.

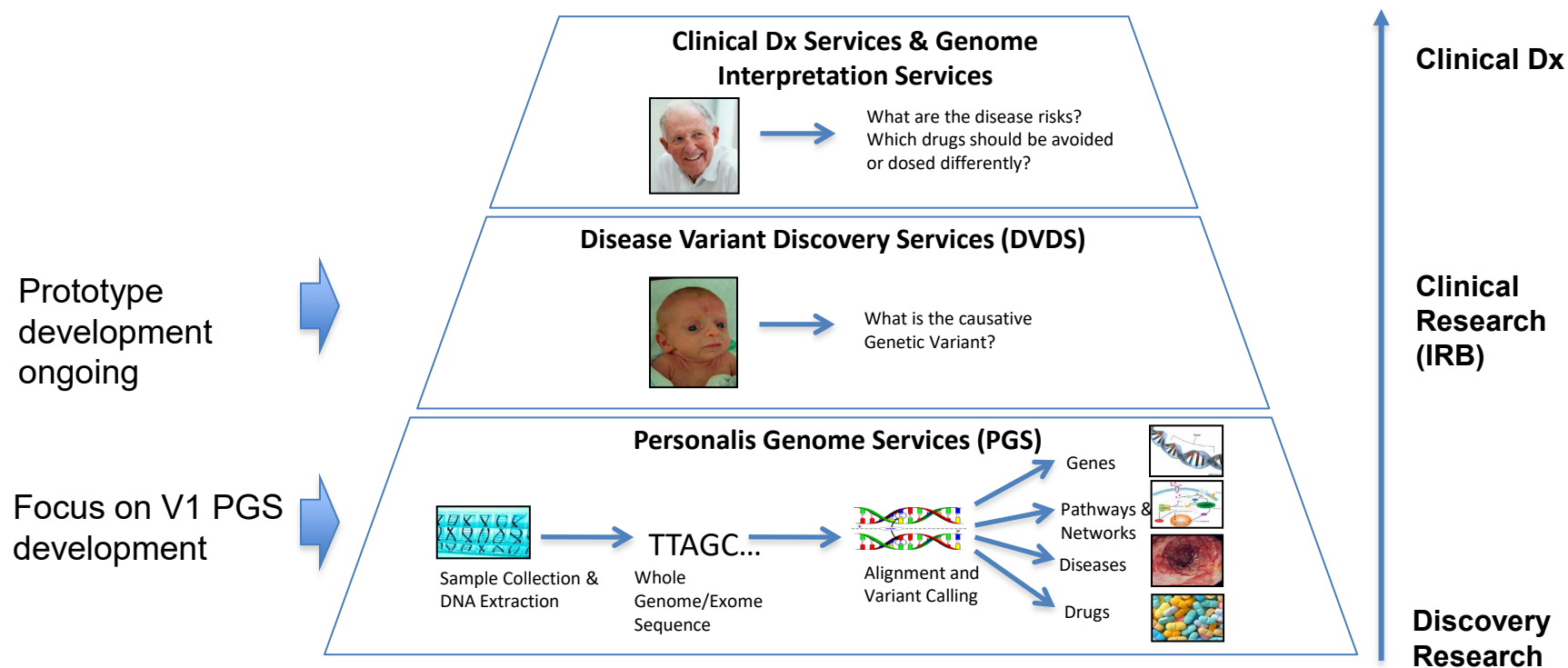
12.14.2012

Richard Chen, CSO

R&D Overview

- Product Development
- Content Development
- Computing Infrastructure
- Hiring

Product Roadmap



Personalis Genome Services for Research

- Currently focused on PGS v1 development
 - ~80 features/enhancements, ~370 tasks, including features required for VA project
 - v1 key differentiating features: Exome+, accuracy, SV detection, analytics leveraging proprietary content, unique visualization and enhanced reporting
 - Improving overall system performance optimization
- Biological testing is critical
 - Obtaining both known and unknown disease data sets to test our algorithms
 - Initiating new collaborations with Dr. Aaron Gilter at Stanford for ALS and Dystonia
 - Objective is to test our algorithms and co-author papers if successful
 - Moyamoya 132 cases sequenced, analyzed with pipeline, now being interpreted
 - GOAL: success stories we can talk about with customers, publish on
- Extending SAB to cover key product areas
 - Prof. Bob Nussbaum UCSF: Recognized world expert in medical genetics, rare pediatric syndromes
- PGS v1 service on track to launch at AGBT conference Feb 2013
 - 3 abstracts accepted to AGBT to support the PGS launch
 - Topics focus on key differentiators including accuracy, proprietary content, and “success stories” applying our technology

Exome Plus

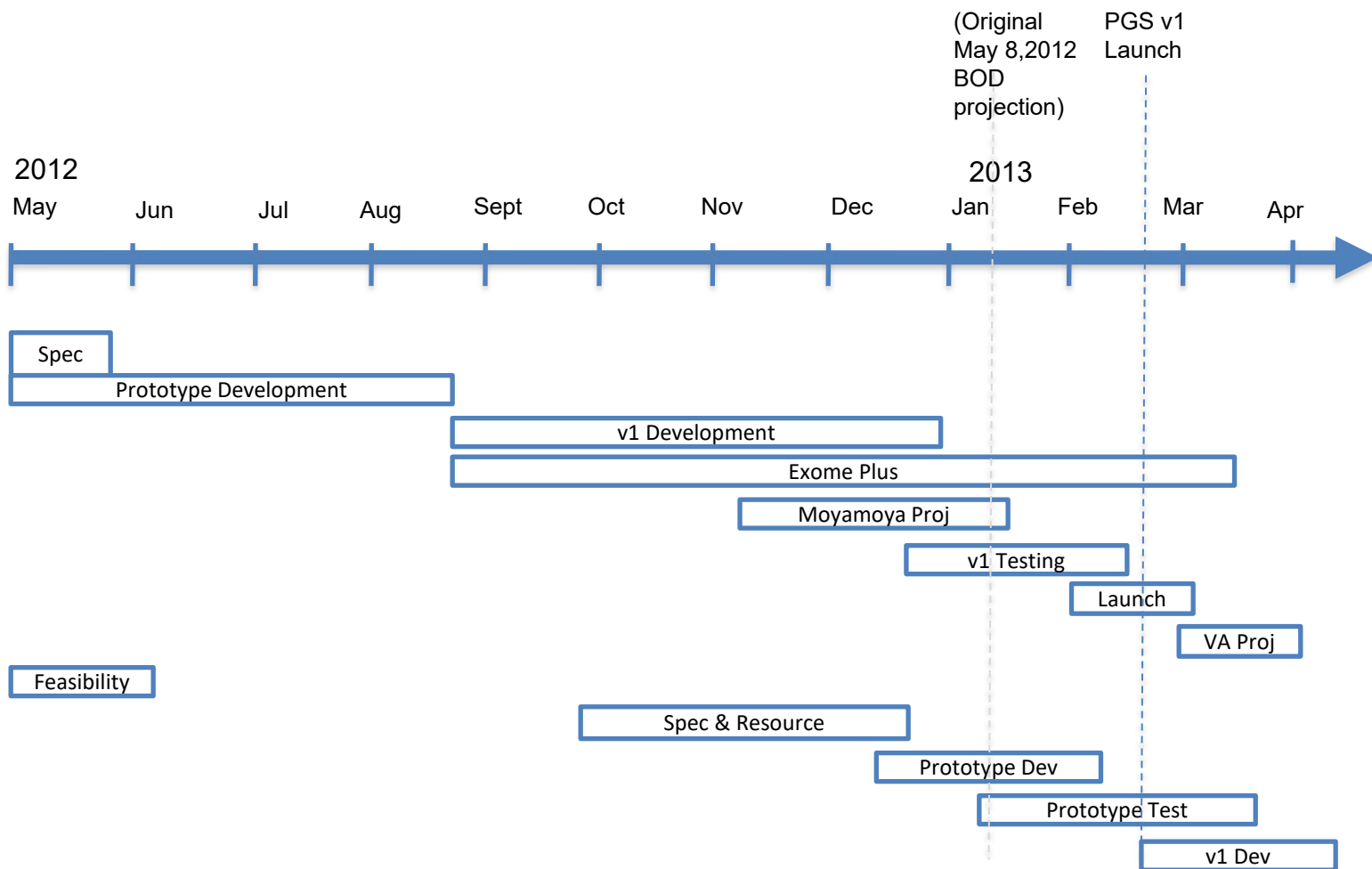
Review of Key Goals & Milestones

- Goal is to fix problems with standard exome sequencing
 - Typical exome sequencing misses a lot of exome (GC regions, etc)
 - Lots of biomedically interpretable content missed on standard exomes
 - The Personalis Exome Plus aims to solve these issues by augmenting standard exomes with custom pullout data
- Milestones
 - Designed and Received Enrichment Probes/Kits from Agilent
 - Prelim analysis shows encouraging results
 - Now working on second iteration of Exome Plus
- Anticipate that this will be launched in 2 phases:
 - Targeting the first release as part of the PGS v1 launch in Feb 2013.
 - More research intensive parts of Exome Plus will be part of a 2nd release in 2013.

Extending PGS to Rare Pediatric Syndromes (DVDS)

- Extending PGS capability to address another key research use case: Rare Pediatric Syndrome Trios/Large Pedigrees
- Consists of new analysis modules built on top of the same sequencing, alignment, variant calling, and annotation pipeline used for PGS
- Near term goal to test our capabilities on real biological examples, and to understand requirements for product
- Biological testing on known and unknown samples including
 - Dystonia family
 - MoyaMoya family
 - Miller syndrome
 - Initiating discussion with Jon Bernstein from Stanford Med Genetics
 - Others

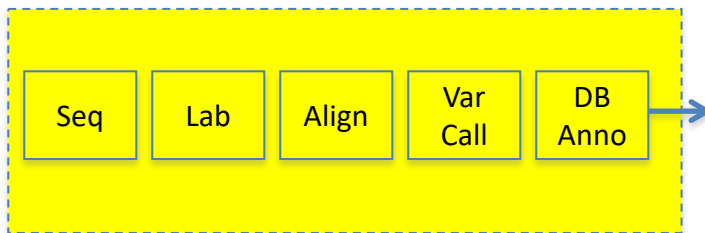
Summary of High-Level Timelines



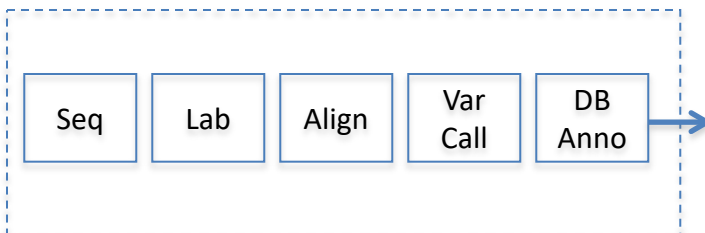
Personalis Genome Services for Research

Key customer use cases addressed in PGS v1 Release

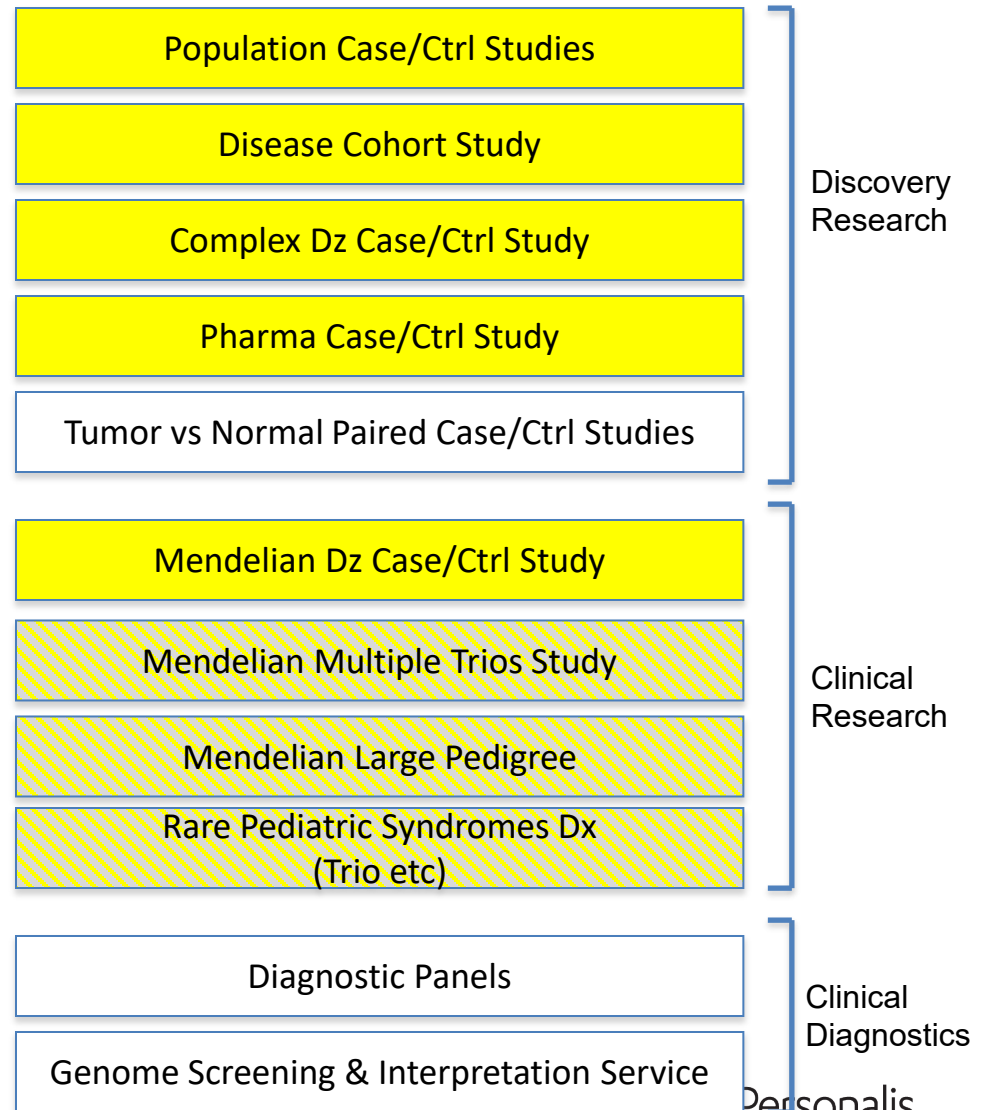
Standard Seq & Pipeline



CLIA Seq and Pipeline



-  PGS v1 Release
-  DVDS Prototype Features



Content: Personalis Genome Library

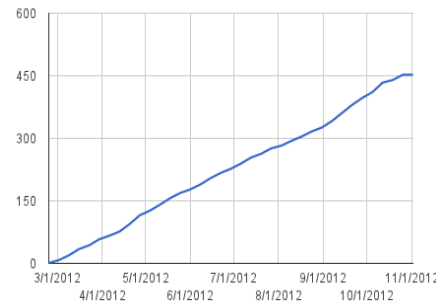
- Gained access to genomes from large public sequencing projects to include as part of our genome “library” including
 - UK10K : 4000 genomes, 6000 exomes, > \$16 M investment from Wellcome Trust
 - NHLBI GO Exome Sequencing Project: ~500 exomes: Heart, Lung, Blood Dz
 - 1000 Genomes (exomes)
 - dbGAP data – Kabuki syndrome, Miller syndrome exomes
 - Represents > 2.5 PB of data in total and > \$20M in research grants to date
- Sequencing exomes/whole genomes in-house with latest chemistries to also serve as potential controls
 - Centenarians
 - 1000 genomes
- These genomes enable us to
 - Establish population allele frequencies to enable filtering of disease causing var
 - Provide potential control sets when customers don’t have controls for comparison
 - Establish normal ranges for genomes for quality control purposes
 - Validate our pipeline and algorithms

Content: MendelDB

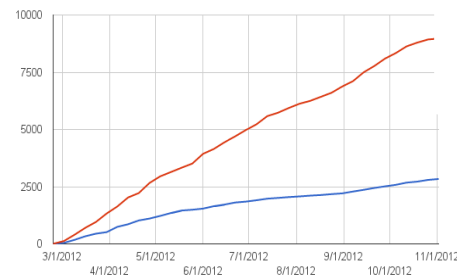
- High quality curated DB of Mendelian phenotypes and their variants
 - Managed by Sarah Garcia and Gemma Chandratillake, both Genetics Ph.D. & Genetic Counselors
- Critical content to support Disease Variant Discovery Service and Genome Interpretation Service
- Finished (~560) GeneReviews > 600 common Mendelian disease phenotypes
- Now finishing QC of that data
- Will then continue phenotype curation and variant curation from other sources
- Flexible workforce for other curation tasks in the future

Curation

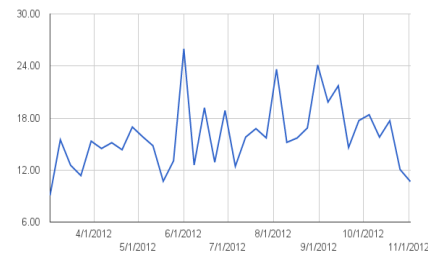
phenotypes



genes (blue) # variants (red)



productivity (rows/hr)



QC Stats

phenotypes remaining for QC



productivity (phenotypes/hour)

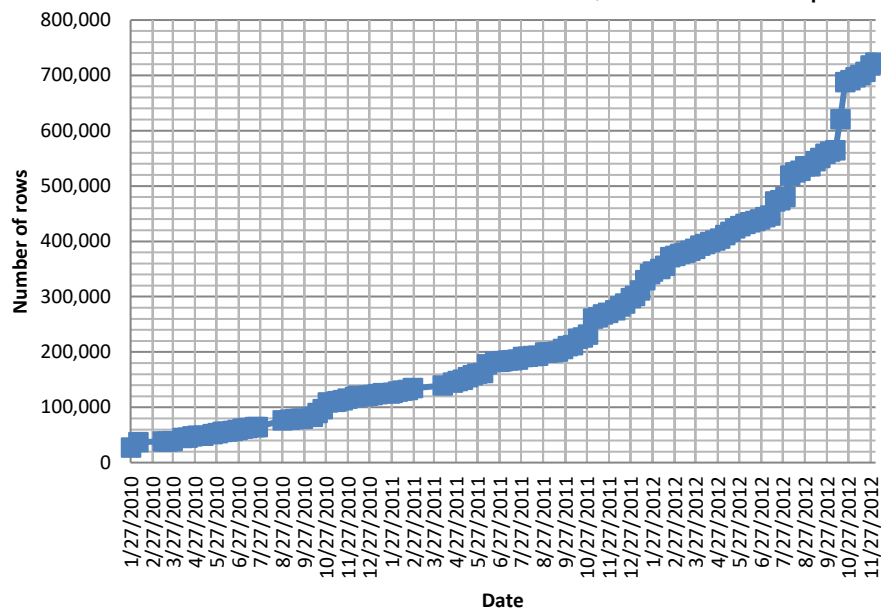


errors/entry

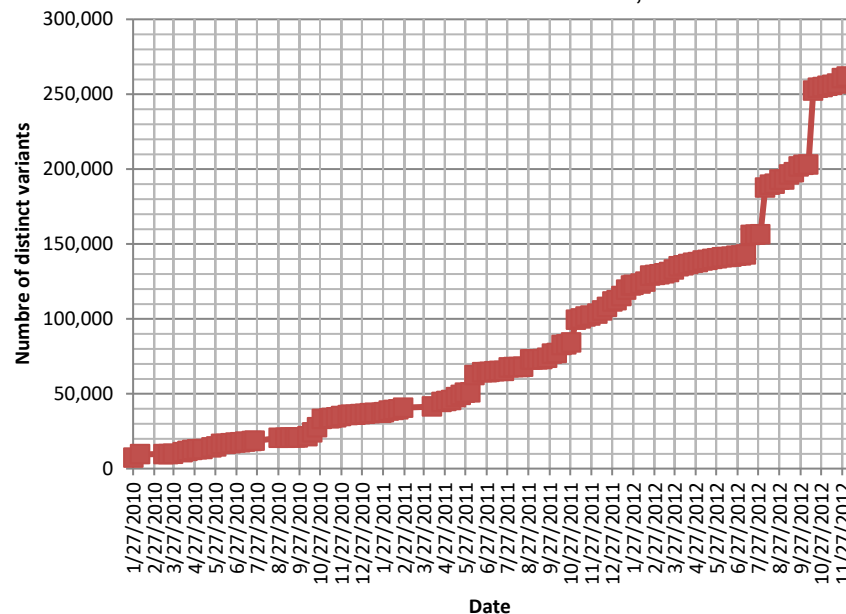


Content: VarimedDB

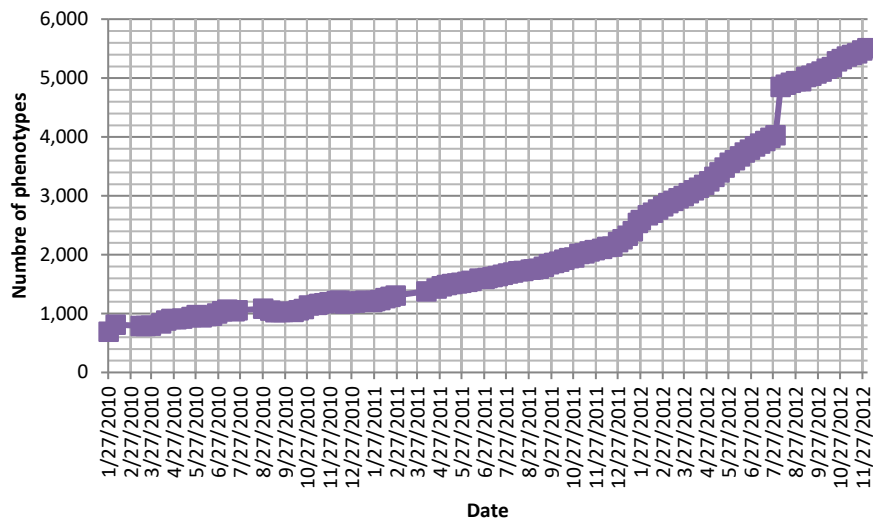
723,195 relationships



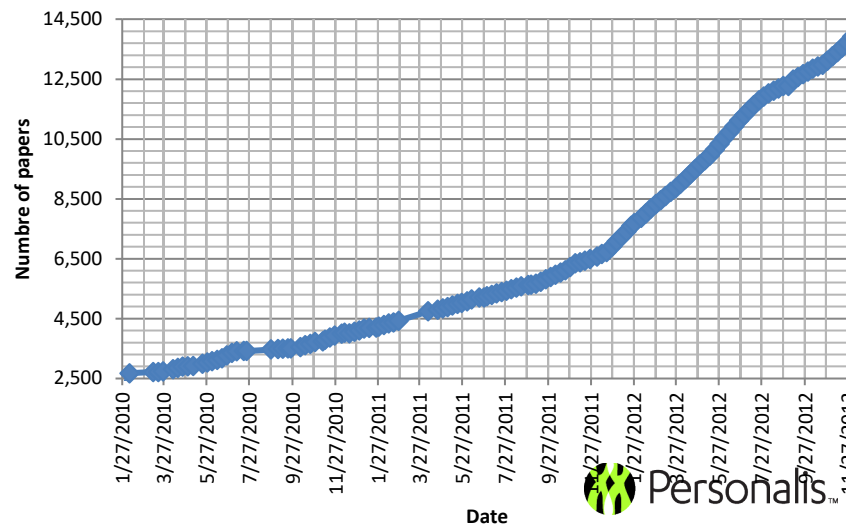
261,861 variants



5,510 phenotypes



13,919 papers



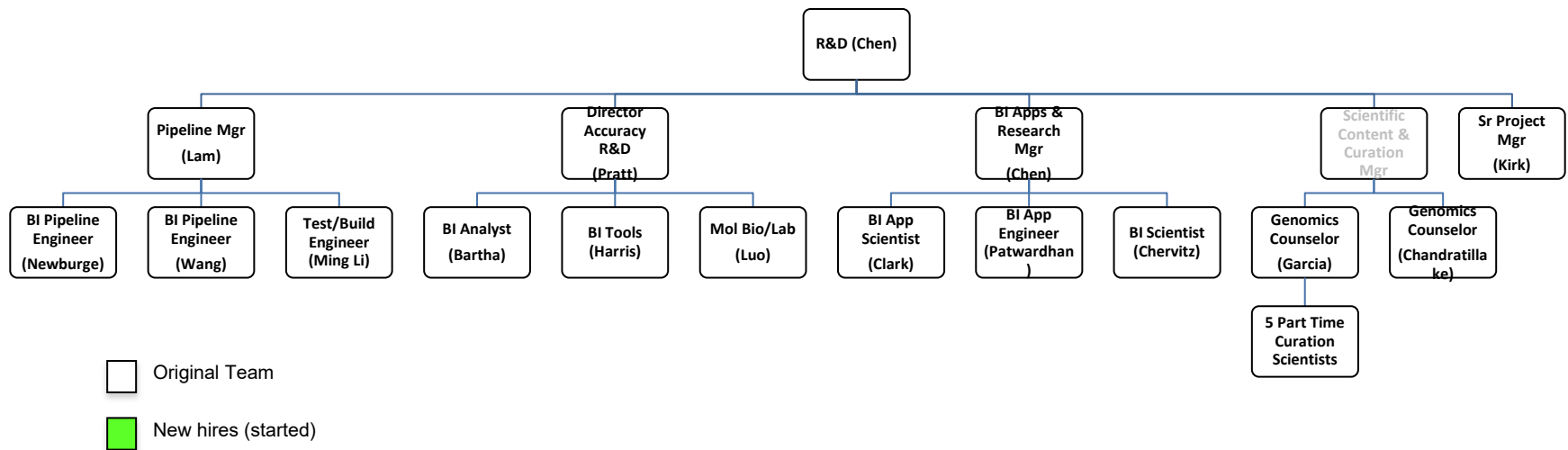
Scientific Computing Infrastructure

- Milestones
 - Installed another 107TB of Hitachi HNAS Storage
 - New backup system currently being installed including disk to disk backup and disk to tape archiving
 - Currently evaluating cost/benefit of cloud implementation with CLIQR
- Hiring is a key challenge:
 - Director of High Performance Computing and Architecture
 - Linux Systems Admin
- Doing a reassessment of scientific computing needs (storage, CPUs) for next 12 months because of recent (good) developments:
 - **Ops: VA project** (processing >300 genomes every 2 months)
 - Ops: Moyamoya and customer projects
 - R&D: Access to very large public genome/exome databases R&D: General R&D needs



Hiring Update

- Open Positions
 - Director of High Performance Computing and Architecture
 - Linux systems admin



ASHG Takeaways

- Huge shift in past year to NGS as the primary discovery research platform in medical genetics community (previously genotyping)
- Increased awareness that having accuracy standards for NGS is critical
 - NIST/FDA (Genome in a Bottle Consortium), CDC, NCBI, CAP
- Also, a large interest in using NGS for clinical
 - Taking place in CLIA certified labs
 - Rare pediatric syndromes most common use case
 - Increasing interest in using NGS to replace current gene panels.

Risks and Mitigation

Risk	Mitigation
• Aggressive timeline	• Minimized “research” features that could result in product delay, focused on achievable, differentiated features for v1
• Pipeline performance risk	• Able to reduce run time per genome from 2 days down to 17 hrs by stacking runs • Assess how we can address with more hardware, cloud
• Product Differentiation	• Prioritized differentiation in three key product areas: Exome+ , SV’s, accuracy/quality, content, visualization • Giving conference talks at AGBT to discuss differentiation, 3 abstracts accepted
• Exome plus costs, may limit margins on product	• Actively working on cost model and ways to reduce cost
• Hiring of Unix sys admin and director of high performance computing.	• Redoubled efforts with in-house recruiter to identify more leads
• Long lead time content curation and content quality items for GIS and DVDS	• Started dev on those items with long lead times to develop concurrently with Pipeline (MendelDB, etc)
• Licensing of applications and content for analysis	• Have systematically reviewing and applied for licenses for key content and algorithms
• Ethical use of Genomes for R&D	• Ethics board approval for all Genomes used for R&D • Part of orientation training

Next Steps & Priorities

- Continue development on PGS v1 priorities with goal of Feb 2013 launch at AGBT
- Execute on product features required for VA project, enable success
- Run biological test cases with the goal of creating success stories for publication, discussion with customers
- Continue implementing DVDS prototype and early test cases/collaborations
- Continue Hiring for open scientific computing positions
- Continue to execute on content priorities, develop longer term content strategy
- Continue to work with OPS team to deliver successes with early customers and collaborators