



SOFTWARE AND SERVICES – THE MISSING LINK FOR CONNECTED THERAPEUTICS

Here, Alexander Dahmani, Co-Founder & Chief Executive Officer, QuiO, explains how the rise of smart devices and connectivity has enabled QuiO to develop ConnectedRx™, the first cloud platform designed for connected therapeutics, and discusses how ConnectedRx™ programmes can be a step towards solving the ongoing problem of adherence.

ADDRESSING THE PROBLEM OF MEDICATION ADHERENCE

Across therapeutic categories and chronic conditions, adherence rates have remained low for decades. This leads to avoidable medical costs, lost pharmaceutical revenue and failed clinical trials.¹ Even with all the attention over time, sustainable and scalable solutions for improving adherence have remained elusive.² An analogy for solving the problem of adherence is the search for a cure for cancer. In point of fact, cancer is actually a collection of hundreds of different diseases rather than a singular condition and, in a similar vein, poor adherence is a multitude of different problematic behaviours.³ In order to actually solve either of these problems, we need to start with detection and characterisation of the specific case at hand.

MISSING LINK: DOSE-LEVEL DETECTION

In order to treat a case of cancer effectively, it must first be detected and characterised. Based on the diagnosis, the correct treatment can then be selected, whether it's surgery, radiation, pharmaceuticals or a combination of the above. We're getting ever better at detecting, characterising and treating cancer,

and a feedback loop exists to continuously improve the treatment selection process based on past outcomes. This system has been lacking for adherence however, because there was no reliable means to detect and characterise poor adherence.

Patient self-reporting and pharmacy refill data are insufficient to support such a system. It's no surprise that people misrepresent their adherence level when self-reporting. It's also a burden for patients to constantly enter in data manually. While pharmacy refill data has been valuable for proving that there is an adherence problem in large observational studies, it doesn't represent a viable option for solving the problem. Picking up a refill on time does not mean the patient took each dose on time, if at all. It is also a lagging indicator of patient behaviour. By the time the pharmacy data

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becomes available for use in calculating an adherence level, the patient has been non-adherent for weeks, if not months.

The optimal means for detecting adherence is at the point of consumption. This is made possible by connected therapeutics. Connected therapeutics refer to pharmaceuticals paired with technologies that enable remote detection of dosing events using sensors and connectivity (Table 1). The most common types are smart devices, including medication containers and drug delivery devices. Figure 1 shows the introduction of smart medication devices over time. It started 10 years ago with medication containers for oral therapies, such as pill bottle caps. The inhaler add-ons were introduced in 2010, and have been deployed at scale across clinical trials and patient support programmes. The most nascent vertical is injectable therapies, with the first devices just now becoming available. You can see in Figure 1 that the rise of connected therapeutic devices closely mirrors the rise of smartphones. This is largely due to the development of low-cost sensors and wireless technology for smartphones, which then becomes available for use in other devices.

The addition of wireless technology to a smart medication device is key, because it allows the device to share its dosing data with remote systems and stakeholders. This means the data can now be used to detect non-adherence in near real-time, and subsequently deliver targeted and personalised interventions. This data also represents an endpoint for measuring the effect of each intervention on adherence, creating a feedback loop that enables continuous improvement of interventions over time.

Container	Add-On	Delivery Device	Other
<ul style="list-style-type: none"> Pill bottle Pill bottle cap Pill tray Pill dispenser Blister packaging Medication storage case Sharps disposable bin 	<ul style="list-style-type: none"> Inhaler sensor Pen injector sensor Pen needle sensor Auto-injector sensor 	<ul style="list-style-type: none"> Inhaler Pen injector Auto-injector Wearable injector 	<ul style="list-style-type: none"> Ingestible smart pill with wearable patch sensor Ingestible smart pill with breath sensor Mobile app with computer vision for confirming pill consumption

Table 1: Types of connected therapeutic solutions currently available.

MISSING LINK: DATA-ENABLED SOLUTIONS

Connected devices and dose-level data are just the first step. Once we can reliably detect adherence, it's still going to require software and clinical services to deliver, track and continuously improve adherence interventions. But who is going to provide such software and services? Many people believe getting the data into the electronic medical record (EMR) and in front of a healthcare professional is the solution. Based on our primary research, physicians are neither willing nor able to take responsibility for the patient outside of the clinic. Rather, they want access to adherence data when the patient is in the clinic in order to make better treatment decisions. Their time is already stretched with diagnosing and prescribing, they don't have any spare time to take on the additional role of remote care services. Healthcare providers also don't have the incentives or resources to become adherence and patient behaviour experts across medications, conditions and patient profiles. That level of expertise and service demands a dedicated, specialised third party.

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Additionally, traditional clinical software is ill-equipped for this task. EMRs represent a static view of patients based on data collected within the clinic. Standard EMR functionality is heavily focused on coding, payments and reimbursement. Care management platforms are basically customer relationship management (CRM) tools for health insurers to communicate with members. This is exemplified by the rise of Salesforce in the care management space. Population health platforms are analytical tools designed for combining EMR and claims data to identify gaps in care and patient segments that represent outliers with regards to utilisation, costs or outcomes.

None of these solutions are designed for, or capable of, continuously collecting data outside the clinic, let alone using that data to remotely monitor and support patients. An opportunity exists for a new kind of solution, one that leverages patient-generated health data and is focused on continuous monitoring and support outside of the clinic. This opportunity is only made possible by the arrival of connected therapeutics.

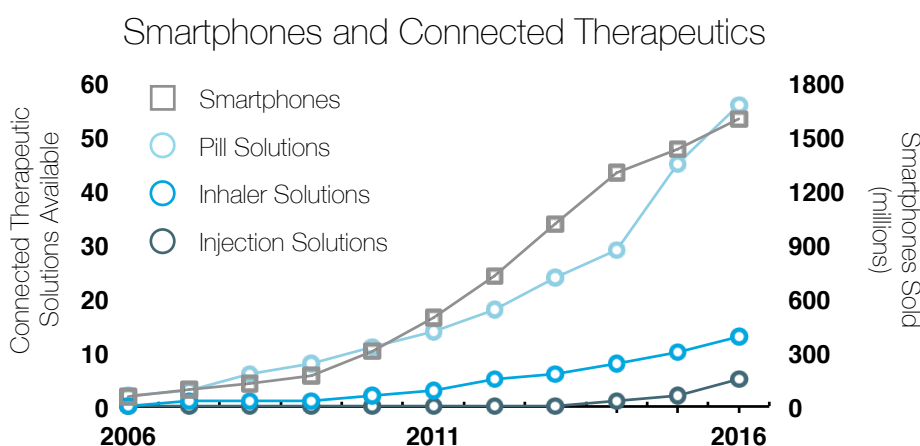


Figure 1: The adoption of smartphones and introduction of connected therapeutic solutions over the past 10 years.

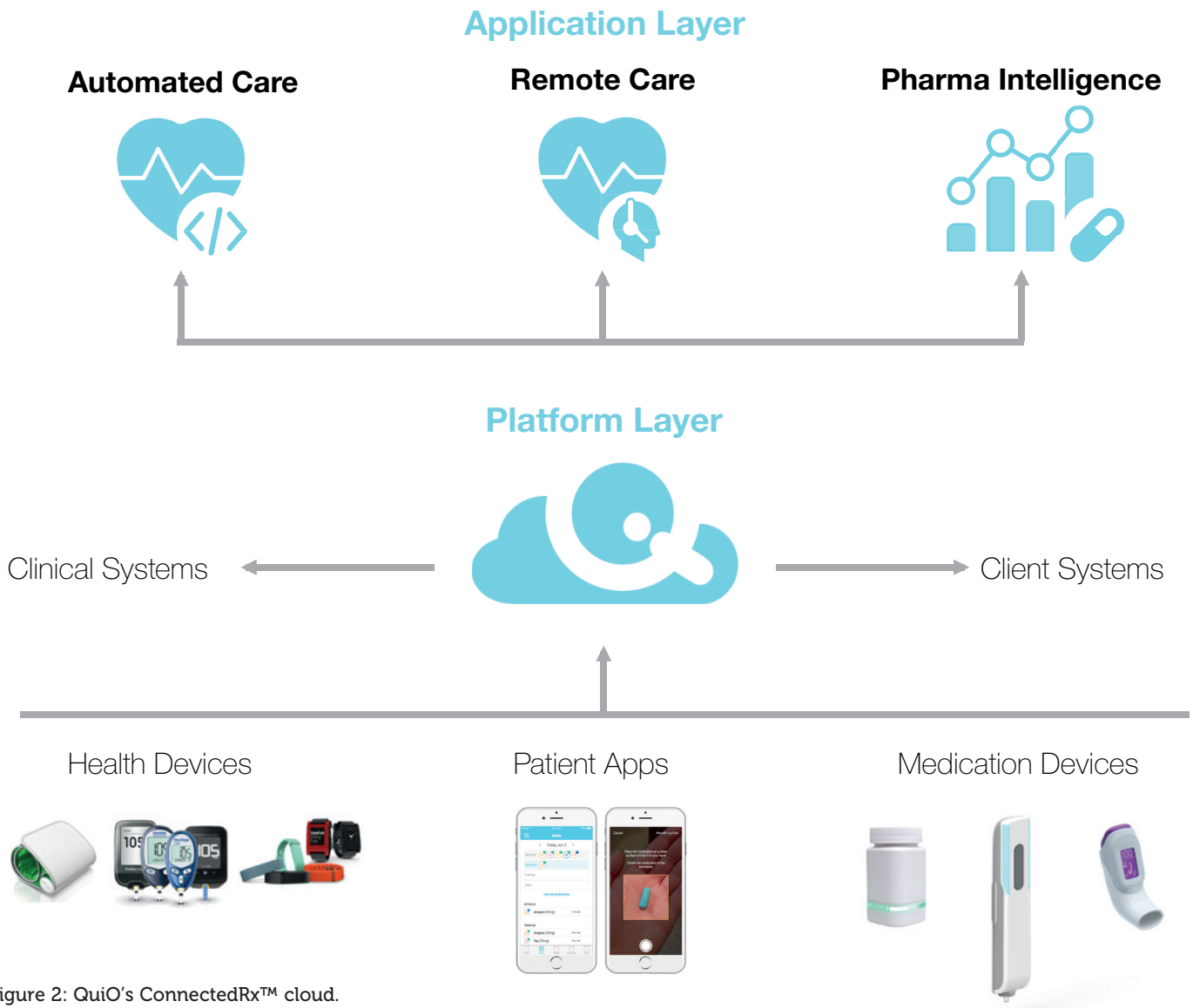


Figure 2: QuiO's ConnectedRx™ cloud.

**CONNECTEDRX™:
A CLOUD SOLUTION FOR
CONNECTED THERAPEUTICS**

The ConnectedRx™ cloud (Figure 2) is a fully managed solution for medical device and pharma companies looking to adopt connectivity. It includes a HIPAA-compliant cloud infrastructure with purpose-built software and services, enabled by patient-level and dose-level data.

Platform Layer

The platform is built from the ground up specifically for secure connected device and patient data management. All the device integrations and software functionality are developed under QuiO's ISO-13485 quality management system. The platform supports companion software use cases ranging from unregulated Medical Device Data Systems (MDDS) up to Class III medical devices. New devices can quickly

be connected to the platform, whether they operate on Bluetooth, WiFi or cellular communication protocols. Over 300 patient monitoring devices have already been integrated, representing a robust ecosystem of connected devices ready for deployment.

The platform is able to structure and securely manage all the data collected from these devices, representing over 40 unique medication and health data points. In addition to connected devices and apps, the platform is compatible with electronic medical record (EMR) data structures, enabling bi-directional communication with clinical systems. Patient data is encrypted within the platform during storage, as well as during transit to and from other clinical or client systems. Most importantly, the platform is designed to meet current and future security and privacy requirements, including HIPAA and GDPR.

Application Layer

The ConnectedRx™ application suite provides the tools and analytics for stakeholders to properly utilise the data collected, including patients, healthcare providers and pharma clients (Figure 3):

- a) **Automated Care**
 - Automated patient communications (app, text, or call) based on medication alerts, with response capture for contextual data.
 - Mobile and web app with features for tracking symptoms, health metrics and multiple medication regimens.
- b) **Remote Care**
 - Stratified patient panel based on device, app and patient response data.
 - Alerts for identifying patients in need of attention.
 - Multi-channel support delivered directly from the web application (in-app chat, SMS or VoIP calls).

c) Pharma Intelligence

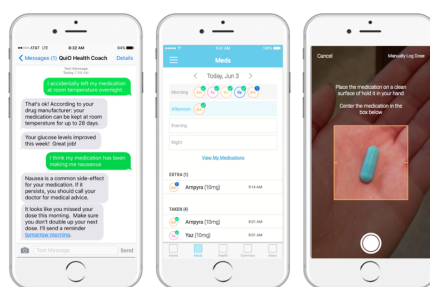
- Anonymised data measuring patient experience, adherence, persistence and health outcomes.
- HIPPA-compliant patient matching with data integrated from EMRs, claims, disease registries and clinical trials.

Pharma clients can choose to offer our own mobile and web app to patients, or we can integrate with the pre-existing patient app of their choice. Our patient app can be transformed into a regulated companion app with therapy specific features by simply entering a unique code supplied to the patient. The code can be distributed with the connected device or prescribed by their physician. Less tech-savvy patients can also choose to receive alerts and information via automated texts and calls instead.

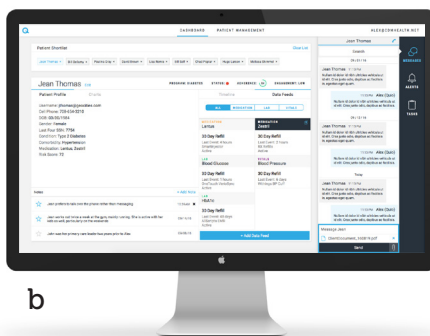
Our automated care service leverages natural language processing (NLP) and interactive voice response (IVR) to accomplish much of the same functionality as the patient app, a feat achieved by capturing patient data through text and voice, respectively. A key benefit of a managed solution like ConnectedRx™ is the continuous improvement in features and functionality. For example, the voice capabilities of our automated care service are being extended into home assistants such as the Amazon Echo. The mobile app experience is also being extended into wearable devices such as the Apple Watch.

Caregivers and clinicians can use the Care Dashboard to monitor and support patients remotely, based on data collected from devices, apps and automated communications. This data enables them to target support to the right patient at the right time. Caregivers can communicate with patients directly from the dashboard, enabling them to review patient data and enter in new data while in contact with them.

Pharma clients can use the Program Dashboard to view the data collected from each patient enrolled in the programme. Data is aggregated, anonymised and



a



b



c

Figure 3: The ConnectedRx™ application suite enables patients to self-manage their health and medications (a), healthcare providers to monitor and support their patients remotely (b), and pharma and device companies to access real-world data and metrics on their therapies (c).

summarised for the client to leverage in a HIPAA-compliant fashion. The Dashboard provides complete transparency into the programme, including how many patients have been enrolled, how many patients are active and the products and services each patient is utilising. Clients are provided valuable, actionable insights they can use to track the real-world performance of their therapeutic product, including adherence rates, persistence rates and patient satisfaction. We can also perform HIPAA-compliant, patient-level matching with third party data sets, including patient registry, EMR and claims data. This enables clients to understand clinical outcomes in the context of dose-level adherence patterns.

Dose-Level Adherence

MedScore™ is our proprietary adherence metric, designed and validated for dose-level data. With the introduction of connected devices capable of collecting dosing data, there needs to be a standard way to measure adherence, just like prescription refill adherence is measured using “proportion of days covered” (PDC) and “medication possession ratio” (MPR). The conventional adherence metrics currently used for dose-level data, such as “percentage of doses taken” (PDT), don’t properly account for the impact dose timing and amount have on therapeutic efficacy.

Figure 4 compares these conventional metrics with our MedScore™, using a twelve dose data set for two patients on a weekly therapy. Both patients received their 90 day supply on time and are considered adherent based on prescription refill data. With dose-level data, you can reveal much more information beyond just the refill date. Conventional metrics don’t calculate adherence level in a clinically meaningful way because they treat late doses, partial doses and missed doses equally, whereas MedScore™ treats dosing mistakes differently by providing distinct weights to these events. It can even be customised for each medication, for example, taking into account its therapeutic index.

As Figure 4 (next page) shows, Patient One missed 25% of the scheduled doses. That significantly diminishes the likely drug efficacy compared with Patient Two, who was more sporadic, but successfully consumed every dose. That’s why Patient One has a much lower MedScore™ than Patient Two. When analysing health outcomes in the context of adherence, Patient One should not be considered more adherent than Patient Two. When limited support resources are a reality, Patient One should receive more time and attention from caregivers. This clinically meaningful metric enables more targeted patient support efforts and more accurate tracking of real-world drug performance, both of which are key for the healthcare system to achieve a return on investment from connected devices.

CONNECTEDRX™ PROGRAMMES: EASY TO ADOPT AND IMPLEMENT

Pharmaceutical Clients

We offer a fully managed solution for pharmaceutical clients interested in

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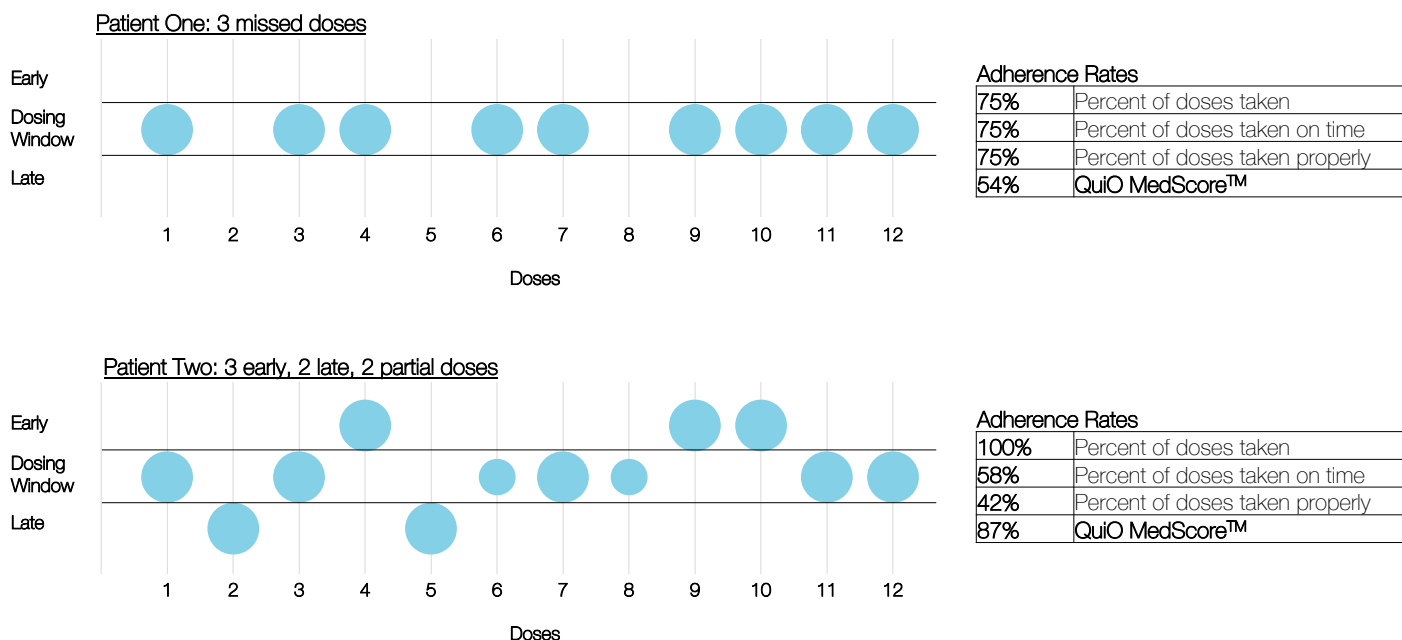


Figure 4: QuiO's MedScore™ compared with conventional adherence metrics. Each blue circle represents a dose taken. Circle size indicates dose size. Circle position indicates dose time.

adopting connected devices. They simply select one or more devices they want to pair with their therapy and we handle the rest. A typical programme starts with customising the patient experience based on the specific therapy and indication(s). The patient experience comprises a mobile app, automated interventions (via app, SMS or phone call), educational content and self-management tools. We also provide our coaching service for enrolment, patient onboarding and high-touch support. Alternatively, we can work with third party service providers, such as speciality pharmacies or support hubs.

Throughout the programme, we provide pharma clients with full transparency into the number of active patients enrolled in the programme, along with their anonymised adherence, persistence and outcomes data. We even provide tools for them to identify and target their support resources to patient subgroups with lower adherence or worse outcomes.

Connected Device Partners

When connected device developers integrate their data into the ConnectedRx™ ecosystem they get the benefits of a fully managed, secure and compliant software stack, designed specifically for connected therapeutics. An example of this is our recently announced partnership with SHL Group. We are integrating their devices into our cloud platform, enabling interested pharma clients to start piloting their connected devices today,

including the ENYA add-on for pen injectors and the Molly® C Recording Unit for auto-injectors.

We enable pharma clients to adopt connected devices easily, without having to build their own software stack or adopt multiple point solutions that don't work well together and require individual maintenance. With ConnectedRx™, device makers can focus on making the best devices possible, pharma clients can focus on getting their innovative therapies into patients' hands and we handle the connected therapeutic experience.

ABOUT THE COMPANY

QuiO is a connected therapeutics company that provides software and services enabled by smart medication devices. The company's solution helps chronic disease patients succeed on long term

therapies, and helps stakeholders track the real-world performance of these therapies.

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2. Choudhry N, Krumme AA, Ercole PM, "Effect of Reminder Devices on Medication Adherence The REMIND Randomized Clinical Trial". JAMA Intern Med, 2017, Vol 177(5), pp 624-631.
3. Neiheisel M, Wheeler K, Roberts ME, "Medication adherence part one: Understanding and assessing the problem". J Am Assoc Nurse Pract, 2014, Vol 26(1), pp 49-55.

ABOUT THE AUTHOR

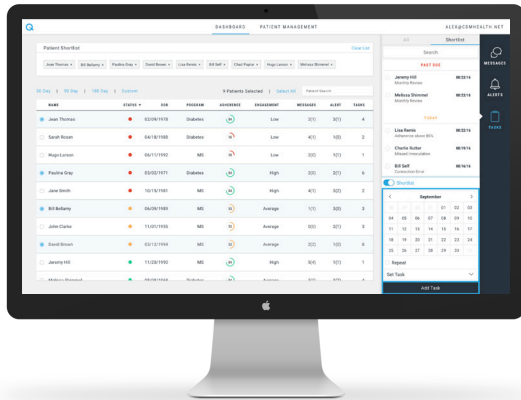
Alexander Dahmani, Chief Executive Officer of QuiO, founded the company in 2014 while pursuing a PhD in Microbiology and Immunology at Columbia University (New York, NY, US). At Columbia, his research focused on human T cell activity using an advanced humanised mouse model. During his PhD he also worked for Columbia Technology Ventures, where he helped review and commercialise new technologies invented on campus, including algorithms, sensors, medical devices and therapeutic molecules. Prior to Columbia, he worked for Heat Biologics (Nasdaq: HTBX), a biotech startup commercialising a novel cellular immunotherapy for multiple cancer indications. Mr Dahmani earned a BS in Genetics with a minor in Business from the University of Wisconsin (Madison, WI, US).



ConnectedRx™

The first cloud solution designed for connected therapeutics

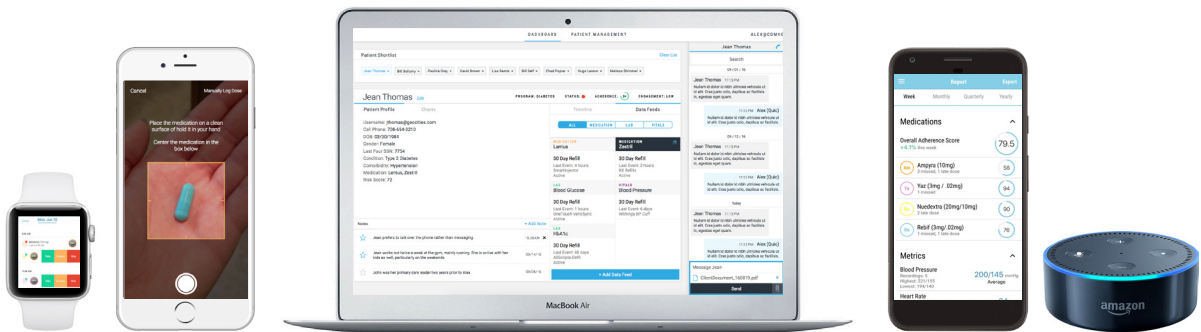
Clinical software for remotely monitoring and supporting patients



Client software for tracking real-world drug performance



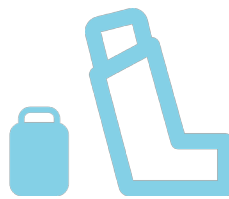
Patient software, services and content for medication and disease management



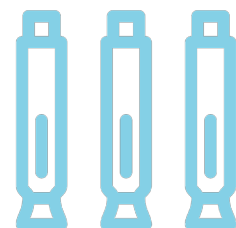
The secure, compliant software stack for all connected therapeutic devices:



Medication Containers



Add-On Sensors



Drug Delivery Devices



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