Strateos™ PLATFORM

High-Throughput Screening (HTS) Overview of Services

Strateos is a pioneer in the development of remote access laboratories and lab control software for life science discovery. The following document contains detailed information regarding our HTS products and services.

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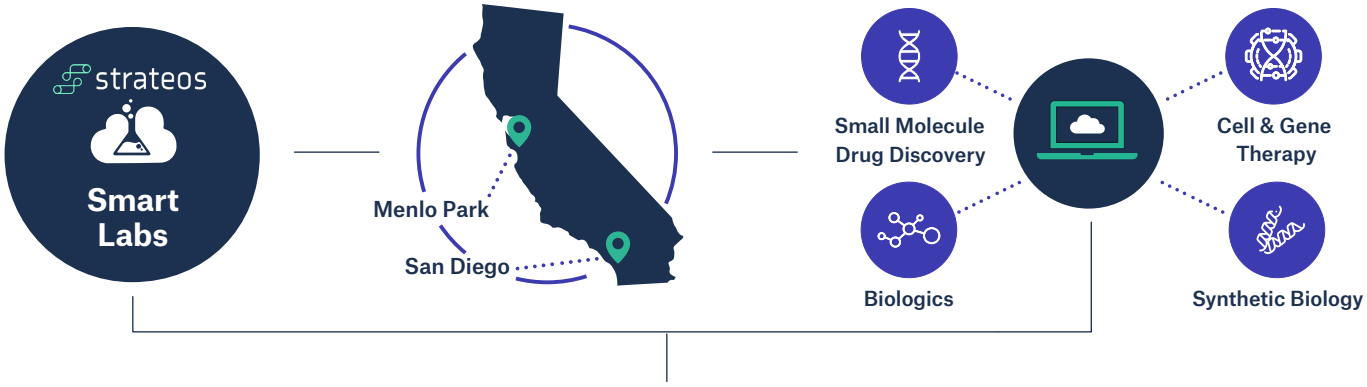
1 | Introduction

Summary of Strateos Platform and Key Capabilities

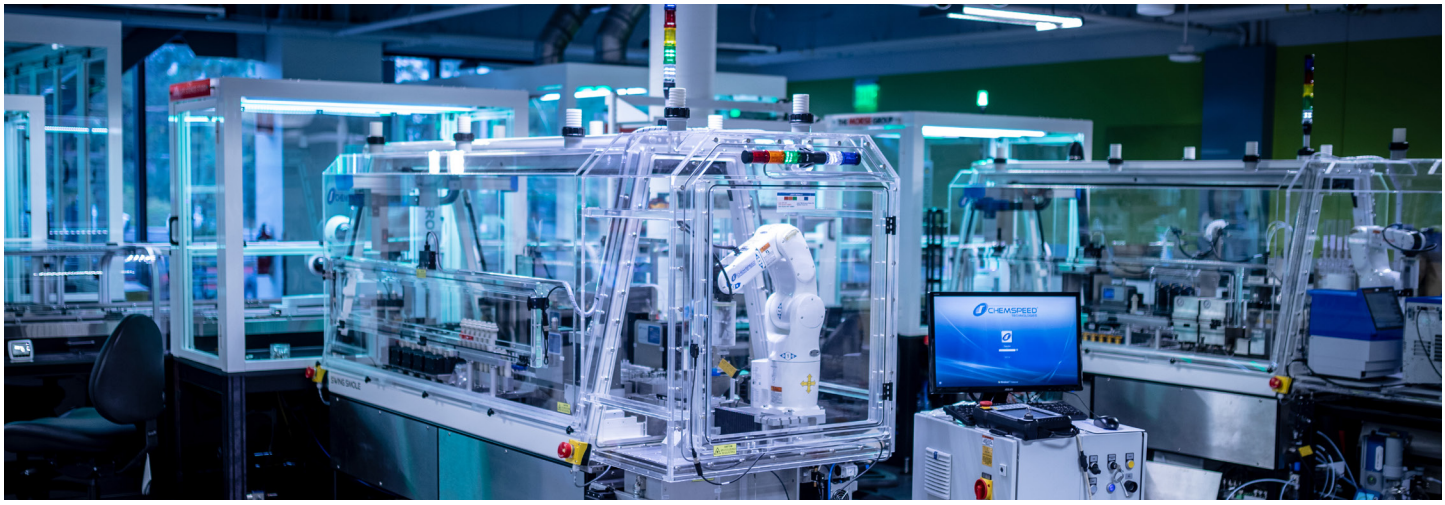
The small molecule drug discovery workflow can be long, complex, and challenging. High throughput screening (HTS) workflows are leveraged for drug discovery campaigns where barriers to in-house execution include significant capital investments, and specialized expertise. Outsourcing to a CRO has been the alternative to investing in HTS infrastructure in-house for many researchers. Strateos offers solutions to enhance the traditional CRO through automation and robotics, enabling scientific organizations to discover and characterize novel drug candidates with greater speed and accuracy.

Small Molecule Drug Discovery and HTS is a key product in our portfolio of life sciences solutions



Strateos smart labs are located in San Diego and Menlo Park, California. The labs collectively span 14K sq. ft. with >200 instruments and 25 Automation Modules tailored to application needs in the areas of small molecule drug discovery.

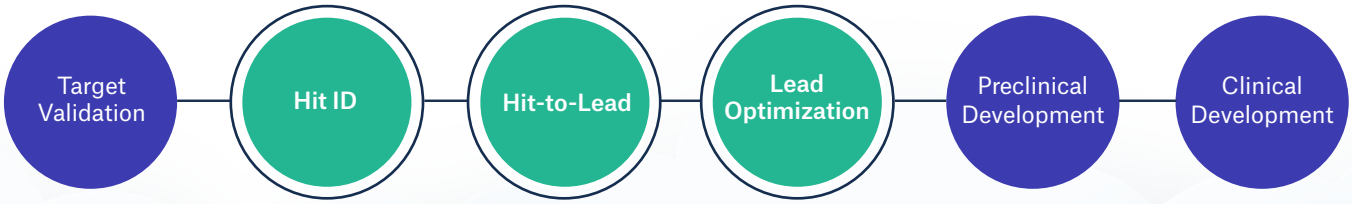
Strateos physically and virtually integrates drug discovery, creating a state-of-the-art automated platform



Medium throughput and high throughput screening (MTS/HTS) of small molecules are offered in a reproducible and agile manner with integration of over 200 instruments through 25 automation modules powered by robotics and software, allowing for a multitude of screening and profiling assays using 384- and 1536-well plates to support every stage of the HTS drug discovery continuum.

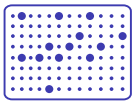
Strateos Platform Value Propositions

- Idea to data becomes agile, fast, and purely operating expense
- Access to robotic scale and novel instrumentation
- Programmatic and closed loop control of the lab
- Massive reduction in fixed capital assets, much more flexibility
- Facilitates collaboration
- Improved reproducibility
- Faster cycle times



Our integrated small molecule discovery workflows for hit ID, hit-to-lead, and lead optimization studies combined with unparalleled scope of capabilities in robotics and automation allow us to deliver quality hits that progress to lead candidates.

Small Molecule Drug Discovery - HTS Workflows and Services

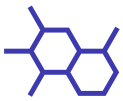


Assay Onboarding & Development

- Bring your assay or save months in development time and use our biochemical, phenotypic and cellular assays for off-the-shelf primary screening, hit confirmation, selectivity, and orthogonal testing

Miniaturization & Automation

- Miniaturize assays for reduced costs, quicker screening times, and leverage our automated laboratory for rapid exploration of large compound libraries



Hit Identification

- Bring your own compound library or use one of our libraries in a platform that combines a comprehensive range of HTS screening technologies including fluorescence intensity, TR-FRET, luminescence, BRET, absorbance, fluorescence polarization, AlphaScreen®, AlphaLISA®, qPCR, mass spectrometry assays and more
- Screen up to 100,000 compounds per day and rapidly identify active compounds

Hit Triaging and Characterization

- Characterize hits for desired biological activity and drug-like properties through the generation of near real-time datasets or collaboratively with our in-house expertise

Hit-to-Lead and Lead Optimization

- Select the most promising hits for lead identification and leverage automated chemical synthesis workflows for faster experimental screening cycles, decreased duration and hands-on-time, reducing the overall drug discovery timeline leading to promising preclinical candidates

Representative Hit Identification Workflow

CUSTOMER ONBOARDING
Custom Assay Development or Assay Transfer, or Off the Shelf Assay

▼

INTAKE AND ASSAY VALIDATION
Assay Feasibility, Miniaturization and Optimization

▼

HTS CAMPAIGN
Single Point Screen

▼

RETESTING AND CONFIRMATION
Retesting and Orthogonal Assays

▼

CHARACTERIZATION
Selectivity, and Secondary Assays

▼

HITS
DRC in Assays, IC50, EC50, 8pt dilution n=2

▼

CONFIRMED HITS
Hit List

Example of Client Onboarding, Execution and Key Milestones

On-boarding

- Feasibility assessment
- Quote acceptance
- SoW finalized
- Approval to transfer assay

Assay Development

- Initiate assay development/ biovalidation phase
- Assay development
- Control validation

- Plate optimization complete
- Autoprotocol code complete
- Pilot screen conducted
- Data analysis & client review meeting
- Approval to initiate primary screen

Primary Screening

- Conduct primary screen
- Perform screen QC
- Data analysis and screening metrics

- Primary screen report generation
- Client review meeting
- Approval to initiate hitpicking

Hit Confirmation

- Receipt of hit pick plates
- Perform single point confirmation screening

- Complete potency screening
- EC50 data analysis and client review meeting
- Approval to reorder stock compounds

Potency Determination:

- Receive compounds
- Complete additional follow-on DRC screening

- Final report generation
- Project finalization approval:

2 | Assays and Readouts

Summary of Assays and Readouts

- Cell-based, phenotypic and biochemical assay development and execution
- 384- and 1536-well plate compatibility
- Homogeneous and heterogeneous assay capabilities
- Luminescence, fluorescence, and TR-FRET readouts
- Threshold of one hundred 1536-well plates per day (equivalent to approximately 140K compounds per day) for simple cell-based and biochemical screens

Hit Finding Approaches

Phenotypic	Biochemical	GPCR	Ubiquintation
PPI	Protease	Transporter	Phosphodieterase
Ion Channel	Enzymatic	Nuclear Receptor	**And Many More**

Screening and Profiling Capabilities

Screening & Profiling Assays

- Compound screening ADP-Glo
- Compound screening UDP-Glo
- Compound screening Alpha
- Compound screening Lance
- Compound screening TR-FRET
- Compound screening fluorescence
- Quenching
- Protease assays
- Dual-Glo luciferase
- Luciferase reporter assay
- Enzymatic assays
- Non-radioactive binding assays
- Immunoassays
- Thermal shift assay
- Protein-protein interaction assays

Cell Based Assays

- Flow Cytometry - 14 color flow
- CellTiter Glow
- Measurement of intracellular [Ca++]
- Intracellular second messengers (cAMP, IP1)
- Cell proliferation, Cytotoxicity
- Reporter assays
- Protein expression/secretion
- Intracellular protein phosphorylation
- Biomarker detection (MSD, qPCR, NGS)
- Expression analysis (NGS, qPCR)
- Flow cytometry (proliferation, cell cycle, viability, apoptosis, surface markers, etc.)

ADME

- Kinetic solubility

Label-free (Mass Spec)

- Rapid fire (HDAC, etc.)

Kinase Assays

- Kinase panels (40)
- HTRF KinEASE-STK
- HTRF KinEASE-TK

3 | San Diego Smart Lab

Automation Modules and Capacity Summary

Testing Module	Capability	Format	Throughput
TST-1	Biochemical Assays, SAR, MTS	96/384	50 plates/day
TST-2	Setup plates for TST6	96/384	20 plates/day
TST-3	Biochemical and cell-based assays, SAR, MTS, HTS	96/384/1536	70 plates/day
TST-4	Biochemical and cell-based assays, SAR, limited MTS	96/384	20 plates/day
TST-5	Biochemical and cell-based assays, SAR, MTS, HTS	96/384/1536	100 plates/day
TST-6	Label-free, affinity selection mass spectrometry(ASMS), RapidFire	96/384	20 plates/day

San Diego Strateos Platform enabling seamless end-to-end laboratory workflows

The custom-engineered MagneMotion track based layout combined with Strateos' scheduling/execution software system integrates and automates the drug discovery process, contextualizing data with the following features:

- Robot transfers to bring samples from track to modules
- Automated high density consumable storage module
- Input / Output module to label and accept sample containers
- Under track utility infrastructure provides power, water, air, exhaust, and various gases to each module
- Video surveillance system throughout the lab and within the track for monitoring of samples in process
- Solvent delivery system supplies solvents to the required modules from a central distribution room in bulk containers

Capabilities by HTS Automation Module

TST-1 | Biochemical Assay Module

- **Format: 96 and 384 well**
- **Throughput: 50 plates/day**
- **Automated Equipment**
  - Formulatrix TEMPEST and BioTek MultiFlo dispensers
  - BMG PHERAstar® FSX multimode plate reader
  - Labcyte Echo® 655T acoustic dispenser
  - Thermo Multidrop Combi dispenser
  - BioNex HiG™ centrifuge
  - KBiosystems Wasp sealer and Brooks XPeel®

TST-2 | Analytical Testing Module

- **Plate configuration and assay setup for TST-6**
- **Set up for RapidFire assays**
- **Set up for Tier 1 ADME assays**
  - Kinetic solubility
  - LogD
- **Sample preparation for affinity selection mass spectrometry (ASMS)**

TST-3 | Biochemical & Cell Based Assay Module

- **Format: 96, 384 and 1536 well**
- **Throughput: 70 plates/day**
- **Automated Equipment**
  - Formulatrix TEMPEST and BioTek MultiFlo dispensers
  - BMG PHERAstar® FSX multimode plate reader
  - Labcyte Echo® 655T acoustic dispenser
  - BioNex HiG™ centrifuge
  - KBiosystems Wasp sealer and Brooks XPeel®
  - LiCONiC automated incubators for 37°C and ambient incubation
  - HRB Lid Valets
  - Hamilton NIMBUS384 pipetter
  - BSL2 compliant

Capabilities by HTS Automation Module contd.

TST-4 | Biochemical & Cell Based Assay Module

- **Format: 96 and 384 well**
- **Throughput: 20 plates/day**
- **Built for prolonged kinetic assays**
- **Automated Equipment**
  - Tissue culture and media changing
  - LiCONiC automated incubator for 37°C
  - Hamilton STAR
  - BioTek Neo2 plate reader
  - BSL2 compliant
  - BioTek 405 dispenser/washer

TST-5 | Biochemical & Cell Based Assay Module

- **Format: 96, 384 and 1536 well**
- **Throughput: 100 plates/day**
- **Automated Equipment**
  - GNF Washer Dispenser II (qty 2)
  - Weigh station
  - Formulatrix TEMPEST and BioTek MultiFlo dispensers
  - BMG PHERAstar® FSX multimode plate reader
  - Labcyte Echo® 655T acoustic dispenser
  - BioNex HiG™ centrifuge
  - KBiosystems Wasp sealer and Brooks XPeel®
  - Cytomat™ automated incubators for 37°C and ambient incubation
  - HRB Lid Valets
  - BSL2 compliant

TST-6 | High Throughput Label-Free Assay Module

- **Format: 96 and 384 well**
- **Throughput: 20 plates/day**
- **Assay Types**
  - ADME
  - Label-free enzymatic assays
  - Affinity Screening by Mass Spec (ASMS)
- **Automated Equipment**
  - Agilent QQQ + RapidFire
  - Thermo Q-Exactive™

4 | Menlo Park Smart Lab

The Menlo Park facility is a deeply integrated technology stack of biology, robotics, automation and software that flexibly supports multiple biochemical and cell based assay types.

This allows for the ability to monitor the lab and instrument environment in real time as well as collect metadata to allow for experimental optimization and troubleshooting, ensuring the quality of experimental design and execution

Capabilities by HTS Automation Module

WC4 | Biochemical & Cell Based Assay Module

- **Automated Equipment**
  - BioNex HiG™ 4 Centrifuge
  - Tecan Infinite® M200 pro plate reader
  - Agilent Bravo multi-channel liquid handler
  - Tecan Cavro® ADP single-channel liquid handler
  - Bio-Rad CFX96 thermocycler
  - Bio-Rad CFX384 thermocycler
  - Thermo Fisher ALPS 3000™ Plate Sealer
  - Tiso* incubators 37°C (qty 2)
  - Tiso* incubator 4°C

WC5 | Biochemical & Cell Based Assay Module

- **Automated Equipment**
  - Agilent Bravo multi-channel liquid handler
  - BioNex HiG™ 4 centrifuge
  - Tecan Infinite® M200 pro plate reader
  - Tecan Cavro® ADP Single channel liquid handler
  - Bio-Rad CFX96 thermocycler
  - Bio-Rad CFX384 thermocycler
  - Thermo ALPS 3000™ plate sealer
  - Tiso* incubator 37°C
  - Tiso* incubator 4°C

*Proprietary to Strateos

Capabilities by HTS Automation Module contd.

WC6 | Biochemical & Cell Based Assay Module

- **Automated Equipment**
  - BlueCatBio Blue®Washer
  - Agilent Bravo multi-channel liquid handler
  - Tecan Infinite® M200Pro
  - Tecan Cavro® ADP single channel liquid handler
  - Bio-Rad CFX96 thermocycler
  - Bio-Rad CFX384 thermocycler
  - Thermo ALPS3000™ plate sealer
  - INHECO Thermoshake
  - Tiso* incubator 4°C
  - Tiso* incubator 37°C
  - Agilent Bravo multichannel liquid handler

WC7 | Biochemical & Cell Based Assay Module

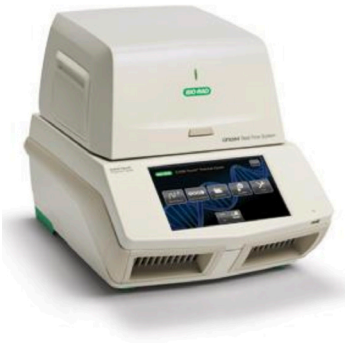
- **Automated Equipment**
  - Perkin Elmer EnVision® plate reader
  - BioNex HiG™ 4 centrifuge
  - Tecan Infinite® M200 Pro plate reader
  - Thermo Fisher Multidrop Combi
  - Precise Automation PF400
  - Formulatrix® TEMPEST® Liquid Handler
  - Brooks XPeel®
  - Labcyte Echo® 525

*Proprietary to Strateos

5 | Key Capabilities by Instrument Type

Bio-Rad CFX96 and 384 qPCR Instruments

The CFX Touch Real-Time PCR Detection System is a powerful and precise real-time PCR instrument in 96-well and 384-well formats, for researchers who require both ease of use and rapid, high-throughput data acquisition. The CFX Touch System utilizes accurate temperature control and sensitive, 4-color detection optics to deliver reliable and repeatable qPCR results for singleplex or multiplex reactions.



Optical Detection

Excitation	5 filtered LEDs
Detection	5 filtered photodiodes
Range of excitation/emission wavelengths, nm	450–690
Dynamic range	10 orders of magnitude

Gradient

Operational range, °C	30–100
Programmable span, °C	1–24

Additional Information

Throughput	96 and 384 well plates
Assay Types	RT-qPCR, Thermal Stability Assay- Thermal Melt and Kinetic stability

Perkin Elmer EnVision®

Designed to give optimized performance in all major multilabel reading applications including reporter gene assays, cell applications, genotyping, enzyme assays, signal transduction, receptor ligand binding, imunnoassays, and quantification, also capable of fluorometry, fluorescence polarization, TR-fluorometry, luminometry, and photometry, features 96-well, 384-well and 1536-well capabilities, high speed dual emission reading, high throughput light source, and top/bottom reading modes for fluorescence.

Detection Modes

- AlphaScreen® and AlphaLISA® Technology
- Fluorescence Intensity
- Fluorescence Polarization

- AlphaScreen® and AlphaLISA® Technology
- Fluorescence Intensity
- Fluorescence Polarization

Measurement Modes

- Supports all main non-radiometric technologies with kinetic and scanning measurements, bottom-reading
- Supports a wide range of filters and dichroic mirrors

Throughput

The maximum throughput for these readers are as follows (single reads):

- 96-well plates are 22 seconds
- 384-well plates are 27 seconds
- 1536-well plates are 36 seconds

Spectral range

- The EnVision with Monochromators enables the user to measure any chromophoreor fluorophore at any wavelength in 0.1 nm increments within the operational wavelength range.
- The range in fluorescence measurements is 230-850 nm, and up to 1000 nm in absorbance assays.

Temperature Control

To ensure reproducibility of cellular and enzyme kinetic assays and other assays that require a defined temperature range, the EnVision platform's temperature control option lets you precisely regulate from +2°C to +45°C above ambient. Temperature control is uniform across the plate, and a top heating plate eliminates condensation problems

BMG PHERAstar® FSX

A multimode plate reader with assay-optimized Optic Modules which contain all application-specific filters, mirrors, dichroics and/or polarizers, and are automatically recognized by the plate reader. In addition, the PHERAstar FSX is equipped with four matched and assay-optimized photomultiplier tubes (PMTs) which are automatically selected for the relevant detection mode. It can also measure assays with two emission wavelengths at the same time using the Simultaneous Dual Emission.

Detection Modes

- Fluorescence intensity - incl. FRET
- Fluorescence polarization
- AlphaScreen®/AlphaLISA®/AlphaPlex™
- Luminescence (flash and glow) - incl. BRET
- Time-resolved fluorescence
- TR-FRET
- UV/Vis absorbance spectra

Measurement Modes

- Top and bottom reading
- Endpoint and kinetic
- Sequential multi-excitation
- Sequential multi-emission
- Simultaneous Dual Emission
- Spectral scanning (absorbance)
- Real-time ratiometric measurements
- Well scanning

Light Sources

- High energy xenon flash lamp
- Dedicated laser for AlphaScreen®/AlphaLISA®/ AlphaPlex™
- Dedicated laser for TRF and TR-FRET

Spectral Range

Filters:
- 230 - 750 nm or 230 - 900 nm for FI, FP
- 230 - 750 nm for LUM
- 230 - 900 nm for TRF

Spectrometer:
- 220 - 1000 nm for ABS

Tecan Infinite® 200 PRO

Designed to give optimized performance in all major multilabel reading applications including reporter gene assays, cell applications, genotyping, enzyme assays, signal transduction, receptor ligand binding, imunnoassays, and quantification, also capable of fluorometry, fluorescence polarization, TR-fluorometry, luminometry, and photometry, features 96-well, 384-well and 1536-well capabilities, high speed dual emission reading, high throughput light source, and top/bottom reading modes for fluorescence.

Capabilities

- Absorbance
- Absorbance spectra
- Fluorescence (top & bottom)
- Fluorescence spectra (top & bottom)
- Time-resolved fluorescence (TRF)
- FRET
- TR-FRET
- Fluorescence polarization (FP)
- Luminescence (glow, flash, multicolor)
- TR-FRET
- Fluorescence polarization (FP)
- Luminescence (glow, flash, multicolor)
- Automated pathlength correction
- Absorbance cuvette port
- NanoQuant Plate™
- Temperature control (RT +5°C to 42°C)
- Plate shaking (linear and orbital)
- Te-Inject™ reagent injectors
- QC tools for IQOQ services
- Connect™ microplate stacker
- ELISA
- DNA/RNA quantification
- Nucleic acid labeling efficiency
- Protein quantification
- ATP quantification
- Ca2+ detection
- HTRF®, DELFIA®, LanthaScreen®
- Transcreener®
- PolarScreen®
- GeneBLAzer®
- DLR®
- BRET (including NanoBRET™)

Read Times

Fastest Read Times	• 96-well plate 20 sec • 384-well plate 30 sec Wavelength Ex / Em-scan • 96-well plate 450 – 550 nm, 5 nm step 150 sec

Spectral Range

Fluorescence sensitivity	Values Infinite F configurations Infinite M configurations
Fluorescence top reading	85 amol / well (100 µl, 384-well plate) 170 amol / well (100 µl; 384-well plate)
Fluorescence bottom reading	5.0 fmol / well (200 µl; 96-well plate) 9.0 fmol / well (200 µl; 96-well plate) TRF 2) 2.8 amol / well (100 µl; 384-well plate) 90 amol / well (100 µl; 384-well plate) FP 1) < 4 mP standard deviation @ 1 nM Fluorescein N/A

Luminescence Sensitivity Values

Glow luminescence	225 amol ATP / well (25 µl; low volume 384-well plate)
Flash luminescence	12 amol ATP / well (55 µl; 384-well plate)
Absorbance Ratio Accuracy	260 / 280 nm ± 0.07 Precision @ 260 nm < 0.2 % Accuracy @ 260 nm < 0.5 % Measurement range 0 – 4 OD

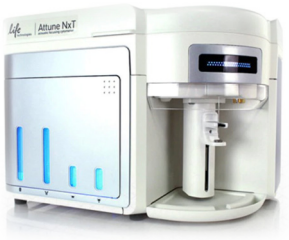
FLIPR Tetra High-Throughput Screening System

The FLIPR Tetra System supports a wide range of assay kits such as GPCRs using Calcium kits and Ion Channel assays using optogenetics, Membrane Potential, Calcium, and Potassium kits. Cardiomyocytes can also be used to evaluate compound effects earlier in the drug discovery process

Specifications

Throughput	Simultaneous liquid transfer to approximately 2,000 cells per well in a 1536-well plate is achieved using a proprietary, contact-based elastomeric technology. Further optimize speed with our Advanced Workflow Engineering Solutions team.
Optics	Two camera options— standard for fluorescence only, or aequorin for both fluorescence and luminescence
Supported Assays	• GPCR • Membrane potential • Cardiomyocytes • Potassium • Ligand gated calcium channels • Optogentics • Aeqourin

Attune NxT Flow Cytometer



The Attune NxT Flow Cytometer is ideal for immunophenotyping and signaling studies, cell cycle analysis, detection of rare events, stem cell analysis, cancer and apoptosis studies, microbiological assays, and more.

Capabilities

- True 35,000 event/sec (+10% coincidence rates)
- Maximum electronic speed of 65,000 events/sec
- Analyze small or limited samples faster than ever
- 96 well autosampler

Additional Information

- Efficiently run traditionally long assays
- Flexibility—1 to 4 lasers, 14 colors, and 16 parameters
- Flexibility in sample concentrations & sample types
- Elimination of time-consuming concentration steps with No-Wash, No-Lyse Filter Kit

High Throughput Agilent RapidFire 400/ Agilent 6495C Triple Quad LC/MS

The Agilent RapidFire 400 is an integrated autosampler for ultrafast sample cleanup based on automated solid phase extraction (SPE) and introduction to mass spectrometry. Designed for highest-throughput laboratories, the large capacity, temperature-controlled, 1536 well-plate handling robot allows unattended weekend operation with sample injection times as short as 2 seconds. RapidFire 400 builds on successful previous models, combining more than 14 years of high-throughput mass spectrometry innovation.

The 6495C Triple Quadrupole LC/MS system is the highest performance LC/TQ available, and is ideally suited for peptide quantitation as well as applications that require ppt sensitivity. The combination of utmost sensitivity, extended mass range, ease of maintenance, and the power and flexibility of MassHunter makes this the system of choice for demanding applications.

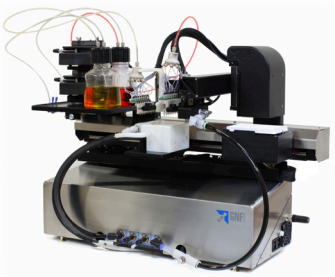
Agilent RapidFire 400 Key Features

- Robot can be used with Agilent triple quadrupole, time-of-flight, and quadrupole time-of-flight mass spectrometers, using a single control software
- Integrating the Ultivo LC/TQ into the RapidFire 400 footprint saves valuable lab space
- Enables different assays in a single batch based on innovative fluidics using proven Agilent 1260 Infinity II quaternary pumps
- Ultra-fast data acquisition reduces data acquisition from minutes to seconds by eliminating chromatography
- Large sample capacity allows longer unattended runs with storage for 138,240 samples in 1536-well plates
- Temperature-controlled sample storage unit stores samples longer without compromising integrity
- Integrated plate handler robot simplifies batch configuration
- Barcode reading ensures sample integrity and tracking from loading to analysis
- With less than 0.5 mL of solvent per sample required and SPE cartridges reusable for thousands of samples, solvent use and waste generation are substantially reduced

Agilent RapidFire 6495C Triple Quadrupole LC/MS Key Features

- Most sensitive Agilent LC/TQ delivers confidence into the ppt range and beyond
- Reliability to match performance with a 3rd-generation all-metal iFunnel design
- Wide mass range of m/z 5-3,000 gives you the flexibility to handle any MRM transition
- Vent-free ion source maintenance with VacShield technology
- Screen, confirm, and quantify with triggered MRM (tMRM), which acts like normal MRM until it sees your compound, then instantly expands to generate a product ion spectrum perfect for a library search to confirm

GNF Washer/Dispenser II

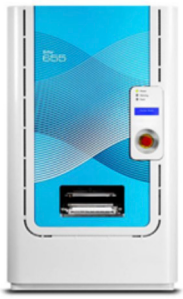


The GNF Systems WDII represents the gold standard in liquid dispensing and aspiration technology for microtiter plates. Available configured as either a bench-top device or integrated into a GNF Systems automation platform, the WDII combines the finesse needed to successfully perform sensitive assays while still providing the throughput required for demanding screens.

Specifications

Dispense Volumes	Minimum 0.5 uL, CV < 5%
Aspiration	16- or 32-pin heads available & control over aspiration heights, velocities, dwell times, and vacuum flow rates
Dispense Heads	Two user-swappable heads (8 tips each), angled or straight

Labcyte Echo® 655



Next generation high-throughput system: Fastest transfer speed available for Acoustic liquid handling | Enables assay miniaturization in a broad range of applications | Transfer from 384-well and 1536-well microplates | Accurate, precise, contact-free acoustic transfer in volumes as low as 2.5 nL.

Specifications

Drop Volumes	2.5 nL
Volume Transfer Range	2.5 to 10,000 nL (the range is dependent on the fluid type, assay, and source plate used)
Transfer Accuracy	<10% deviation from target volume
Transfer Precision	<8% CV (excluding protein crystallography fluid class)
DMSO Hydration Accuracy	<8% deviation from target
DMSO Hydration Precision	<5% CV
Source Labware Compatibility	All ECHO qualified 384- and 1536
Destination Labware Compatibility	96-,384-,1536-well, low profile and standard height, user-definable

6 | Data Analysis

Data Analysis Overview

It is our goal to provide customers with highly robust and reproducible results. To achieve these goals, we employ state of the art robotic platforms directed through a web-based software interface. This interface instructs the robotics to perform assay tasks in a rapid, yet highly reproducible manner. As in any experimental setting, however, the quality of screening results is highly dependent on many factors including the complexity of the assay, the quality of the reagents, the screening format, and more.

Our reports offer quantitative summary of the results obtained on your behalf. It includes details collected throughout the different stages of the screening process and may include the following information, if appropriate:

- Assay overview and screening objectives (e.g., inhibitory screen, up-regulation, target type, etc.)
- Exact assay protocol conducted including lot numbers for reagents
- Description of any cell lines used along with culturing conditions and lot numbers
- Plate layout including location and number of controls
- Equipment and consumables employed during the screening process
- Details regarding the library screened, assuming it was provided by Strateos
- Screening statistics summarizing successful and failed results
- Representative heat maps of the plate-based screening results
- Potency determination and representative EC50 curves
- Lists of all data files provided to the client

Screen Quality Control

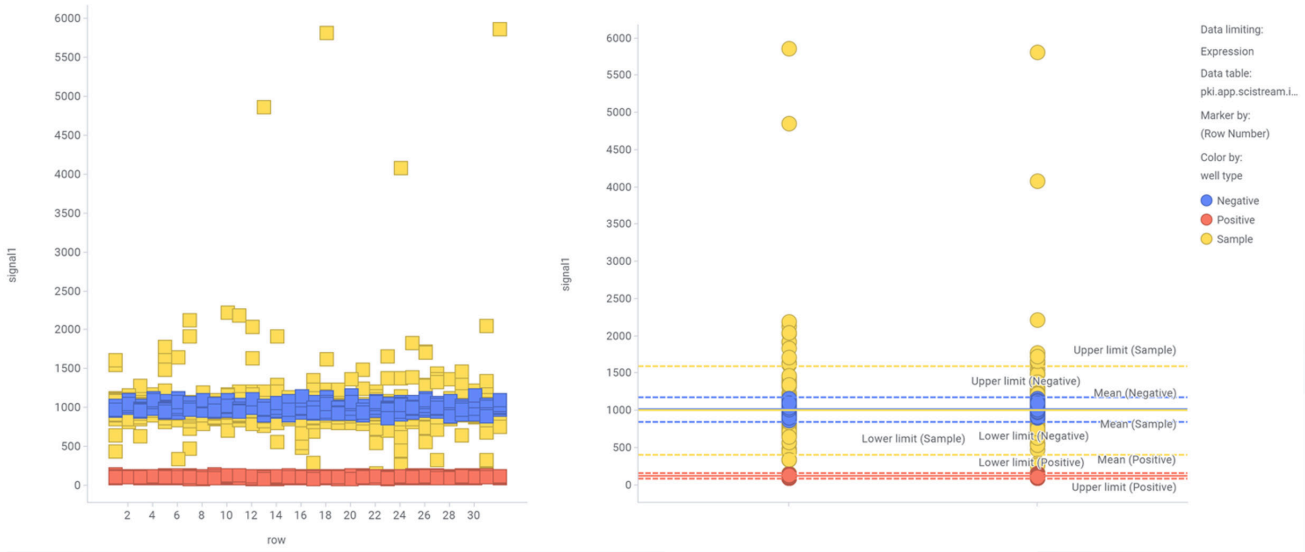
Throughout the full execution of a screen, multiple statistical parameters are monitored watching for deviations in plate CV, SNR, and Z-prime measurements. As with any mechanical device, errors can occur during use, and it is important to us to identify any such errors quickly during a screening program. Therefore, we are constantly monitoring screen progression with a particular eye towards common errors such as tip clogging, evaporative edge effects, signal loss over time, along with a host of other events that can negatively affect the quality of data. Below is an example of 100 microtiter plates that were used to complete both the primary and confirmatory screens.

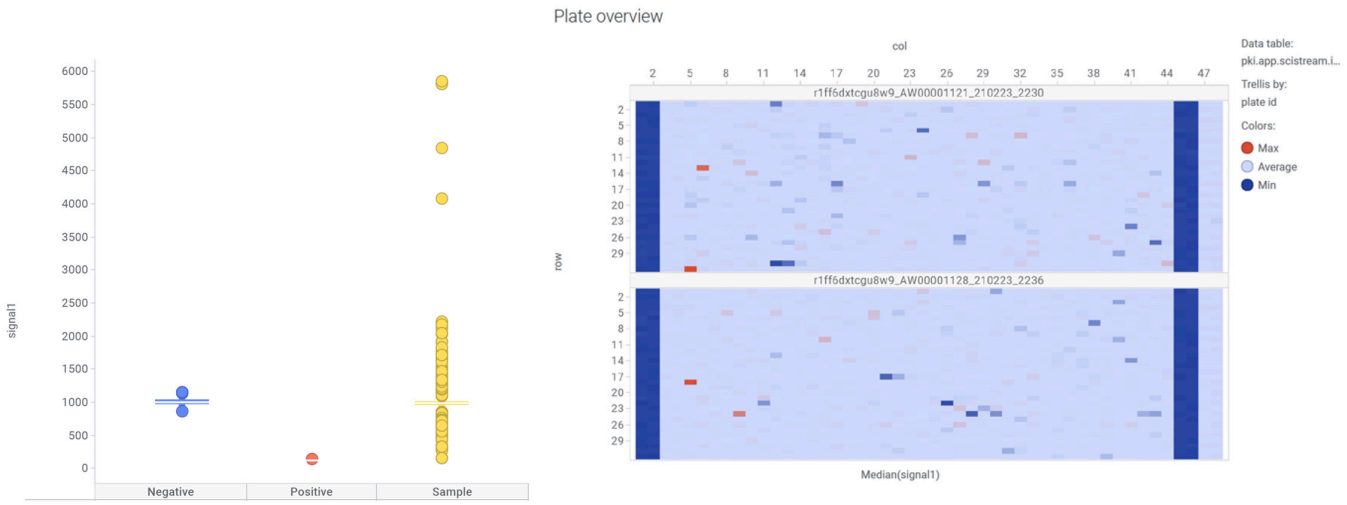
Screen Performance

Primary Screen

We screened 100,000 chemicals from the ChemDiv Diversity library at a final concentration of 5 µM in 1% DMSO in a single-compound, single-well format with control wells containing 1% DMSO on each plate. Most plates had a Z' > 0.55, and those with values lower than Z' < 0.45 were repeated (~5%).

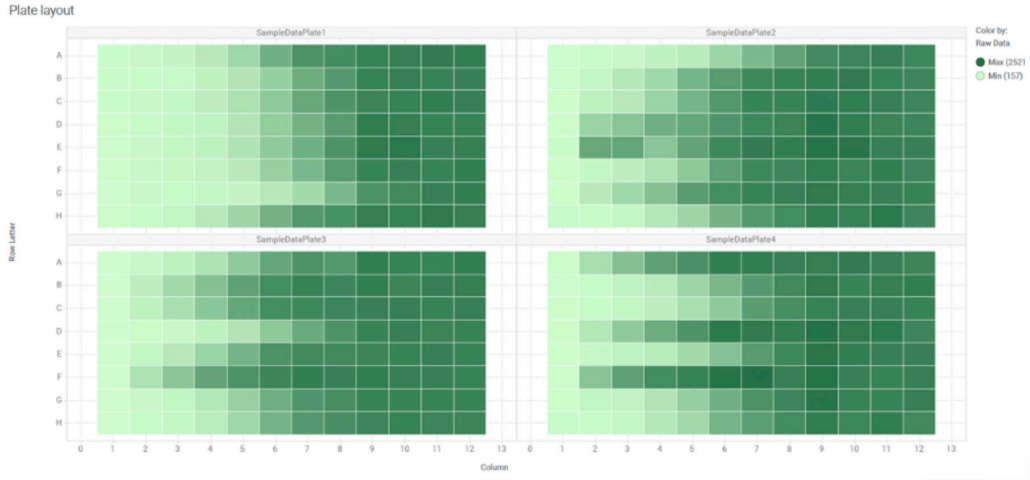
The following graphs show a representative sample of the signal distribution across rows as well as with the mean distribution, upper limit, and lower limits of both the controls and sample wells. These distributions are shown to compare the control vs screening well distribution plots. We observed very tight distributions among both the Positive and Negative control wells, contributing to the relatively high Z'-Factor. We also observed no edge or evaporative effects across individual plates. The plate heat maps shown below are representative of the SNR and common hit patterns achieved while conducting the primary screening of the diversity library.





Secondary Screen

Based on filtering for unwanted chemical properties and discussions with our client we removed approximately 4,000 compounds, leaving 1502 compounds of potential interest. 417 of the most potent compounds were selected for additional testing. The following dose response heat maps show representative potency responses observed during the second round of potency screening.

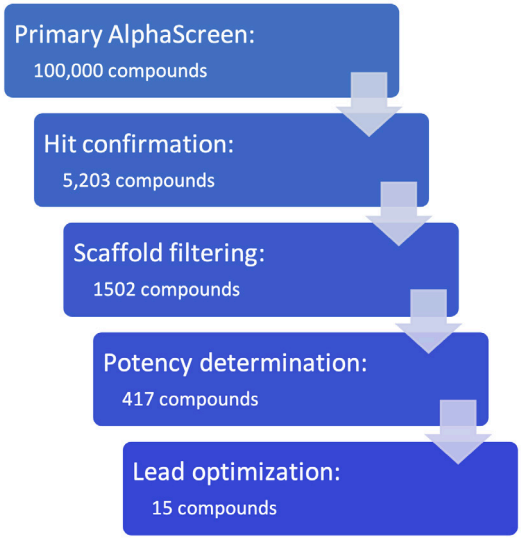


Screening Results

Compounds of interest (COI) identified by this screen were subjected to the decision process shown in below. We selected 9890 compounds with a standard deviation more than 3.5 compared to on-plate controls. Based on filtering for unwanted chemical properties we removed a significant number of candidates, leaving 1502 compounds of interest. The most potent compounds from each cluster were selected for additional testing. After setting aside the less active analogues, 417 compounds remained.

Compound Filtering Scheme

The process for selecting compounds that suppress glucagon at each stage of the screening process followed the filtering scheme outlined here.



Potency Determination

After reviewing the scaffolds with the Medicinal Chemistry team, 417 compounds were selected for potency determination in a dose response format (EC50). The following graphs show representative curves and datasets from the dose response screening phase.