



# Viking Therapeutics

Novel therapeutics for metabolic diseases

# Forward Looking Statements

This presentation contains statements about our future expectations, plans and prospects that constitute forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including risks relating to: both our and our collaborators' ability to successfully research, obtain regulatory approvals for, develop and commercialize products based upon our technologies; our ability to obtain and maintain proprietary protection for our technologies and product candidates, including our liver-targeting drug candidates; competitive pressures; our ability to obtain and maintain strategic collaborations; our ability to successfully execute on, and receive favorable results from, our proprietary drug development efforts; and our ability to raise additional funds to finance our operations.

The forward-looking statements included in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. While we may elect to update these forward-looking statements in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

# Investment Highlights

- First-in-class program for type 2 diabetes, VK0612
- Novel small molecule gluconeogenesis inhibitor
- Clinical POC completed; phase IIb planned
- Differentiated commercial profile; potentially superior efficacy, excellent preliminary safety
- Attractive market positioning, opportunity
- Experienced management team and advisors

# Diabetes, A Growing Healthcare Challenge

## 25.8M U.S. Cases

- 18.8M diagnosed
- 7.0M undiagnosed
- >90% Type 2

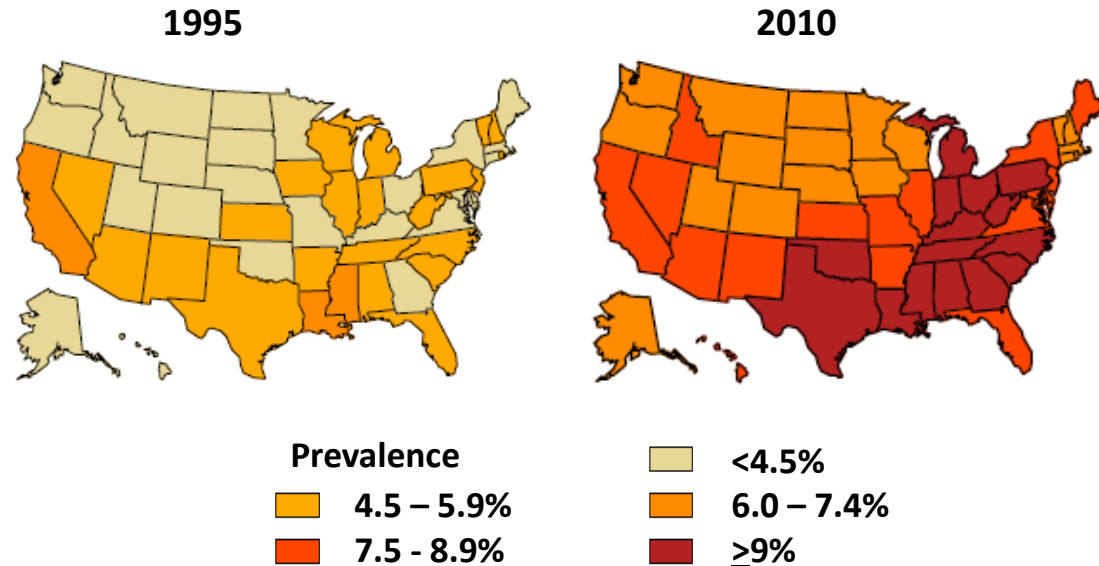
## Economic impact

- \$245B in healthcare costs in 2012

Long-term complications: renal failure, vision loss, amputation, death

Global prevalence projected to exceed 500M by 2030

## Prevalence of Diabetes, U.S. Adults



# Robust Appetite for New Therapies

- Market size suggests multiple blockbusters possible, as with hypertension, statins
- Demand for new mechanisms despite existing options
- Recent launches have enjoyed rapid adoption even with modest antiglycemic effects; e.g. DPP-4 inhibitors

Drug	2007	2008	2009	2010	2011	2012	2013
Januvia/Janumet (sitagliptin)	\$668	\$1,397	\$2,580	\$3,339	\$4,687	\$5,745	\$5,833
Tradjenta (linagliptin)	-	-	-	-	\$30	\$177	\$498
Onglyza/Kombiglyze (saxagliptin)	-	-	\$24	\$158	\$473	\$709	\$877
Galvus (vildagliptin)	-	\$55	\$181	\$391	\$677	\$910	\$1,200
Nesina/Liovel (alogliptin) (2)	-	-	-	-	\$196	\$451	\$513
<b>Total DPP-4 sales (1)</b>	<b>\$668</b>	<b>\$1,452</b>	<b>\$2,785</b>	<b>\$3,888</b>	<b>\$6,063</b>	<b>\$7,992</b>	<b>\$8,921</b>
<b>Global growth rate</b>	<b>-</b>	<b>117%</b>	<b>92%</b>	<b>40%</b>	<b>56%</b>	<b>32%</b>	<b>12%</b>

Notes: (1) Global sales, in \$M. (2) Japan only through 1H13, U.S. launch June 2013.

# Existing Landscape Presents Opportunities

- Strengths: Current Landscape
  - Weight neutral (metformin, DPP-4, SGLT inhibitors)
  - Improved side effect profiles vs. older therapies
- Weaknesses: Current Landscape
  - Generally modest efficacy; HbA1c  $\delta$  -0.6% to -0.8%
  - Questionable durability, long-term safety concerns
  - Differentiation; 93 ongoing phase III trials, 0 new targets/mechanisms
- Opportunities for New Therapies
  - Differentiated, complementary mechanisms to be embraced
  - Improved efficacy, durability, safety key competitive advantages

# VK0612 Market Potential: Base Case >5M Patients

**18.8M patients**

- 58% on OAD
- 14% OAD + injectible
- 12% Insulin only
- 16% No medication

**1.7M Annual Diagnoses**

CDC 2011 Diabetes Fact Sheet



**Diet and Exercise**

**10.9M patients**

**2.6M patients**

**1st-Line**  
(16%)

**2nd-Line**  
(27%)

**3rd-Line**  
(28%)

**4th-Line**  
(14%)

**5th-Line**  
(15%)

**Annual New Patients**

35% of 1st-line OADs are non-metformin

**600K Patients/yr**  
**\$1.7B**

Metformin or SU (1 drug)

Add-on DPP-4, TZD, SU (2 drugs)

Add-on 2nd OAD (3 drugs)

Injectible GLP-1, Insulin +/- OADs

**Existing Patients**

5% Metformin intolerant

15% Metformin contraindicated

25% Metformin switch at 1 year

42% to 52% Metformin refractory within 5 years

**Substantial base opportunity:**

**Base case = no metformin combo**  
**Total Mkt = \$17-22B**

**550K Patients**  
**\$1.6B**

**1.6M Patients**  
**\$4.7B**

**2.2M Patients**  
**\$6.3B**

**2.8M Patients**  
**\$7.9B**

**5.5M to 7.1M Existing patients; 600K new starts annually**

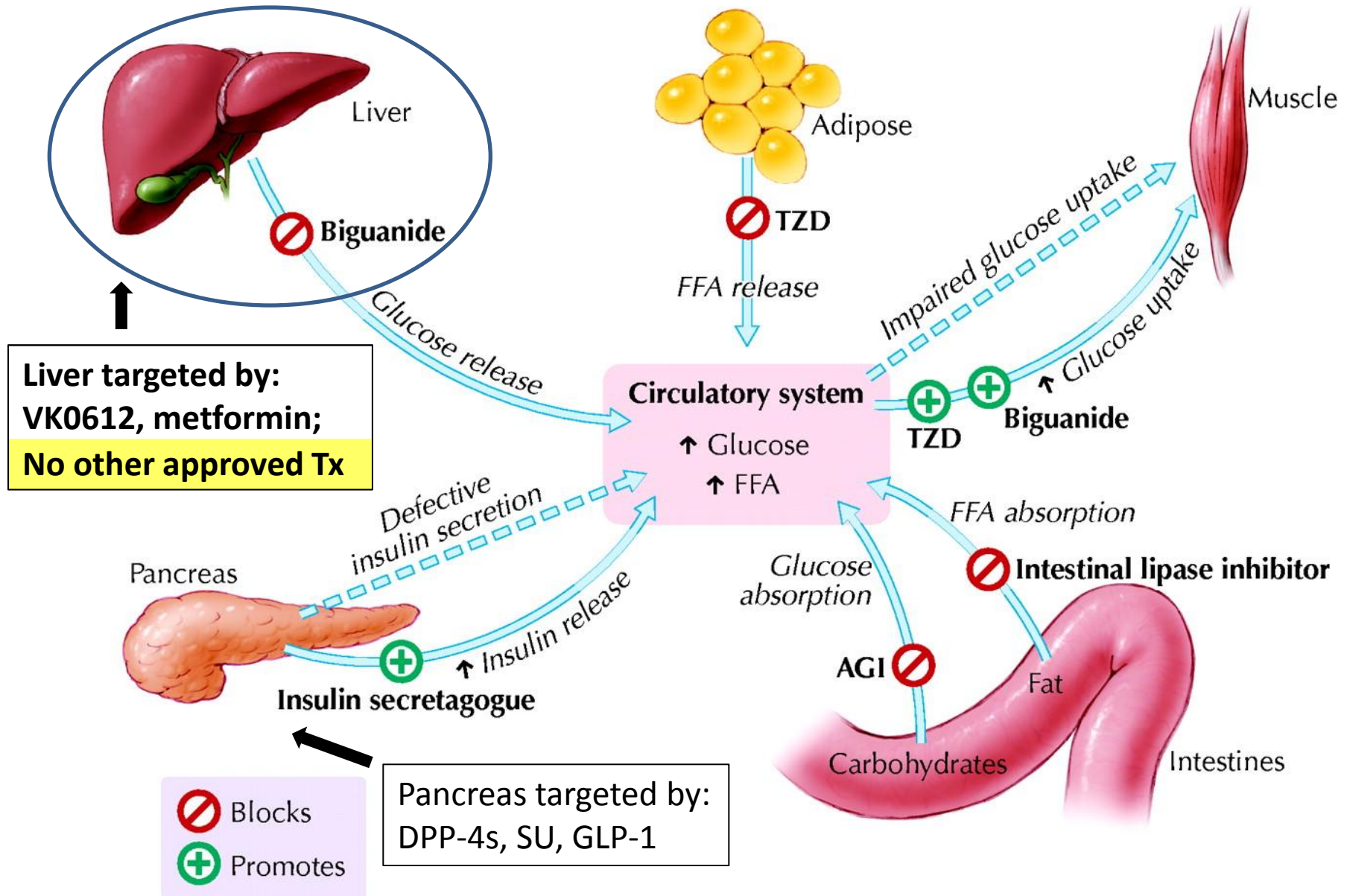
**Best case = all combination possibilities**

**13.5M Existing patients;**  
**1.7M new diagnoses annually**

**VK0612 Target Markets: Severe 1<sup>st</sup>-line patients, 2<sup>nd</sup>-line and refractory patients, metformin-intolerant, contraindicated, switches**

References: 1) *Am J Med*, **125**(3), 302.e1-e7 (2012). 2) *Diabetes Care*, **33**, 501-506 (2010). 3) Garber, *Diabetes Mellitus*, 3<sup>rd</sup> ed., 1123-1138, (2000). 4) CADTH Optimal Therapy Report; Current Utilization of 2nd- and 3rd-Line Therapies in Patients with Type 2 Diabetes, **4**, (2010). 5) *N Engl J Med*. 366(24), 2247-2256 (2012). 6) L.E.K. Consulting, LLC, market research (2007)

# Targets for Therapeutic Intervention

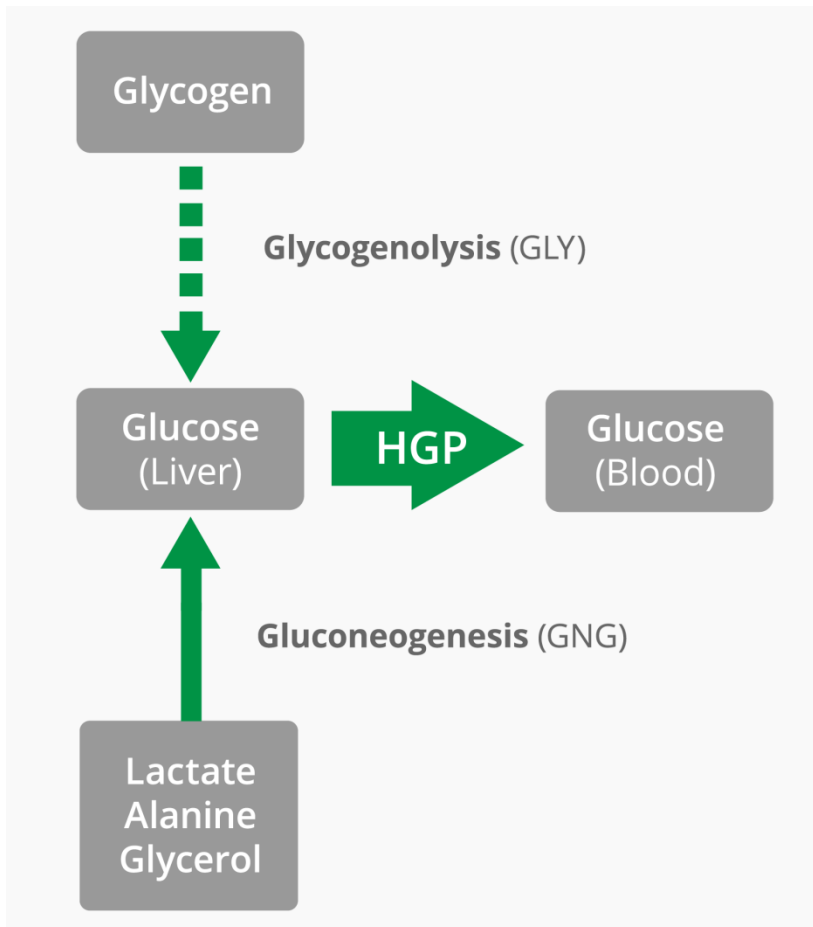




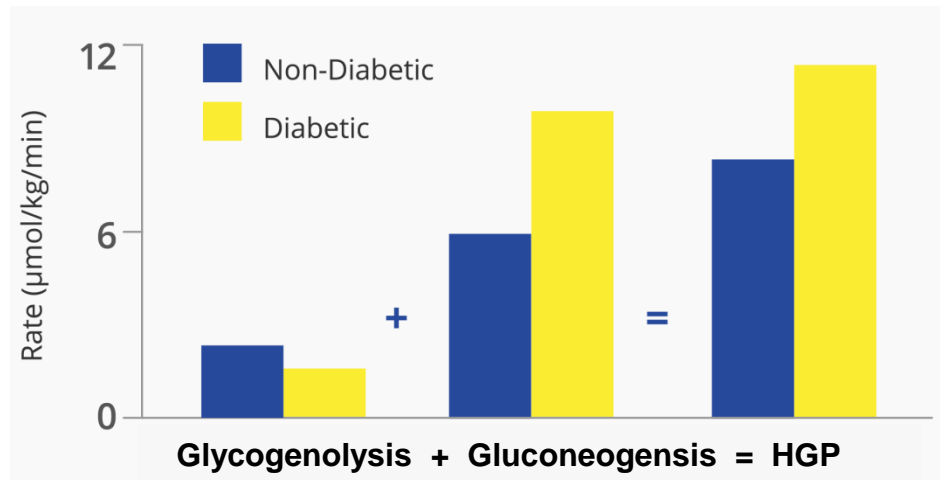
# Hepatic Gluconeogenesis

## Attractive pathway for diabetes therapy

### Hepatic Glucose Production (HGP)

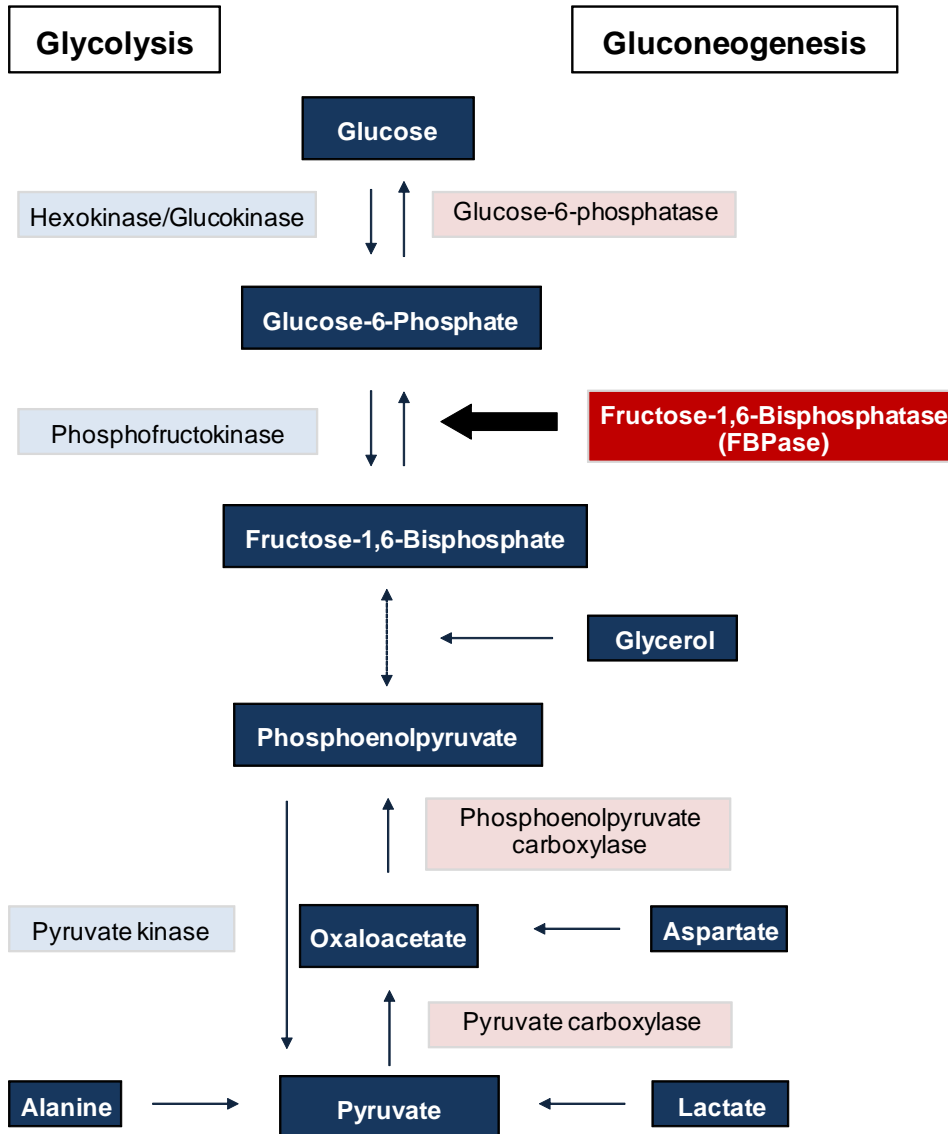


### Contributions to HGP



- **GNG Elevated in type 2 diabetes**
- **Major source of glucose output**
- **Contributes ~70% of FPG**

# Fructose-1,6-Bisphosphatase, FBPase



- Target of VK0612
  - Low nM inhibitor
- Plays critical role in GNG
  - Increased activity in T2D
  - Rate-limiting enzyme
- Primarily expressed in liver
- Independent of glycogenolysis
  - Reduces risk of hypoglycemia

# Known Genetic Deficiency Provides Insight

- Baker-Winegrad Disease, 1970
- Patients lack functional fructose-1,6-bisphosphatase
  - Effectively a human knock-out model
- Once diagnosed, controlled through diet and behavior; patients otherwise healthy with normal lifespan
- Suggests attractive target for type 2 diabetes
  - Lack of long-term complications/comorbidities encouraging

# Our Lead Program: VK0612

- Selective 31nM inhibitor of fructose-1,6-bisphosphatase
- Successful phase IIa study: Highly clinically and statistically significant effects on plasma glucose
- Safe, well-tolerated
- PK, formulation conducive to QD dosing
- Differentiated mechanism, facilitates combinations
- Significant target markets: Poorly controlled patients, metformin-refractory, contraindicated, intolerant, switches

# VK0612: Clinical Overview

- Five Phase I studies completed
  - Evaluated safety/tolerability and PK
    - Single doses of up to 1000 mg
    - Multiple doses of up to 400 mg QD for 14 days
- Promising safety, tolerability (>300 patients)
  - No hypoglycemia, no lacticemia
  - GI events similar across treatment groups
- Successful 14-day phase Ib, 28-day phase II
  - Highly clinically, statistically significant antiglycemic effects
  - Attractive HbA1c-lowering potential

# VK0612: 28-Day Phase IIa Highlights

- Five arm, dose-ranging study, QD dosing (n=100)
- Day 28 vs. Baseline  $\Delta$ FPG (mg/dL): Statistically and clinically significant glucose lowering

Patients			$\Delta$ FPG		PBO-adjusted $\Delta$ FPG	
Cohort	N	Baseline FPG *	Mean	95% CI	Mean	95% CI
Placebo	23	185.0 (41.7)	8.2	(-8.4, 24.7)	-----	-----
10 mg	13	177.7 (46.9)	7.4	(-14.7, 29.5)	-0.7	(-28.3, 26.9)
50 mg	23	174.8 (39.0)	5.3	(-11.4, 22.0)	-2.9	(-26.4, 20.6)
100 mg	23	187.6 (38.0)	8.1	(-8.4, 24.7)	0	(-23.5, 23.4)
<b>200 mg</b>	<b>23</b>	<b>206.4 (50.7)</b>	<b>-20.7</b>	<b>(-37.7, -3.8)</b>	<b>- 28.9 **</b>	<b>(- 52.6, - 5.1)</b>

\* mean (SD)

\*\* p = 0.0177

- Linear regression suggests efficacious dose = 200 - 400mg

# VK0612: Phase IIa Data, Advanced Patients

Patients with baseline FPG  $\geq 180$  mg/dL

Patients			$\Delta$ FPG		PBO-adjusted $\Delta$ FPG	
Cohort	N	Baseline FPG *	Mean	95% CI	Mean	95% CI
Placebo	12	216.3 (30.0)	15.2	(-12.6, 43.0)	-----	-----
10 mg	6	215.5 (40.3)	18.2	(-21.2, 57.5)	3	(-45.1, 51.1)
50 mg	8	218.4 (19.3)	-2.6	(-36.6, 31.4)	-17.8	(-61.7, 26.1)
100 mg	14	212.3 (20.7)	0.6	(-25.3, 26.6)	-14.5	(-52.4, 23.4)
<b>200 mg</b>	<b>16</b>	<b>230.6 (39.0)</b>	<b>-34.6</b>	<b>(-59.1, -10.0)</b>	<b>- 49.7 **</b>	<b>(- 87.0, - 12.5)</b>

\* mean (SD)

\*\* p = 0.0099

- Efficacy increases with disease severity, mirrors prior experience
- Excellent profile for advanced, poorly controlled patients
- Typical FPG to HbA1c conversion  $\sim 35\text{mg/dL} = 1\%$  HbA1c

# VK0612: 14-Day Phase Ib Highlights

- Four arm, placebo-controlled, BID dosing (n=42)
  - Important enrollment criterion: FPG  $\geq$  180mg/dL
- Results: Clinically, statistically significant effect on FPG
- 200mg, 400mg BID: Potential HbA1c effect -1% to -1.5%

Patients			Day 15 $\Delta$ FPG	PBO-adjusted $\Delta$ FPG	
Cohort	N	Baseline FPG *	Mean (SD)	Mean	p-value
Placebo	10	245.1 (33.1)	-14.4 (66.4)	-----	-----
50 mg	12	219.8 (34.6)	-30.0 (55.2)	-15.6	0.48
<b>200 mg</b>	<b>10</b>	<b>218.3 (31.8)</b>	<b>-72.4 (56.6)</b>	<b>-58.0</b>	<b>0.01</b>
<b>400 mg</b>	<b>10</b>	<b>202.5 (34.9)</b>	<b>-69.3 (54.6)</b>	<b>-54.9</b>	<b>0.03</b>

\* mean (SD)



## Safety Takeaways

- Safe at all doses; No drug-related SAEs
- Dose-limiting nausea, vomiting at 400mg BID
- Well-tolerated at 200mg BID
- No hypoglycemia
- No lactic acidosis
- No discontinuations due to lab abnormalities

# VK0612: Development Summary

Human POC successfully demonstrated

- Glucose-lowering observed throughout the day
  - Preliminary FPG data: Outstanding HbA1c potential
  - Weight-neutral, lipid-neutral
- Safe and well-tolerated
  - MTD, dose-limiting tolerability identified
  - >300 patients in database; no drug-related SAEs
- Promising benefit/risk profile vs. competitive landscape

# VK0612: Attractive Competitive Profile

Drug	Target	$\Delta$ FPG mg/dL (wks) <sup>1</sup>	$\Delta$ HbA1c % (wks)	$\Delta$ Weight	Safety, Tolerability, Other
<b>VK0612</b>	<b>FBPase</b>	<b>-50<sup>2</sup> to -58<sup>3</sup> (2 to 4)</b>	<b>Expect -1.0 or greater</b>	<b>Neutral</b>	<b>Dose limiting nausea at &gt;2x potential commercial doses</b>
<b>Sitagliptin</b>	DPP4	-20 (12)	-0.6 (12)	Neutral	Modest efficacy, pancreatitis, pancreatic lesions, HF risk (?)
<b>Metformin</b>	Unknown	-59 <sup>4</sup> (24)	-1.8 (24)	Neutral	GI intolerance, renal contraindications, elderly, rare lactic acidosis
<b>Pioglitazone</b>	PPAR	-41 <sup>5</sup> (26)	-1.0 (26)	Modest weight gain	CHF, edema, oncogenic signal, bone fractures
<b>Canagliflozin</b>	SGLT	-43 (26)	-1.2 (26)	Modest weight loss	Genital infections, increased hepatic glucose output, durability, increased LDL, renal contraindication, bone fractures
<b>Glucokinase activators<sup>6</sup></b>	Glucokinase	-6 to -11 (14-16)	-0.4 to -0.9 (14-16)	Modest weight gain	Lipidemia, waning efficacy, hypoglycemia, liver enzymes
<b>Glucagon antagonists</b>	Glucagon	-30 to -40 (4)	-0.6 to -0.8 (12)	Neutral	Variable dose-response; LDL, liver enzyme elevations; hypoglycemia

Notes and references: (1) Placebo-adjusted. (2) Baseline FPG 231mg/dL. (3) Baseline FPG 221mg/dL.

(4) Baseline FPG 242mg/dL. (5) 30mg QD, baseline FPG 269mg/dL. (6) Various MK-0941, AZD1656 data.

# VK0612 vs. Existing Landscape

Commercial profile compares favorably to existing agents

- Efficacy, safety, durability, convenience, mechanism

	VK0612	Metformin	Sulfonylurea	TZD	DPP-4	SGLT2
Glycemic impact						
Durability						
Safety, preclinical						
Safety, clinical						
Safety, long-term	NA					
Tolerability						
Weight neutral						
Convenience						
Insulin independence						

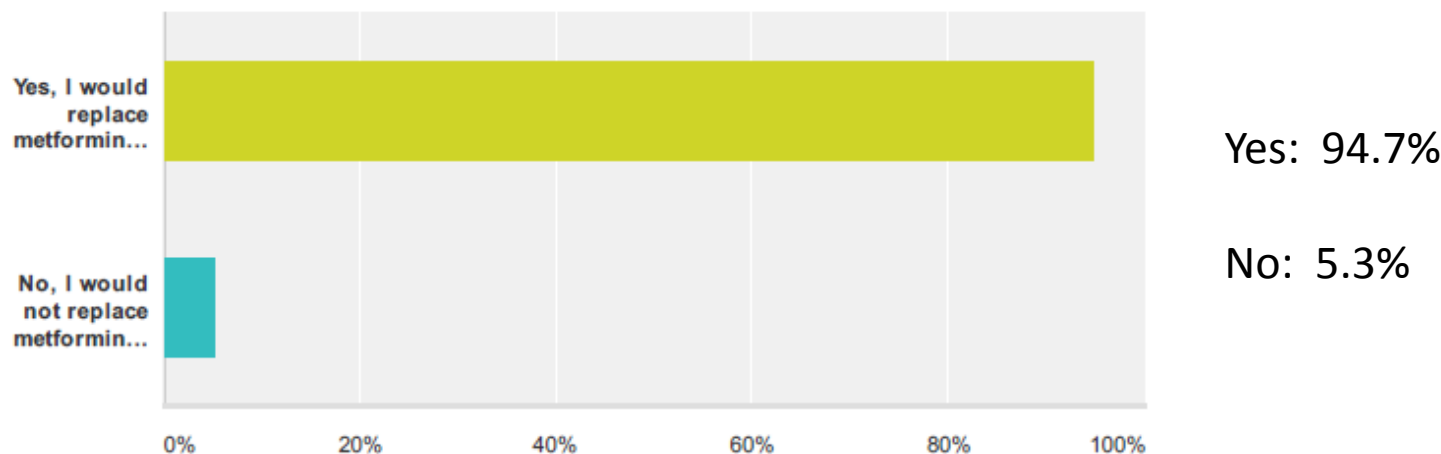
Key  = Favorable  Inadequate or potential concern  = Negative

# What do endocrinologists think?

Market research: Significant opportunity in multiple settings

Example, poorly-controlled patients:

**Q:** Suppose the therapy above demonstrated efficacy in patients no longer receiving benefit from a metformin-containing regimen. Would you replace metformin with the new drug in a combination regimen?



- Secondary failure rate for metformin ~17%/year, >40% at 3-5yrs
- Prescribing trends suggest ~200K new patients/yr = \$600M market/yr

# VK0612: Efficacy in Metformin-Experienced

Phase Ib: Patients receiving metformin at screening visit

Cohort	N	Mean FPG at screening (mg/dL) <sup>1</sup>	Mean FPG, Day 14 <sup>2</sup>	Day 14 $\Delta$ FPG vs. Screening visit	Placebo-adjusted Day 14 $\Delta$ FPG vs. Screening visit
Placebo	9	172	236	65	-
200mg	8	183	151	-32	-97
400mg	7	170	138	-32	-97

Notes: 1) Screening visit 2-4 weeks prior to first dose. 2) Primary efficacy analysis.

- Glucose-lowering effect observed in refractory patients
- Highlights differentiated mechanism vs. metformin
- Survey: Significant interest in 1<sup>st</sup>-line, additional settings

# FBPase: Extensive Prior Validation

- Historically attractive but difficult to approach
  - PFE, ABT, Roche, NVO, others
  - Challenges: potency, selectivity, PK
- Daiichi-Sankyo/Metabasis; Most successful
  - Discovered novel class of potent, selective, pharmaceutically relevant small molecule inhibitors
  - Lead CS-917, first-generation FBPase inhibitor
  - Demonstrated *in vitro*, *in vivo*, and clinical POC
  - Completed 3 phase II trials, ~900 patient database

# Daiichi-Metabasis CS-917, Clinical Summary

## Phase II Overview

- 14 and 28 day studies demonstrated human POC
- Statistically significant anti-glycemic effects

## Phase IIb Highlights: 12 week BID dosing, 400 patients

- Sub-optimal (low) dose, mild patient population = low chance of success
- Trial failed to demonstrate statistically significant change in HbA1c
- CS-917 program discontinued; Daiichi-Metabasis partnership terminated

## Phase IIb Extension: 24-week, promising longer-term efficacy, safety

- Statistically significant reduction in HbA1c (-0.37%,  $p = 0.0036$ )
- Durable effect; 24-week safety; no problematic lactate elevation



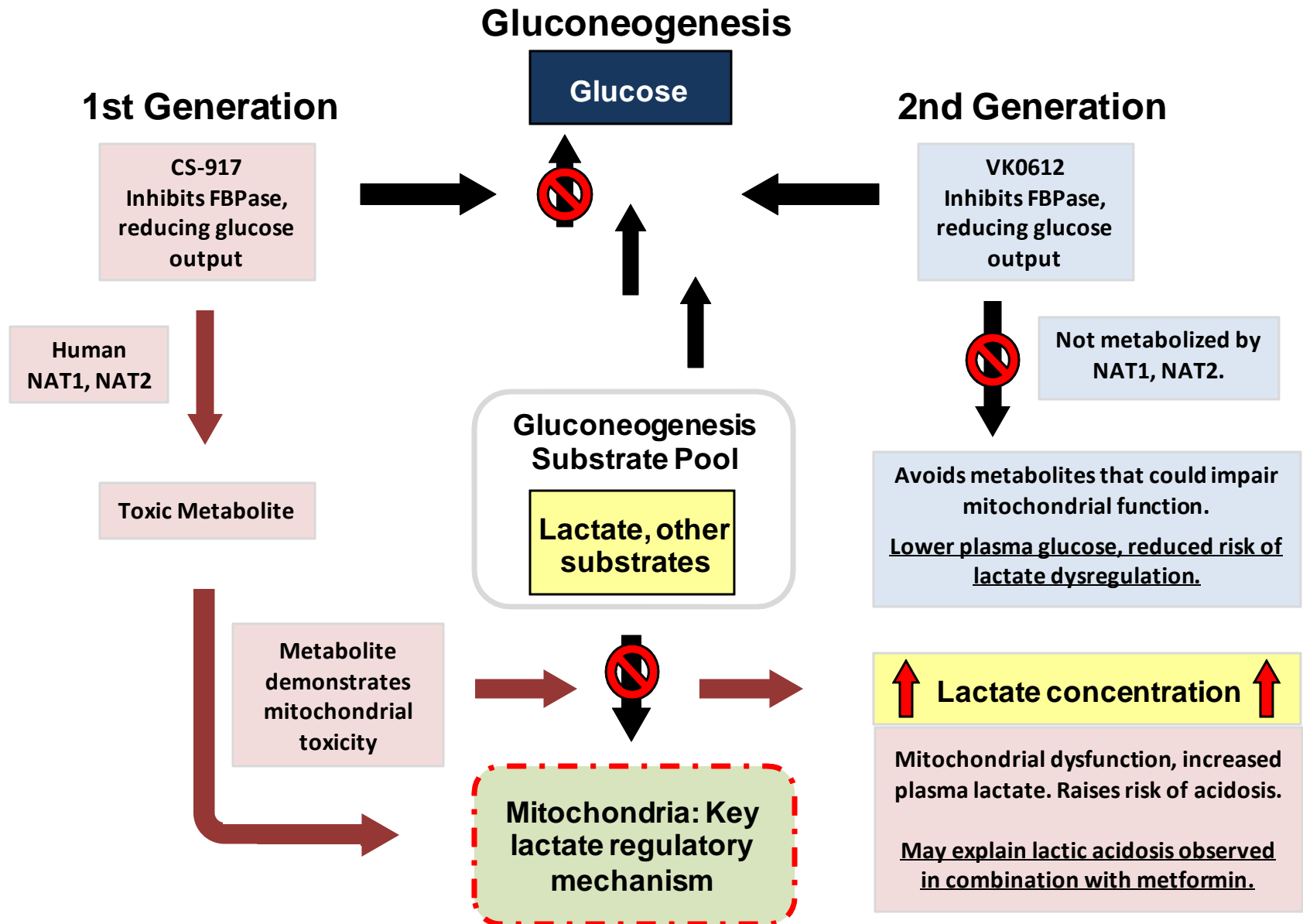
# Daiichi-Metabasis CS-917: Takeaways

## Clinical Experience Validates FB Pase Target for T2D

- Best efficacy in poorly controlled patients; baseline FPG  $\geq 180$ mg/dL

	Placebo	50 BID	100 BID	200 BID	Metformin
<b><u>4 Week Phase 2a Trial, All Patients (Study 202)</u></b>					
N =	35		37	36	
$\Delta$ FPG at 4 weeks, all patients (mg/dL)	+30.2		-1.4	-11.1	
Placebo-corrected $\Delta$ FPG			-31.6 p=0.0018	-41.3 p<0.0001	
<b><u>12 Week Phase 2b Trial, Subgroup With FPG <math>\geq 180</math>mg/dL (Study 205)</u></b>					
N =	20	23	26		35
$\Delta$ FPG at 12 weeks (mg/dL)	+25.0	-21.0	-13.1		-42.4
Placebo-corrected $\Delta$ FPG		-46.0 p=0.0104	-38.1 p=0.0295		-67.4 p<0.0001

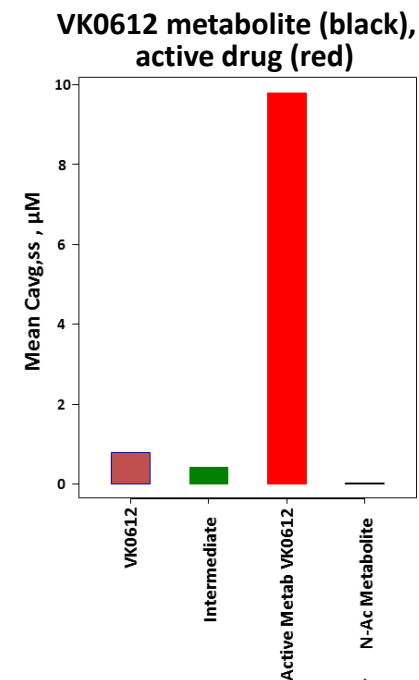
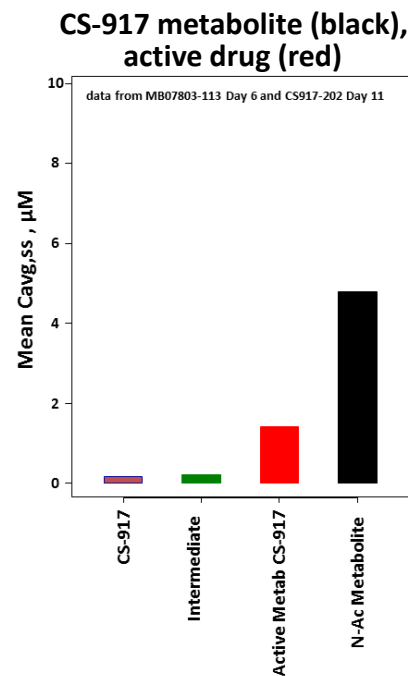
# VK0612 vs. CS-917, Issues and Implications



# VK0612 vs. CS-917 Comparative Profile

## Key differences: VK0612 vs CS-917

- Resistant to metabolic inactivation
- Not toxic to mitochondria
- Increased oral bioavailability
- ~5x higher plasma levels
- Longer  $T_{1/2}$  (~20h)
- Potential for QD dosing
- Reduced drug variability
- Results in higher, more durable, consistent, safer exposures



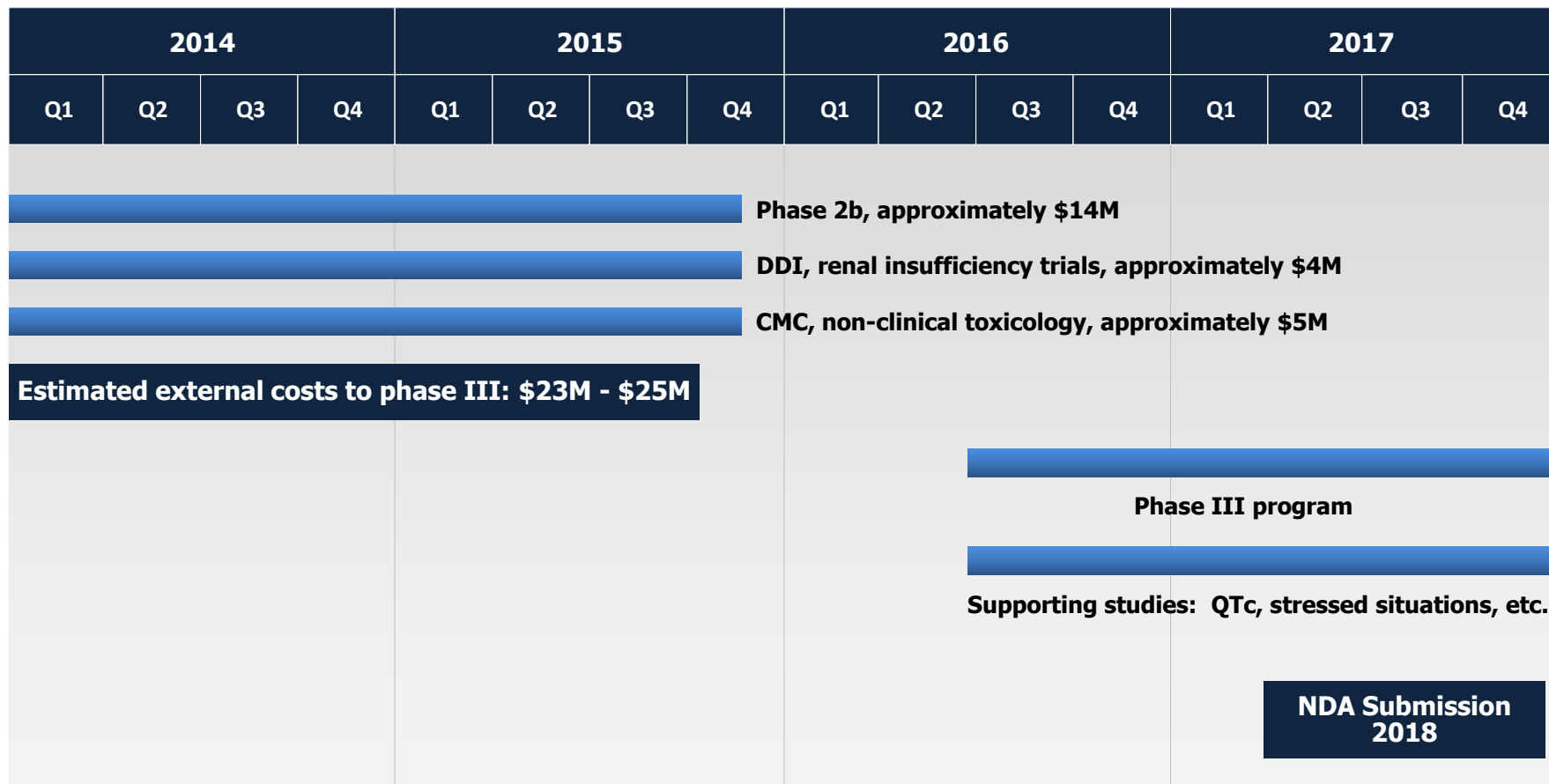
>100-Fold exposure difference in key problematic metabolite

# VK0612: Development Plans

- Conduct phase IIb trial
  - Multi-arm dose ranging
  - 12-Week study to assess HbA1c
  - Metformin comparator (not powered for superiority)
- Conduct parallel exploratory phase I trials
  - Metformin combination
  - Renally impaired population
- Data possible 2H15

# VK0612: Development Timelines, Costs

## Development Timeline



# Summary of Potential Phase III and CV Plans

- FDA diabetes requirements:  $\geq 2500$  exposures,  $\geq 1,300$  for 1 year,  $\geq 300$  for 18 months
- CV safety analysis from  $\geq 1,300$  patients; focus on 95% Confidence Interval around Hazard Ratio, relative risks
  - If upper bounds of HR CI  $> 1.8$ , pre-market CV study
  - If upper bounds of HR CI  $> 1.3 - 1.8$ , post-mkt CV study
- Many possible scenarios, two examples:

Scenario 1	Scenario 2
5 - 6 phase III trials; total N=4,900	5 phase III trials; total N=8,250
No dedicated CV study; phase III trials enroll up to 30% high risk patients	Dedicated 6,500 patient CV study with interim analysis; embeds 2 phase III trials
Events sufficient for HR analysis and NDA filing in approximately 2 years	Events sufficient for HR analysis and NDA filing in approximately 1.5 - 2 years
Estimated external cost to NDA = \$165M	Estimated external cost to NDA = \$180M

# Licensing Terms, Intellectual Property

- \$1M Up-front to Ligand
- \$38M Clinical and regulatory milestones
  - Includes \$33M post-phase III
  - No commercial/sales milestones
- \$10M Each for EU, Japan approvals
- Tiered royalties to low double-digit
- Composition of matter to 2025
- Additional filings planned
  - Expect runway to extend >2030

Nimble model minimizes expenses, accelerates decisions

CEO: Brian Lian, Ph.D.

SunTrust, CIBC World Markets, Amgen

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GSK, QuatRx, Pfizer, Parke-Davis, Duke University

COO: Misha Dinerman, MD

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Portola, Millennium, COR Therapeutics

VP, Clinical Operations: Confidential

Pfizer, Metabasis, 20+ years clinical operations experience



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- **Paul van Poelje, Ph.D.**

Former Head, Biological Sciences, Metabasis Therapeutics. Former Sr. Director, Cardiovascular, Metabolic, Endocrine Diseases, Pfizer.

# Viking Therapeutics, Summary

- Lead program VK0612: Novel, first-in-class drug candidate for type 2 diabetes
- Differentiated mechanism with competitive advantages
- Excellent clinical POC data suggest potency, safety, combinability, attractive commercial profile
- Phase IIb, metformin, renal insufficient studies planned
- Significant market opportunities: Poorly-controlled, refractory, metformin contraindicated, intolerant
  - Base Case: 5M patients; Best Case: 13.5M patients