

!" #&/

4;O <548G=>3> 70AB>AC20==O ;V:0@AL:>3> 70A>1C

!::04:

4VNG0 @5G>28=0: rabeprazole;

1 B01;5B:0 ;C =0B@VN 10 <3 01> 20 <3;

4>?>28=8: B01;5B:8 ?> 10 <3: <0=VB (421), 3V4@>:A8?@>?V;F5;N;>70 =87L:>70B01;5B:8 ?> 20 <3:
<0=VB (421), 3V4@>:A8?@>?V;F5;N;>70 =87L:>70 B@85B8;F8B@0B.

V:0@AL:0 D>@<0. "01;5B:8, 2:@8BV >1>;>=:N, :8H:>2>@>7G8==V.

A=>2=V DV78:>-EVABV:

B01;5B:8 ?> 10 <3: :@C3;V 42>>?C;;V B01;5B:8, 2:@8BV >1>;>=:N, :8H:>2>@>7G8==V, @>652>3>
>;L>@C, 7 =0?8A>< «R» 7 >4=>3> 1>:C B0 3;04:V 7 V=H>3>;

B01;5B:8 ?> 20 <3: :@C3;V 42>>?C;;V B01;5B:8, 2:@8BV >1>;>=:N, :8H:>2>@>7G8==V, 6>2B>3>
>;L>@C, 7 =0?8A>< «R2» 7 >4=>3> 1>:C B0 3;04:V 7 V=H>3>.

\$0@<0:>B5@0?52B8G=0 3@C?0.

0A>18 4;O ;V:C20==O ?5?B8G=>W 28@07:8 B0 30AB@>57>D0350;L=>W @5D;N:A=>W E2>@>18.
=3V1VB>@8 ?@>B>=>W ?>4 "% 02!04.

\$0@<0:>;>3VG=V 2;0AB82>ABV.

\$0@<0:>48=0

5E0=V7< 4VW. 015?@07>; =0B@VN =0;568BL 4> ;:0AC 0=B8A5:@5B>@=8E A?>;C:, 70;V2, =5 <0T
0=B8E>;V=5@3VG=8E 2;0AB82>AB59 V =5 T 0=B03>=VAB< 3VAB028E 2-@5F5?B>@V2, 0;5
?@83=VGCT A5:@5FVN H;C=:>2>W :8A;>B8 H;OE< A?5F8DVG=>3> ?@83=VG5==O D5@<5=BC +/□+
"\$-078 =0 A5:@5B>@=V9 ?>25@E=V ?0@VTB0;L=8E ;:VB8= H;C=:0 (:8A;>B=89, 01? ?@>B>==89
=0A>A). D5:B T 4>7>70;56=8< B0 ?@872>48BL 4> V=3V1C20==O O: 1070;L=>3>, B0: V AB&20=>3>
284V;5==O :8A;>B8, =570;56=> 2V4 ?>4@07=8:0. >A;V465==O =0 B20@8=0E ?>:070;8, I> ?VA;O
22545==O 2 >@30=V7< @015?@07>; =0B@VN H284:> 7=8:0T O: V7 ?;07<8, B0: V 7V A;87>2>W
>1>;>=:8 H;C=:0. 015?@07>; =0B@VN <0T A;01>;:C6=V 2;0AB82>ABV, 2 CAVE 4>7C20==OE H284:>
01A>@1CTBLAO V :=F5=B@CTBLAO C ?0@VTB0;L=8E ;:VB8=0E. 015?@07>; =0B@VN
?5@5B2>@NTBLAO 2 0:B82=C AC;LD5=0@< ?@>B>=C20==O V B0:8< G8=>< @503CT 7 4>ABC?=8<8
70;8H:0<8 F8AB5W=C ?@>B>=>W ?>

=B8A5:@5B>@=0 0:B82=VABL. VA;O ?5@>@0;L=>3> ?@89> 0=B8A5:@5B>@=89 5D5:B
A?>AB5@V30TBLAO G5@57 1 3>48=C V 4>AO30T <0:A8 2-4 3>48=8. D5:B ?@83=VG5==O
1070;L=>W DC=:FVW B0 AB8B8 G5@57 23 3>48=8 ?VA;O ?@89>W 4>78 @015?@07>;C =0B@VN
AB0=>282 69 B0 82 % 2V4?>2V4=>, 0 B@820;VABL FL>3> 5D5:BC 4>AO30;0 48 3>48=. D5:B82=VABL
@015?@07>;C =0B@VN I>4> ?@83=VG5==O A5:@5FVW :8A;>B8 45I> ?>A8;NTBLAO C ?@>F5AV
I>45==>3> ?@89>AO30TBLAO G5@57 3 4=V ?VA;O ?>G0B:C ?@89>3> ?@5?0@0BC. VA;O
7025@H5==O ?@89>;C =0B@VN A5:@5B>@=0 0:B82=VABL =>@<0;V7CTBLAO ?@>BO3>< 2-3 4=V2.
=865==O :8A;>B=>ABV H;C=:0 =570;56=> 2V4 1C4L-O:8E G8==8:V2, 2;;NG0NG8 V=3V1VB>@8
?@>B>=>W ?>;, 71V;LHCT :V;L:VABL 10:B5@V9 C H;C=:>2>-.8H:>2>@0<8 ?@>B>=>W ?>65
71V;LHC20B8 @878: H;C=:>2>-.8H:>28E V=D5:FV9, B0:8E O: Salmonella, Campylobacter B0 Clostridium
difficile

?;82 =0 :=F5=B@0FVN 30AB@8=C C A8@>20BFV :@>2V.VA;O ?@89>20 <3 @015?@07>;C =0B@VN
1 @07 =0 4>1C ?@>BO3>< 43 =F5=B@0FVO 30AB@8=C C A8@>20BFV :@>2V 71V;LHCTBLAO, I>
2V4>1@060T ?@83=VG5==O A5:@5FVW :8A;>B8. :=F5=B@0FVW 30AB@8=C ?>25@B0NBLAO 4>
?>G0B:>28E @V2=V2, O: ?@028;>, ?@>BO3>< 1-2 B86=V2 ?VA;O ?@8?8=5==O ;V:C20==O.
82G5==O 1V>?B0BV2 4=0 B0 0=B@0;L=>3> 2V44V;C H;C=:0 C 1030BL>E ?0FVT=BV2, O:V >B@8; 01>
?@5?0@0B ?>@V2=O==O ?@>BO3>< 8 B86=V2, =5 28O28;> =VO:8E 3VAB>;>3VG=8E 73> 30AB@8BC,
71V;LH5==O G0AB>B8 0B@>DVG=>3> 30AB@8BC, <5B0?;07VW :8H5G=8:C B0 @>7?>2AN465==O
V=D5:FVW . pylori. V4 G0A B@820;>3> ;V:C20==O ?@>BO3>< 36 28O2;5=> 6>4=8E VAB>B=8E 7
=HV 5D5:B8. 0 40=89 G0A =5<0T 40=8E I>4> A8AB5<=8E 5D5:BV2 7 1>:C F5=B@0;L=>W =5@2>2>W
A8AB5<8 (&!), A5@F52>-AC48==>W V 48E0;L=>W A8AB5<8, A?@8G8=5=8E 70AB>AC20==O<
@015?@07>;C =0B@VN. 5@>@0;L=89 ?@89>< 20 <3 @015?@07>;C =0B@VN =0 4>1C ?@>BO3>< 2
B86=V2 =5 2?;820T =0 DC=:FVN I8B>284=>W 70;>78, <5B01>;V7< 2C3;52>4V2, 0 B0:>6 =0

:=F5=B@0FVW C :@>2V ?0@0B8@5>W4=>3> 3>@<>=C, :=@B87>=C, 5AB@>35=C, B5AB>AB5@>=C, ?@>;0:B8=C, E>;5F8AB>:V=V=C, A5:@5B8=C, 3;N:03>=C, D>;V:C;>AB83> 3>@<>=C (FSH), ;NB5W=V7CNG>3> 3>@<>=C (LH), @5=V=C, 0;L4>AB5@>=C B0 A<0B>B@>?=>3> 3>@<>=C. # 4>A;V465==OE 28O2;5=0 2V4ACB=VABL ;;V=VG=> 7=0GCI8E 270T<>4V9 ;< B0 0<:A8F8;V=> 015?@07>; =5 <0T =530B82=>3> 2?;82C =0 @V2=V C ?;072V 0<:A8F8;V=C B0 ;:0@8B@>4=>G0A=> AC20==V 7 <5B>N 5@048:0FVW V=D5:FVW H. pylori C 25@E=L>3> B@0:BC. \$0@<0>.:V=5B8:0.

IA>@1FVO. 01V<0: B01;5B:0, 2:@8B0 :8H:>2>@>7G8==>N >1>;>=:>N. 1A>@1FVO @015?@07>;C =0B@VN @>7?>G8=0TBLAO ;8H5 ?VA;O B>3>, O: B01;5B:0<8=0T H;C=>.: 015?@07>; =0B@VN H284:> 01A>@1CTBLAO 7 :8H5G=8:C. V:>2V :=F5=B@0FVW @015?@07>;C C ?;07AO30NBLAO ?@81;87=> G5@57 3,5 3>48=8 ?VA;O ?@89>78 C 20 <3. V:>2V :=F5=B@0FVW C ?;072V (!_{m0E}) B0 ?;>I0 ?V4 :@82>N <<:=F5=B@0FVO-G0A» (AUC) @015?@07>;C <0NBL ;V=V9=89 E0@0:B5@ C 4V0?07>=V 4>7 2V4 10 4> 40 <3. 1A>;NB=0 1V>4>ABC?=VABL ?VA;O ?5@>@0;L=>3> ?@89>;C =0B@VN. 5@V>4 =0?V2282545==O 7 ?;07<8 :@>2V AB0=>282 ?@81;87=> 1 3>48=C (2V4 0,7 4> 1,5 3>48=8), 0 AC<0@=89 ;;V@5=A AB0=>28BL 2V4?>2V4=> 4> >FV=>: 283±98<;/E2. >7?>4V;. # ;N48=8 ABC?V=L 7207C20==O @015?@07>;C =0B@VN 7 1V;:0<8 ?;07<8 :@>2V AB0=>28BL 1;87L:> 97 %.

5B01>;V7< B0 5:A:@5FVO. /: V V=HV ?@54AB02=8:8 ;:0AC V=3V1VB>@V2 ?@>B>==>W ?>; <5B01>;V7CTBLAO F8B>E@><< 450 (CYP450) ?5GV=>2>W A8AB5<8 <5B01>;V7A;V465==O in vitro 7 ;N4AL:8<8 ?5GV=>28<8 A><0<8 ?>:070;8, I> @015?@07>; =0B@VN <5B01>;V7CTBLAO V7>5=78<0<8 CYP450 (CYP2C19 B0 CYP3A4). @8 >GV:C20=>2V ;N48=8 @015?@07>; =5 V=4C:CT V =5 ?@83=VGCT CYP3A4. 4=0: 4>A;V465==O in vitro=5 <>6CBL 702648 1CB8 5:AB@0?>;L>20=V 2V4=>A=> A8BC0FV9 in vivo, FV @57C;LB0B8 ?>:07CNBL, I> 270T<>4V0 ;< B0 F8;:>A?>@8=>< =5 >GV:CTBLAO.# ;N48=8 3>;>2=8<8 <5B01>;VB0<8, ?@8ACB=V<8 C ?;072V, T BV>5DV@ (1) V :0@1=>20 :8A;>B0 (6), 0 4@C3>@O4=V <5B01>;VB8, ?@8ACB=V C =87L:8E :=F5=B@0FVOE, ?@54AB02;5=V AC;LD>=>< (2), 48<5B8;BV>5DV@>< (4) V :=N30B<< <5@:0?BC@>2>W :8A;>B8 (5). 57=0G=C 0=B8A5:@5B>@=C 0:B82=VABL<0T BV;L:8 48<5B8;>289 <5B01>;VB (), >4=0: 2V= =5 ?@8ACB=V9 C ?;072V. VA;O >4=>@07>2>3> ?@89>3> 14! @015?@07>;C =0B@VN =573> @015?@07>;C C A5GV =5 28O2;O;8. @81;87=> 90 % 2.070=>W 4>78 5;VAO 7 A5G5N ?5@5206=> C 283;O4V 42>E <5B01>;VBV2: :=N30BC <5@:0?BC@>2>W :8A;>B8 (5) B0 :0@1=>2>W :8A;>B8 (6); :@V< B>3>, C B>:A8:>;>3VG=8E 4>A;V465==OE C ;01>@0B>@=8E B20@8= 1C;> 7=0945=> I5 420 =5V45=B8DV:>20=V <5B01>;VB8. '0AB8=0 4>78, I> 70;8H8;0AL, 1C;0 7=0945=0 C :0;>28E <0A0E.

!B0B52V >A>1;82>ABV. A:V;L:8 @07>20 4>70 20 <3 @015?@07>;C =0B@VN ?V4V1@0=0 70 <0A>N BV;0 B0 7@>AB< ;N48=8, AB0B52V >A>1;82>ABV =5 2?;820NBL =0 D0@<0>.:V=5B8G=V ?0@0<5B@8. 8@:>20 =54>AB0B=VABL. # ?0FVT=BV2 7 B5@N E@>=VG=>N =8@:>2>N =54>AB0B=VABN, O:V ?5@51C20NBL =0 ?V4B@82), @>7?>4V; @015?@07>;C =0B@VN 1C2 4C65 ?>4V1=89 4> B0:>3> C 74>@>28E 4>1@>2>;LFV2. AUC @015?@07>;C =0B@VN B0 !_{m0E} 4;O B0:8E ?0FVT=BV2 1C;8 <0965 =0 35% ?V428I5=V ?>@V2=O=> 7 B0:8<8 C 74>@>28E 4>1@>2>;LFV2. !5@54=T 7=0G5==O ?5@V>4C =0?V2282545==O AB0=>28BL 0,82 3>48=8 C 74>@>28E 4>1@>2>;LFV2, 0,95 3>48=8 C ?0FVT=BV2, O:V ?5@51C20NBL =0 35<>4V0;V7V, B0 3,6 3>48=8 C ?>AB4V0;V7=8E E2>@8E. ;V@5=A ;V:0@AL:>3> 70A>1C 4;O ?0FVT=BV2 7 =8@:>2>N =54>AB0B=VABN, O:V ?5@51C20NBL =0 35<>4V0;V7V, 1C2 ?@81;87=> 242VGV 1V;LH8<, =V6 C 74>@>28E 4>1@>2>;LFV2.

5GV=>20 =54>AB0B=VABL. VA;O >4=>@07>2>W @015?@07>;C =0B@VN 4>78 20<3 @015?@07>;C =0B@VN C ?0FVT=BV2 7 ?>7V 20 <3 ?@>BO3<< 7 4=V2 AUC ?>28==> 71V;LHC20B8AO =5<5=H =V6 C 1,5 @070, 0 728E :=F5=B@0FV9 C ?;07_{m0E} 4> 1,2. 5@V>4 =0?V2282545==O C ?0FVT=BV2 7 C@065==O< ?5GV=:8 AB0=>282 12,3 3>48=8 ?>@V2=O=> 7 2,1 3>48=0<8 4;O 74>@>28E 4>1@>2>;LFV2. \$0@<0>48=02V4L (@<-5B@VO H;C=>2>3> 2E 3@C? ?0FVT=BV2 1C;0 ?>4V1=0 70 B5@0?52B8G=8<8 ?>:07=8:0<8.

0FVT=B8 ;VB=L>3> 2V:C. # ?0FVT=BV2 ;VB=L>3> 2V:C 5;V;C =0B@VN 45I> 7=865=0. VA;O 7 4=V2 ?@89>;C =0B@VN ?> 20 <3 =0 4>1C C >AV1 ;VB=L>3> 2V:C AUC 1C;0 ?@81;87=> 42VGV 1V;LH>N, !_{m0E} 71V;LHC20;0AO =0 60 %, 0 "1/2 71V;LHC202AO =0 30 % ?>@V2=O=> 7 B0:8<8 C <>;>48E 74>@>28E 4>1@>2>;LFV2. 4=0: A;V4 2V47=0G8B8 2V4ACB=VABL >7=0: 0;C C =0B@VN.

>;V<>@DV7< CYP2C19. @8 ?@87=0G5==V ?@>BO3<< 7 4=V2 4>78 20 <3 @015?@07>;C =0B@VN =0 4>1C C ?0FVT=BV2, O:V <0NBL A?>2V;L=5=89<5B01>;V7< CYP2C19, @V2=V AUC B0 ?5@V>4 =0?V2282545==O 1C;8 28IV ?@81;87=> 2 1,9 B0 1,6 @070 2V4?>2V4=> ?>@V2=O=> 7 B0:8<8 C ?0FVT=BV2 7V H284:8< <5B01>;V7<<<; C B>9 65 G0A !_{m0E} 71V;LHC20;0AO ;8H5 =0 40 %.

;V=VG=V E0@0:B5@8AB8:8.

>:070==O.

:B82=0 ?5?B8G=0 28@07:0 420=04FOB8?0;>W :8H:8;

0:B82=0 4>1@>O:VA=0 28@07:0 H;C=:0;

5@>782=0 01> 28@07:>20 30AB@>57>D0350;L=0 @5D;N:A=0 E2>@>10 (%);

4>23>B@820;5 ;V:C20==O 30AB@>57>D0350;L=>W @5D;N:A=>W E2>@>18 (?V4B@8

A8<0B8G=5 ;V:C20==O 30AB@>57>D0350;L=>W @5D;N:A=>W E2>@>18 2V4 ?>3> 4> 4C65 B06:>3> ABC?5=O (A8<0B8G=5 ;V:C20==O %);

A8=4@><>;V=35@0-;;VA>=0;

C :><1V=0FVW 7 2V4?>2V4=8<8 0=B810:B5@V0;L=8<8 B5@0?52B8G=8<8 AE5<0<8 4;O 5@048:0FVW *Helicobacter pylori* (*H. pylori*)C ?0FVT=BV2 7 ?5?B8G=>N 28@07:>N H;C=:0 B0 420=04FOB8?0;>W :8H:8.

@>B8?>:070==O.

@5?0@0B ?@>B8?>:070=89 ?0FVT=B0< 7 3V?5@GCB;82VABN 4> @015?@07>;C =0B@VN, 70;V2 01> 1C4L-O:>3> V=H>3> V=3@54VT=B0 ?@5?0@0BC.

5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.

70T<>4V0 7 V=H8<8 ;V:0@AL:8<8 70A>10<8 B0 V=HV 2848 270T<>4V9.

!8AB5<0 CYP450

015?@07>; =0B@VN <5B01>;V7CTBLAO A8AB5<>N ?5GV=:>28E D5@<5=BV2 CYP450, 0 A0<5 CYP2C19 B0 CYP3A4.

>A;V465==O 28O28;8, I> @015?@07>; =0B@VN =5 <0T D0@<0>:V=5B8G=8E 01> ;V=VG=> 7=0GCI8E 270T<>4V9 7 20@D0@8=><, D5=VB>W=><, B5>DV;V=>< G8 4V075?0<><, :>65= 7 O:8E <5B01>;V7CTBLAO CYP450.

70T<>4VW, A?@8G8=5=V ?@83=VG5==O< A5:@5FVW H;C=:>2>W :8A;>B8

015?@07>; =0B@VN A?@8G8=OT A8;L=5 B0 B@820;5 7=865==O ?@>4C:C20==O H;C=:>2>W :8A;>B8.

"0:8< G8=>< @015?@07>; <>65 270T<>4VOB8 7 ?@5?0@0B0<8, 01A>@1FVO O:8E 70;568BL 2V4

?>:07=8:0 @H;C=:>2>3> 2G0A=5 70AB>AC20==O @015?@07>;C =0B@VN B0 :5B>:>=07>;C 01> VB@0:>=07>;C <>65 ?@8725AB8 4> 7=865==O :>=F5=B@0FVW >AB0==VE C ?;072V, 0 70AB>AC20==O 7 483>:A8=>< <>65 ?@8725AB8 4> ?V428I5==O :>=F5=B@0FVW >AB0==L>3>. "0:8< G8=><, >:@5<8< ?0FVT=B0<, O:V 70AB>A>2CNBL 707=0G5=V ?@5?0@0B8 @07< V7 01V<0:><, A;V4 ?5@51C20B8 ?V4 =03;O4<< ;V:0@O 4;O 287=0G5==O =5>1EV4=>ABV :>@83C20==O 4>78.

=B0F848

V4 G0A ;V=VG=8E 28?@>1C20=L ?0FVT=B8 >4=>G0A=> 7 01V<0:>< ?@89<0;8 ?@8 =5>1EV4=>ABV 0=B0F848; C E>4V A?5FV0;L=>3> 4>A;V465==O =5 A?>AB5@V30;>AO 270T<>4VW ?@5?0@0BC 7 0=B0F840<8, B0:8<8 O: 0;N <03=VN 3V4@>:A84.

B070=02V@

4=>G0A=5 70AB>AC20==O 0B070=02V@C 300 <3/@8B>=02V@C 100 <3 7 ><5?@07>;<< (40 <3 1 @07 =0 4>1C) 01> 0B070=02V@C 400 <3 7 ;0=7?@07>;<< (60 <3 1 @07 =0 4>1C) C 74>@>28E

4>1@>2>;LFV2 ?@872>48;> 4> 7=0G=>3> 7=865==O 5:A?>78FVW 0B070=02V@C. 1A>@1FVO

0B070=02V@C 70;568BL 2V4 @. %>G0 4>A;V465==O =5 ?@>2>48;8, >GV:CNBLAO AE>6V

@57C;LB0B8 70AB>AC20==O V=H8E V=3V1VB>@V2 ?@>B>=>W ?>@8 ?@>B>=>W ?>;, =5 A;V4 70AB>A>2C20B8 C :><1V=0FVW 7 0B070=02V@>

5B>B@5:A0B

>2V4><;5==O ?@> ?>1VG=V @50:FVW, >?C1;V:>20=V 40=V ?>?C;OFV9=8E D0@<0>:V=5B8G=8E 4>A;V465=L B0 @5B@>A?5:B82=V 0=0;V78 ?@8?CA:0NBL, I> >4=>G0A=5 70AB>AC20==O

<5B>B@5:A0BC B0 V=3V1VB>@V2 ?@>B>=>W ?> 70 28A>:8E 4>7) <>65 ?@8725AB8 4> 71V;LH5==O @V2=V2 <5B>B@5:A0BC B0/01> 9>3> <5B01>;VBC 3V4@>:A8<5B>B@5:A0BC C A8@>20BFV :@>2V.

%>G0 6>4=8E D>@<0;L=8E 4>A;V465=L =5 ?@>2>48;8.

4=>G0A=5 70AB>AC20==O ;:>?V4>3@5;N B0 @015?@07>;C 74>@>28< 4>1@>2>;LFO< =5 <0;>
 ;;V=VG=> 206;82>3> 2?;82C =0 :=F5=B@0FVW 0:B82=>3> <5B01>;VBC ;:>?V4>3@5;N. >@5:FVO 4>78
 =5 ?>B@V1=0.

60

>A;V465==O ?>:070;8, I> 26820==O W6V 7 =87L:8< 2< 68@V2 =5 2?;820T =0 01A>@1FVN @015?@07>;C
 =0B@VN. @89>< @015?@07>;C =0B@VN 7 68@=>N W65N <>65 70B@8<0B8 01A>@1FVN =0 4 3>48=8
 V 1V;LH5, ?@>B5 <0:A8<0;L=0 :=F5=B@0FVO B0 @V25=L 01A>@1FVW 70;8H0NBLAO =57

?>A?>@8=

>A;V465==O *in vitro* 28O28;8, I> @015?@07>; =0B@VN V=3V1CT <5B01>;V7< F8;;>A?>@8=C. &59
 @V25=L V=3V1C20==O 0=0;>3VG=89 @V2=N V=3V1C20==O <5?@07>;>

V:0@AL:V 70A>18 =5 @5:<5=4>20=V 4;O >4=>G0A=>3> 70AB>AC20==O 7 @015?@07>;<

V:0@AL:89 70AV1	7=0:8 270T<>4VW	5E0=V7< B0 D0:B>@8 @878:C
B070=02V@C AC;LD0B	"5@0?52B8G=0 4VO 0B070=02V@C <>65 7 <5=H8B8AO	024O:8 A2>W9 0=B8A5:@5B>@=V9 4VW @015?@07>; ?V428ICT @H;C=:0, 7 <5=HCT @>7G8==VABL 0B070=02V@C AC;LD0BC V B8< A0<8< 7=86CT 9>3> :=F5=B@0FVN C ?;072V

V:0@AL:V 70A>18, O:V A;V4 ?@87=0G0B8 7 >15@56=VABN

V:0@AL:89 70AV1	7=0:8 270T<>4VW	5E0=V7< B0 D0:B>@8 @878:C
83>:A8= 5B8;483>:A8=	V25=L :=F5=B@0FVW 483>:A8=C B0 <5B8;483>:A8=C C :@>2V <>65 71V;LH8B8AO	024O:8 A2>W 0=B8A5:@5B>@=V9 4VW @015?@07>; <>65 71V;LHC20B8 @H;C=:0, I> ?@872>48BL 4> ?@8A:>@5=>W 01A>@1FVW 483>:A8=C B0 <5B8;483>:A8=C
B@0:>=07>; 5DVB8=V1	V25=L :=F5=B@0FVW VB@0:>=07>;C B0 35DVB8=V1C C :@>2V <>65 7<5=H8B8AO	024O:8 A2>W9 0=B8A5:@5B>@=V9 4VW @015?@07>; 740B5= 71V;LHC20B8 @H;C=:0, I> ?@872>48BL 4> V=3V1C20==O 01A>@1FVW VB@0:>=07>;C B0 35DVB8=V1C
=B0F848, I> :A84/ <03=VN 3V4@>:A84	>=F5=B@0FVO @015?@07>;C <>65 7=86C20B8AO ?@8 >4=>G0A=>AC20==V 7 0=B0F840<8.	

A>1;82>ABV 70AB>AC20==O.

!;V4 4>B@815@56=>ABV ?@8 ?@87=0G5==V @015?@07>;C ?0FVT=B0< 7 2V4><>N
 3V?5@GCB;82VABN 4> ;V:V2. 878: ?5@5E@5A=>W 3V?5@GCB;82>ABV 7 V=H8<8 V=3V1VB>@0<8
 ?@>B>=>W ?> 70;0<8 =5 28;;NG0TBLAO.

0AB>AC20==O ?0FVT=B0< ;VB=L>3> 2V:C

015?@07>; <5B01>;V7CTBLAO 28=OB:>2> C ?5GV=FV. A:V;L:8 7 2V:< DV7V>;>3VG=0 DC=:FVO
 ?5GV=:8 <>65 ?>A;01;N20B8AO, C ?0FVT=BV2 ;VB=L>3> 2V:C <>6CBL 28=8=:CB8 ?>1VG=V
 @50:FVW. "<5=40FV9 I>4> 4>7C20==O B0 B@820;>ABV ;V:C20==O.

!8<0B8G=5 ?>;V?H5==O 2V4 ;V:C20==O @015?@07>;< =5 28;;NG0T =002=>ABV 7;>O:VA=>W ?CE;8=8
 H;C=:0 01> AB@02>E>4C, B>

0FVT=BV2, O:V ?@>E>4OBL B@820;89 :C@A ;V:C20==O (>A>1;82> B8E, EB> ;V:CTBLAO 1V;LH5
 1 @>:C), A;V4 @53C;O@=> >1AB56C20B8.

878: @>728B:C @50:FV9 ?5@5E@5A=>W 3V?5@GCB;82>ABV ?@8 70AB>AC20==V 7 V=H8<8
 V=3V1VB>@0<8 ?@>B>=>W ?> 70;0<8 =5 28;;NG0TBLAO.

0FVT=BV2 A;V4 ?>?5@548B8, I> B01;5B:8 01V<0:C =5 <>6=0 @>76>2C20B8 01> 4@V1=8B8, 0 B@510
:>2B0B8 FV;8<8.
015?@07>; =5 @5:><5=4CTBLAO 70AB>A>2C20B8 4VBO<, >A;V;L:8 =5<0T 4>A2V4C 70AB>AC20==O
FV9 :0B53>@VW ?0FVT=BV2.
>2V4><;O;>AO ?@> ?0B>;>3VG=V 72V (B@><1>F8B>?5=VO B0 =59B@>?5=VO). # 1V;LH>ABV
28?04:V2 V=H>W 5BV>;>3VW =5 7=0E>48;8; 72V 1C;8 =5CA;:04=5=V B0 7=8:0;8 ?VA;O ?@8?8=5==O
70AB>AC20==O @015?@07>;C.
V4E8;5==O ?5GV=:>28E D5@<5=BV2 2V4 =>@<8 A?>AB5@V30;8AL O: C E>4V ;;V=VG=8E
4>A;V465=L, B0: V ?V4 G0A ?>AB<0@:5B8=3>2>3> ?5@V>4C. # 1V;LH>ABV 28?04:V2 V=H>W
5BV>;>3VW =5 7=0E>48;8; ?>@CH5==O 1C;8 =5CA;:04=5=V B0 7=8:0;8 ?VA;O ?@8?8=5==O
70AB>AC20==O @015?@07>;C.
E>4V 4>A;V465=L C ?0FVT=BV2 7 ;53:8<8 01> ?>;C ?>@V2=O=> 7 B0:>N C :>=B@>;L=V9 3@C?V
2V4?>2V4=>W AB0BV B0 2V:C. V:0@N A;V4 4>B@85@56=>ABV ?@8 ?@87=0G5==V @015?@07>;C
=0 @0==VE AB04VOE B5@0?VW ?0FVT=B0< V7 B06:8<8 ?>@CH5==O<8 DC=:FVW ?5GV=:8, >A;V;L:8
2V4ACB=V ;;V=VG=V 40=V I>4> 70AB>AC20==O ?@5?0@0BC ?0FVT=B0< FVTW 3@C?8.
V4 G0A ;V:C20==O @015?@07>;< @5:><5=4CTBLAO ?5@V>48G=> ?@>2>48B8 35<0B>;>3VG=V B0
1V>EV
4=>G0A=5 70AB>AC20==O 0B070=02V@C B0 @015?@07>;C =5 @5:><5=4CTBLAO.
V:C20==O V=3V1VB>@0<8 ?@>B>==>W ?>;, <>65 ?V428IC20B8 @878: 28=8:=5==O H;C=:>2>.:8H:>28E
V=D5:FV9, B0:8E O: *Salmonella, Campylobacter B0 Clostridium difficile*
878: ?5@5;>
=3V1VB>@8 ?@>B>==>W ?>A>1;82> ?@8 70AB>AC20==V 28A>:8E 4>7 B0 ?@>BO3<< B@820;>3>
G0AC (1V;LH5 1 @>:C), <>6CBL ?V428IC20B8 @878: ?5@5;> C ?0FVT=BV2 ;VB=L>3> 2V:C 01> C
?0FVT=BV2 7 =0O2=8<8 V=H8<8 D0:B>@0<8 @878:C. 1A5@20FV9=V 4>A;V465==O ?@8?CA:0NBL, I>
V=3V1VB>@8 ?@>B>==>W ?>6CBL ?V428IC20B8 7030;L=89 @878: ?5@5;>6 @878: <>65 1CB8
?V428I5=8< G5@57 V=HV D0:B>@8. 0FVT=B0< 7 @878:<< >AB5?>@>7C A;V4 ?@>E>48B8
2V4?>2V4=5 ;V:C20==O B0 ?@89<0B8 2VB0
V?><03=VT
@> 28?04:8 B06:>W 3V?<03=VT2V4><;O;>AO C ?0FVT=BV2, O:V ?@89<0;8 V=3V1VB>@8
?@>B>==>W ?>BO3<< I>=09<5=H5 3 ABV 28?04:V2, ?@>BO3<< @>:C. >6CBL 28=8:=CB8 A5@9>7=V
?@>O28 3V?<03=VT<8, 70?0<>@>G5==O B0 25=B@8:C;O@=0 0@8BABV ?0FVT=BV2 3V?<03=VT
AC20==O V=3V1VB>@V2 ?@>B>==>W ?>W B5@0?VW ?@5?0@0B0<8 <03=VN.
0FVT=B0< ?@8 B@820;>4=>G0A=>:A8=>< G8 ?@5?0@0B0<8, O:V ?@872>4OBL 4> 3V?<03=VT
\$C=:FVO I8B>284=>W 70;>78
E>4V 4>A;V465=L =0 B20@8=0E A?>AB5@V30;>AO 71V;LH5==O<0A8 I8B>284=>W 70;>78 B0
?V428I5==O @V2=V2 B8@>:A8=C C :@>2V. 5:>5=4CTBLAO A;V4:C20B8 70 DC=:FVTN I8B>284=>W
70;>78 ?V4 G0A ;V:C20==O @015?@07>;>
A>I;82>ABV ?@>2545==O 48E0;L=8E B5ABV2
57C;LB0B8 !-C@507=8E 48E0;L=8E B5ABV2 <>6CBL 1CB8 E81=>=530B82=8<8 ?V4 G0A ?@89>@V2
?@>B>==>W ?>;, B0 0=B81V>B8:V2, B0:8E O: 0<>:A8F8;V=, ;:0@8B@>ABV *Helicobacter pylori*
48E0;L=V B5AB8 A;V4 ?@>2>48B8 =5 @0=VH5 =V6 G5@57 4 B86=V ?VA;O 70:V=G5==O ;V:C20==O
B0:8<8 ?@5?0@0B0<8.
V:C20==O =55@>782=>W @5D;N:A=>W E2>@>18 ?>:070=5 ?0FVT=B0<, O:V <0NBL ?>2B>@N20=V
@5D;N:A A8<8, 7>:@5<0 ?5GVN B0 :8A;>B=89 @5D;N:A (1;87L:> 2 @07V2 =0 B8645=L). 0AB>AC20==O
@015?@07>;C <>65 ?@8E>2C20B8 A8<8 7;>O:VA=>W ?CE;8=8 (=0?@8;:04 @0:C H;C=:0 01> :8H5G=8:C)
B0 V=HV 70E2>@N20==O B@02=>3> B@0:BC. ">@N20=L ?5@54 ?@87=0G5==O< @015?@07>;C.
0 C<>28 ?@87=0G5==O @015?@07>;C ?0FVT=BC 7 @5D;N:A=>N E2>@>1>N 157 5@>7V9 ;V:0@N A;V4
70A2V4G8B8 5D5:B82=VABL ;V:C20==O ?VA;O 2 B86=V2 70AB>AC20==O ?@5?0@0BC. /:I> A88 =5
7=8;:8, T V<>2V@=VABL, I> @5D;N:A=0 E2>@>10 =5 T ?@8G8=>N WE 28=8:=5==O. # B0:>28=5=
70AB>AC20B8 V=H89 <5B>4 ;V:C20==O.
/:I> @015?@07>; ?@87=0G0NBL 7 <5B>N 5@048:0FVW *Helicobacter pylori*, 206;82> 725@=CB8 C203C =0
?@>B8?>:070==O, >A>1;82>ABV 70AB>AC20==O, ;:V=VG=> 7=0GCIV ?>1VG=V @50:FVW B0 V=HV
70AB5@565==O, 2:070=V 2 V=AB@C:FVW 4;O <548G=>3> 70AB>AC20==O V=H8E ;V:0@AL:8E
70A>1V2, O:V 70AB>A>2CNBL 7 <5B>N 5@048:0FVW.

VB5@0BC@=V 40=V ?@8?CA:0NBL, I> >4=>G0A=5 70AB>AC20==O V=3V1VB>@V2 ?@>B>==>W ?>
B@5:A0BC (?5@5206=> C 28A>:8E 4>70E) <>65 ?V428I8B8 @V25=L <5B>B@5:A0BC B0/01> 9>3>
<5B01>;VBV2 C A8@>20BFV :@>2V, I><>65 ?@8725AB8 4> <5B>B@5:A0B-70;56=>W B>:A8G=>ABV.
@07V =5>1EV4=>ABV 70AB>AC20==O 28A>:8E 4>7 <5B>B@5:A0BC A;V4 @>73;O=CB8 ?8B0==O
?@> ?@8?8=5==O ;V:C20==O V=3V1VB>@0<8 ?@>B>==>W ?>

0AB>AC20==O C ?5@V>4 203VB=>ABV 01> 3>4C20==O 3@C44N.

03VB=VABL

5<0T 40=8E I>4> 157?5:8 70AB>AC20==O @015?@07>;C C ?5@V>4 203VB=>ABV.

0AB>AC20==O 01V<0:C C ?5@V>4 203VB=>ABV ?@>B8?>:070=>.

>4C20==O 3@C44N

52V4><>, G8 ?@>=8:0T @015?@07>; =0B@VN C 3@C4=5 <>;>: 6V=>.: V4?>2V4=V 4>A;V465==O =5
?@>2>48;8AO.

01V<0: =5 A;V4 ?@87=0G0B8 6V=:0< C ?5@V>4 3>4C20==O 3@C44N.

**40B=VABL 2?;820B8 =0 H284:VABL @50:FVW ?@8 :5@C20==V 02B>B@0=A?>@B< 01> V=H8<8
<5E0=V7<0<8.**

>3;O4C =0 D0@<0:>48=0;C =0B@VN B0 2;0AB8289 9>DV;L ?>1VG=8E 5D5:BV2 <>6=0 22060B8, I> 01V
<0: =5 ?>28=5= =530B82=> 2?;820B8 =0 :5@C20==O 02B>B@0=A?>@B< 01> V=H8<8 <5E0=V7<0<8.

07>< 7 B8< C @07V 28=8:=5==O A>;82>ABV @5:<5=4CTBLAO C=8:0B8 :5@C20==O

02B>B@0=A?>@B< 01> V=H8<8 <5E0=V7<0<8.

!/?>AV1 70AB>AC20==O B0 4>78.

>@>A;V, C B>3> 2V:C.

:B82=0 ?5?B8G=0 28@07:0 420=04FOB8?0;>W :8H:8 B0 0:B82=0 4>1@>O:VA=0 28@07:0 H;C=:0: @5:>
<5=4>20=0 4>70 ?@8 F8E 70E2>@N20==OE AB0=>28BL 20<3 1 @07 =0 4>1C 2@0=FV.

1V;LH>ABV ?0FVT=BV2 7 0:B82=>N ?5?B8G=>N 28@07:>N 420=04FOB8?0;>W :8H:8 G0A,
=5>1EV4=89 4;O 703>T==O 28@07:8, AB0=>28BL 4> 4 B86=V2. 4=0: 45O:8< ?0FVT=B0< 4;O >4C60==O
A;V4 ?@89<0B8 ?@5?0@0B 4>40B:>2> ?@>BO3<< I5 4 B86=V2. # 1V;LH>ABV ?0FVT=BV2 7 0:B82=>N
4>1@>O:VA=>N 28@07:>N H;C=:0 703>T==O 2V41C20TBLAO 70 6 B86=V2, 0;5 45O:8< ?0FVT=B0<,
=5GCB;828< 4> ;V:C20==O, 4;O 703>T==O 28@07>: A;V4 ?@89<0B8 ?@5?0@0B 4>40B:>2> ?@>BO3<<
I5 6 B86=V2.

@>782=0 01> 28@07:>20 30AB@>57>D0350;L=0 @5D;N:A=0 E2>@>10: @5:<5=4>20=0 4>70 ?@8
F8E 70E2>@N20==OE AB0=>28BL 20<3 1 @07 =0 4>1C ?@>BO3<< 4-8 B86=V2.

>23>B@820;5 ;V:C20==O 30AB@>57>D0350;L=>W @5D;N:A=>W E2>@>18 (?V4B@84;O B@820;>3>
;V:C20==O <>6=0 70AB>A>2C20B8 ?V4B@878 ?@5?0@0BC 10 <3 01> 20 <3 1 @07 =0 4>1C (70;56=>
2V4 5D5:B82=>ABV ;V:C20==O).

!8<0B8G=5 ;V:C20==O % 2V4 ?>3> 4> 4C65 BO6:>3> ABC?5=O: ?0FVT=B0< 157 57>D03VBC
?@5?0@0B ?@87=0G0NBL C 4>7V 10<3 1 @07 =0 4>1C. /:I> ?VA;O 4 B86=V2 ;V:C20==O A8<8 =5
7=8:0NBL, A;V4 ?@>25AB8 4>40B:>25 >1AB565==O ?0FVT=B0. /: BV;L:8 A8<8 7=8:=CBL, ?>40;LH>3>
:=B@>;N A8

!8=4@>< >;;V=35@0-;;VA>=0: 4>7C ?V418@0NBL V=482V4C0;L=>.

5:<5=4>20=0 ?>G0B:>20 4>70 60 <3 1 @07 =0 4>1C. >7C <>6=0 ?>ABC?>2> ?V428IC20B8 4> 120 <3 =0
4>1C ?@8 ;;V=VG=V9 =5>1EV4=>ABV. >6=0 70AB>A>2C20B8 @07>2C 4>7C 4> 100<3 =0 4>1C. @8
=5>1EV4=>ABV ?@89>

5O:V E2>@V =0 A8=4@<> ;;V=35@0-;;VA>=0 >B@8;<< =0B@VN ?@>BO3<< 1 @>:C.

@048:0FVO . pylori: ?0FVT=B0< 7 . pylori A;V4 70AB>A>2C20B8 2V4?>2V4=V :<<1V=0FVW

?@5?0@0BC 7 0=B81V>B8:0<8. 5:<5=4CTBLAO ?@87=0G5==O ?@>BO3<< 7 4=V2:

01V<0: 20 <3 2 @078 =0 4>1C + ;:0@8B@>

0 ?>:070==O<8, I> ?>B@51CNBL ?@89>1C, B01;5B:8 A;V4 ?@89<0B8 2@0=FV 4> ?@89>G0 =V ?@89<<

C ?5@HC ?>;>28=C 4=O, =V 26820==O W6V =5 ?@>45<>=AB@C20;8 2?;82C =0 4VN @015?@07>;C

=0B@VN, F59 @568< 70AB>AC20==O T 1V;LH A?@8OB;828< 4;O ;V:C20==O. "01;5B:8 =5 <>6=0

@>76>2C20B8 01> 4@V1=8B8, WE A;V4 :>2B0B8 FV;8<8.

>@CH5==O DC=:FVW =8@>: B0 ?5GV=:8. 0FVT=B8 7 ?>@CH5==O<8 DC=:FVW =8@>: 01> ?5GV=:8 =5 ?>B@51CNBL :>@83C20==O 4>78 ?@5?0@0BC. ;O V=D>@<0FVW I>4> 70AB>AC20==O ?@5?0@0BC 4;O ;V:C20==O ?0FVT=BV2 7 BO6:8<8 ?>@CH5==O<8 DC=:FVW ?5GV=:8 482. @>74V;< A>1;82>ABV 70AB>AC20==O».

VB8.

01V<0: =5 @5:<5=4CTBLAO ?@87=0G0B8 4VBO<, >A:V;L:8 =0 40=89 G0A =5<0T 4>AB0B=L>3> 4>A2V4C 9>3> 70AB>AC20==O ?0FVT=B0< FVTW 2V:>2>W 3@C?8.

5@54>7C20==O.

>A2V4 =02<8A=>3> 01> 28?04:>2>3> ?5@54>7C20==O >1<565=89. >4=8E A82O70=8E V7 ?5@54>7C20==O<, =5 28O2;5=>. 0:A8<0;L=0 4>A;V465=0 4>70 =5 ?5@528IC20;0 180 <3 @015?@07>;C =0B@VN 1 @07 =0 4>1C ?V4 G0A ;V:C20==O A8=4@>;V=35@0-;;VA>=0. !?5F8DVG=89 0=B84>B 4;O 01V<0:C =52V4><89. 015?@07>; =0B@VN 4>1@5 72O7CTBLAO 7 1V;:0<8 ?;07<8 :@>2V B0 =5 282>48BLAO ?V4 G0A 4V0;V7C. @8 ?5@54>7C20==V =5>1EV4=> ?@>2>48B8 A8 <0B8G=C B0 ?V4B@8

>1VG=V @50:FVW.

09G0ABVH8<8 ?>1VG=8<8 @50:FVO<8, ?@> O:V ?>2V4><;O;>AO, 1C;8 3>;>2=89 1V;L, 4V0@50, 014> =D5:FVW B0 V=207VW: V=D5:FVW.

I>:C A8AB5<8 :@>2V: 0=578=>DV;VO, 5@8B@>F8B>?5=VO, ;V?5=VO, =59B@>?5=VO, ;59:>?5=VO, B@><1>F8B>?5=VO, ;59:>F8B>7.

I>:C VW A8AB5<8: 3V?5@GCB;82VABL (2;;NG0NG8 :@>?82O=C, =01@O: >1;8GGO, 0@B5@V0;L=C 3V?>B5=7VN B0 48A?=>5; 5@8B57=V @50:FVW B0 3>AB@V A8AB5<=V 0;5@3VG=V @50:FVW, I> 70728G09 7=8:0NBL ?VA;O ?@8?8=5==O ;V:C20==O).

I>:C <5B0I>;V7 0=>@5:AVO, 3V?<03=VT=0B@VT

I>:C ?A8EV:8: 157A>=O, 7=5@2>20=VABL, 45?@5AVO, A?;CB0=VABL A2V4>ABV.

I>:C =5@2>2>W A8AB5<8: 3>;>2=89 1V;L, 70?0<>@>G5==O, A>;82VABL, A;01:VABL C :V=FV2:0E, >=V;, 3V?5AB57VO, 7=865==O A8;8 AB8A=5==O :8ABV, ?>@CH5==O<>2;5==O, 457>@VT=B0FVO, 45;V@V9, :><0.

I>:C >@30=V2 7>@C: @>7;048 7>@C, 71V;LH5==O 2=CB@VH=L>>G=>3> B8A:C.

I>:C A5@F52>-AC48==>W A8AB5<8: ?5@8D5@8G=V =01@O:8, 0@B5@V0;L=0 3V?5@B5=7VO, ?0;L?VB0FVO.

I>:C 48E0;L=>W A8AB5<8: :0H5;L, D0@8=3VB, @8=VB, 1@>=EVB, A8=CA8B, 3;>A8B.

I>:C B@02=>3> B@0:BC: 4V0@50, 1;N20==O, =C4>B0, 1V;L C 682>BV, 70?>@, <5B5>@87<, 2V4GCBBO ?5@5?>2=5==O B0 BO6:>ABV C H;C=C, :0=484>7, 48A?5?AVO, ACEVABL C @>BV, 2V4@86:0, 30AB@8B, AB<0B8B, ?>@CH5==O 2V4GCBBO A<0:C, 5=B5@8B, 57>D03VB, E59;VB, ?5GVO, 35<>@>9.

I>:C 35?0B>1V;V0@=>W A8AB5<8: 35?0B8B, 6>2BO=8FO, ?5GV=:>20 5=F5D0;>?0BVO1.

I>:C H:V@8 B0 ?V4H:V@=8E B:0=8=: 28A8?0==O, 5@8B5<0 (1C;L>7=V @50:FVW B0 @50:FVW 3V?5@GCB;82>ABV, I> 70728G09 7=8:0NBL ?VA;O ?@8?8=5==O ;V:C20==O), A25@1V6, ?V428I5=0 ?VB;82VABL, 1C;L>7=V @50:FVW,@<=0 5@8B5<0, B>:A8G=89 5?V45@<0;L=89 =5:@>;V7 (!), A8=4@> <!BV25=A0-6>=A>=0.

I>:C :VAB:>2>-<O7>2>W A8AB5<8: =5A?5F8DVG=89 1V;L, 1V;L C A?8=V,<8 =V3, 0@B@0;3VO, ?5@5;>< H89:8 AB53=0, 70?OAB:0 01> E@51B0.

I>:C A5G>282V4=>W A8AB5<8: V=D5:FVW A5G>282V4=8E H;OEV2, V=B5@AB8FV0;L=89 =5D@8B.

I>:C @5?@>4C:B82=>W A8AB5<8: 3V=5:><0ABVO, ?>A8;5==O 5@5:FVW.

030;L=V @>7;048: 0AB5=VO, 3@8?>?>4V1=89 A8=4@><, =574C60==O, 1V;L C 3@C4OE, >7=>1, ?V@5:AVO, A?@030, 0;>?5FVO.

01>@0B>@=V 4>A;V465==O: 71V;LH5==O @V2=O ?5GV=:>28E D5@<5=BV2 (" !), , 30<<0-3;CB0W D>AD0B078, 7030;L=>3> 1V;V@C1V=C, 71V;LH5==O<0A8 BV;0, ?@>B5W=C@VO, 71V;LH5==O @V2=O 7030;L=>3> E>;5AB5@8=C, B@83;VF5@84V2, 07>BC A5G>28=8, ?V428I5==O @V2=O !, \$, A5G>2>W :8A;>B8, 3;N:>78 A5GV, 3V?5@0<>=VT

1# ?>>48=>:8E 28?04:0E ?5GV=:>20 5=F5D0;>?0BVO A?>AB5@V30;0AL C ?0FVT=BV2 V7 F8@>7>

!;V4 1CB8 >15@56=8<8 ?@8 ?@87=0G5==V ;V:C20==O @015?@07>;> ?0FVT=B0< 7 BO6:8<8 ?>@CH5==O<8 DC=:FVW ?5GV=:8.

>1VG=V @50:FVW, O:V<0NBL ;;V=VG=5 7=0G5==O: H>: B0 0=0DV;0:B8G=V @50:FVW; ?0=F8B>?5=VO, ;59:>?5=VO, 03@0=C;>F8B>7, 35<>;VB8G=0 0=5@<0 35?0B8BC, ?>@CH5==O DC=:FVW ?5GV=:8, 6>2BO=8FO; V=B5@AB8FV0;L=0 ?=52<>=VO; B>:A8G=89 5?V45@<0;L=89 =5:@>;V7, A8=4@>< !BV25=A0-6>=A>=0, @<=0 5@8B5<0; 3>AB@0 =8@:>20 =54>AB0B=VABL, V=B5@AB8FV9=89 =5D@8B; 3V?>=0B@VT;V7.
>1VG=V @50:FVW, O:V<0NBL ;;V=VG=5 7=0G5==O B0 2;0AB82V V=3V1VB>@0< ?@>B>==>W ?> @CH5==O 7>@C, 0=3V>=52@>B8G=89 =01@O:, 1@>=EV0;L=89 A?07<, A?;CB0=VABL A2V4<>ABV.

"5@ABV.2 @>:8.

#<>28 715@V30==O.

15@V30B8 ?@8 B5@83V=0;L=V9 C?0:>2FV.

15@V30B8 C =54>ABC?=>

#?0:>2:0.

> 7 B01;5B>: C AB@8?V, ?> 2 AB@8?8 2 :0@B>==V9 C?0:>2FV.

0B53>@VO 2V4?CA:C. 0 @5F5?B>

8@>1=8:.

0;;5>4A \$0@<0ALNB8:0;A V.

VAF57=0E>465==O 28@>1=8:0 B0 9>3> 04@5A0 20465==O 4VO;L=>ABV.

V;546 "E540, >4EV 09@0, "5EAV; 0;030@E, VAB. !>;0= %V<0G0; @045H (Block 2), =4VO.